WHAT IS CLAIMED IS:

1. A method of detecting a target nucleic acid, the method comprising:

providing a detection chamber that has at least one nucleic acid detection array on at least one surface of the chamber;

loading a sample into the detection chamber, which sample comprises one or more copies of the target nucleic acid to be detected;

hybridizing in a first hybridizing step an amplification primer and a probe to the one or more copies;

amplifying at least a portion of one or more of the target nucleic acid copies in an amplification primer dependent amplification reaction, wherein the amplification reaction results in cleavage of the probe and release of a first probe fragment;

hybridizing in a second hybridizing step the first probe fragment to the array; and,

detecting a signal produced by binding the first probe fragment to the array, thereby detecting the target nucleic acid, wherein one or more of the detection chamber and the probe are configured to reduce background signal proximal to the array.

2. The method of claim 1, wherein the probe comprises a labeled probe and the first probe fragment comprises a labeled probe fragment.

3. The method of claim 2, wherein the labeled probe fragment comprises a label that produces a detectable signal upon hybridizing to the array.

4. The method of claim 1, wherein in the providing step, the detection chamber is provided configured to reduce signal background proximal to the array.

5. The method of claim 1, wherein the array comprises a non-rate limiting number of capture nucleic acids probes that hybridize to the first probe fragment.

6. The method of claim 1, wherein the first probe fragment is not complementary to the target nucleic acid.

7. The method of claim 1, wherein the sample is loaded through at least one port or fluidic channel in operable communication with the chamber.

8. The method of claim 1, wherein the target nucleic acid is amplified for at least 5 amplification cycles prior to said detecting.

9. The method of claim 1, wherein the target nucleic acid is amplified in a plurality of amplification cycles prior to said detecting, wherein the target nucleic acid portion is additionally amplified after said detecting, in the presence of additional copies of the probe, with resulting released first probe fragments being subsequently hybridized to the array and detected, wherein detected signal intensity is correlated to a quantity of the target nucleic acid present in the sample.

10. The method of claim 1, wherein the signal is detected by detecting one or more optical signal wavelengths.

11. The method of claim 1, wherein detecting the signal comprises detecting a plurality of optical signal wavelengths from a plurality of signals.

12. The method of claim 1, wherein the second hybridizing step is carried out at the same temperature of an extension reaction in the amplifying step.

13. The method of claim 1, wherein the first probe comprises a first orthogonal flap that is not complimentary to the target nucleic acid, which flap is cleaved from the labeled probe to produce the labeled probe fragment.

14. The method of claim 13, wherein the probe comprises a second orthogonal flap which is at least partially complimentary to the first flap, wherein the second flap has a higher T_m for binding to the first flap than the first flap has for binding to the array.

15. The method of claim 2, wherein the labeled probe comprises a fluorescent or luminescent label.

16. The method of claim 1, wherein the probe comprises a label and a label quencher, wherein cleavage of the probe results in separation of the label and the quencher, thereby unquenching the label.

17. The method of claim 1, wherein the probe comprises an unquenched label.

18. The method of claim 1, wherein the signal is an optical signal.

19. The method of claim 18, wherein the signal detected comprises a signal from an intercalating dye indicating hybridization of the first probe fragment to the high-efficiency array.

20. The method of claim 1, comprising detecting local background for one or more regions of the array, and normalizing signal intensity measurements by correcting for said background.

21. The method of claim 20, further comprising normalizing signal intensity by correcting for variability in array capture nucleic acid probe spotting, or uneven field of view of different regions of the array.

22. The method of claim 1, wherein the sample comprises a plurality of different target nucleic acids.

23. The method of claim 22, wherein the array comprises a plurality of different capture nucleic acid probe types spatially separated on the array.

24. The method of claim 23, comprising incubating a plurality of amplification primers, each primer specific for a different nucleic acid target, and a plurality of different probe types, each probe type specific for a different nucleic acid target, with the target nucleic acids.

25. The method of claim 24, comprising;

incubating a plurality of labeled probe types, each specific for a different target nucleic acid, with the target nucleic acids;

amplifying at least a portion of the target nucleic acids in the amplification primer dependent amplification reaction to cleave a plurality of different labeled probe types releasing a plurality of different labeled probe fragment types; and

wherein said second hybridizing step comprises hybridizing the plurality of probe fragment types to the array, wherein each of the different probe fragment types hybridizes to a different spatially discrete capture nucleic acid probe type, and wherein detecting the label signal comprises detecting a plurality of label signals from a plurality of spatially discrete regions corresponding to the spatially discrete capture nucleic acids probes on the array.

26. The method of claim 25, wherein the labeled probe types comprise the same label moiety.

27. The method of claim 25, wherein the labeled probe types comprise a plurality of different label moieties.

28. The method of claim 25, wherein the labeled probe types comprise one or more different label moieties, wherein the number of different moieties is less than the number of labeled probe types.

29. The method of claim 1, wherein the amplifying step and the step of hybridizing the first probe fragment to the high-efficiency array are carried out at the same temperature.

30. The method of claim 25, wherein there are between about 5 and about 100 different spatially discrete capture nucleic acid probe types on the array, and between about 5 and about 100 different labeled probe fragment types produced during the amplification reaction, each different spatially discrete capture nucleic acid types on the array is complementary to a different labeled probe fragment.

WHAT IS CLAIMED IS:

1. A method of detecting a target nucleic acid, the method comprising:

providing a detection chamber that has at least one high efficiency nucleic acid detection array on at least one surface of the chamber;

loading a sample into the detection chamber, which sample comprises one or more copies of the target nucleic acid to be detected;

hybridizing an amplification primer and a probe to the one or more copies;

amplifying at least a portion of one or more of the target nucleic acid copies in an amplification primer dependent amplification reaction, wherein the amplification reaction results in cleavage of the probe and release of a first probe fragment;

hybridizing the first probe fragment to the high-efficiency array; and,

detecting a signal produced by binding the first probe fragment to the array, thereby detecting the target nucleic acid, wherein the detecting step is carried out under conditions that reduce background signal proximal to the array.

2. The method of claim 1, wherein the probe comprises a labeled probe and the first probe fragment comprises a labeled probe fragment.

3. The method of claim 2, wherein the labeled probe fragment comprises a label that produces a detectable signal upon hybridizing to the array.

4. The method of claim 1, wherein the detection chamber is configured to reduce signal background proximal to the array.

5. The method of claim 1, wherein the detection chamber is less than 500 μm in at least one dimension proximal to the array.

6. The method of claim 1, wherein the detection chamber is between about 10 μm and about 200 μm in at least one dimension proximal to the array.

7. The method of claim 1, wherein the array comprises a non-rate limiting number of capture nucleic acids that hybridize to the first probe fragment.

8. The method of claim 1, wherein the first probe fragment is not complementary to the target nucleic acid.

9. The method of claim 7, wherein the first probe fragment that hybridizes to the capture nucleic acids of the array is less than about 30 nucleotides in length.

10. The method of claim 7, wherein the first probe fragment that hybridizes to the capture nucleic acids of the array is less than about 20 nucleotides in length.

11. The method of claim 7, wherein the first probe fragment that hybridizes to the capture nucleic acids of the array is about 15 nucleotides or less in length.

12. The method of claim 1, wherein the sample is loaded through at least one port or fluidic channel in operable communication with the chamber.

13. The method of claim 1, wherein the target nucleic acid is amplified for at least 5 amplification cycles prior to said detecting.

14. The method of claim 1, wherein the target nucleic acid is amplified in a plurality of amplification cycles prior to said detecting, wherein the target nucleic acid portion is additionally amplified after said detecting, in the presence of additional copies of the probe, with resulting released first probe fragments being subsequently hybridized to the array and detected, wherein detected signal intensity is correlated to a quantity of the target nucleic acid present in the sample.

15. The method of claim 1, wherein the signal is detected by detecting one or more optical signal wavelengths.

16. The method of claim 1, wherein detecting the signal comprises detecting a plurality of optical signal wavelengths from a plurality of signals.

17. The method of claim 1, wherein the hybridization temperature is less than the temperature of the amplification reaction.

18. The method of claim 1, wherein the first probe comprises a first orthogonal flap that is not complimentary to the target nucleic acid, which flap is cleaved from the labeled probe to produce the labeled probe fragment.

19. The method of claim 14, wherein the probe comprises a second orthogonal flap which is at least partially complimentary to the first flap, wherein the second flap has a higher T_m for binding to the first flap than the first flap has for binding to the array.

20. The method of claim 2, wherein the labeled probe comprises a fluorescent or luminescent label.

21. The method of claim 20, wherein the label is a fluorescent dye.

22. The method of claim 1, wherein the probe comprises a label and a label quencher, wherein cleavage of the probe results in separation of the label and the quencher, thereby unquenching the label.

23. The method of claim 1, wherein the probe comprises an unquenched label.

24. The method of claim 1, wherein the signal is an optical signal.

25. The method of claim 24, wherein the signal detected comprises a signal from an intercalating dye indicating hybridization of the first probe fragment to the high-efficiency array.

26. The method of claim 1, comprising detecting local background for one or more regions of the array, and normalizing signal intensity measurements by correcting for said background.

27. The method of claim 1, wherein the signal detected in the detecting step has a signal to background noise ratio of greater than 2.5.

28. The method of claim 1,wherein the signal detected in the detecting step has a signal to background noise ratio of greater than 5.

29. The method of claim 26, further comprising normalizing signal intensity by correcting for variability in array capture nucleic acid spotting, or uneven field of view of different regions of the array.

30. The method of claim 1, wherein the sample comprises a plurality of target nucleic acids and the array comprises a plurality of capture nucleic acid types.

31. The method of claim 30, wherein the capture nucleic acid types are spatially separated on the array.

32. The method of claim 30, comprising incubating a plurality of amplification probes, each specific for a different nucleic acid target, with the target nucleic acids.

33. The method of claim 30, wherein there are between about 5 and about 100 capture nucleic acid types, and between about 5 and about 100 corresponding labeled probe

types in the amplification reaction, wherein up to 5 to 100 different signals can be detected based upon positioning of the signals in the array.

34. The method of claim 30, wherein the capture nucleic acids are arrayed at a density of about between about 350 fmoles/cm^2 and about 5,000 fmoles/cm^2 or greater.

35. The method of claim 30, wherein the capture nucleic acids are arrayed at a density greater than 2000 fmoles/cm^2.

36. The method of claim 32, comprising incubating a plurality of labeled probes, each specific for a different target nucleic acid, with the target nucleic acids, wherein amplifying at least a portion of the target nucleic acids in the amplification primer dependent amplification reaction results in cleavage of a plurality of labeled probe types and resulting release of a plurality of labeled probe fragment types, wherein said hybridizing comprises hybridizing the plurailty of probe fragment types to the array, wherein each of the different probe fragment types hybridizes to a spatially discrete capture nucleic acid type, and wherein detecting the label signal comprises detecting a plurality of label signals from a plurality of spatially discrete regions corresponding to the spatially discrete capture nucleic acids on the array.

37. The method of claim 36, wherein the labeled probe types comprise the same label moiety.

38. The method of claim 36, wherein the labeled probe types comprise a plurality of different label moieties.

39. The method of claim 36, wherein the labeled probe types comprise one or more different label moieties, wherein the number of different moieties is less than the number of labeled probe types.

40. The method of claim 1, wherein the amplifying step and the step of hybridizing the first probe fragment to the high-efficiency array are carried out at the same temperature.

41. A method of analyzing a sample for a plurality of target nucleic acid sequences, comprising:

contacting the sample with a first plurality of labeled probes, each of the first plurality labeled probes comprising a first portion complementary to a different target sequence of interest in a first panel of target nucleic acid sequences and a second portion complementary to a different capture probe on a high efficiency probe array, wherein the second portion has a label attached thereto and is not complementary to the target sequence of interest;

amplifying any target sequences from the first panel of target nucleic acid sequences that are present in the sample, in an amplification primer dependent amplification reaction, wherein the amplification reaction results in cleavage of labeled probes hybridized to the target sequences and release of the second portion of the labeled probes bearing the label;

hybridizing the released second portion of the labeled probes to the high-efficiency array;

detecting binding of the second portion of the labeled probe to a capture probe in the high efficiency array; and

identifying the target sequences present in the sample from the second portions of the labeled probes that hybridize to the high efficiency array.

42. The method of claim 41, further comprising:

contacting the sample with a second plurality of labeled probes, each of the second plurality labeled probes comprising the second portion, and a third portion complementary to a different target sequence of interest in a second panel of target nucleic acid sequences;

amplifying any target sequences from the second panel of target nucleic acid sequences that are present in the sample, in an amplification primer dependent amplification reaction, wherein the amplification reaction results in cleavage of labeled probes hybridized to the target sequences and release of the second portion of the labeled probes bearing the label; and

repeating the hybridizing, detecting and identifying steps.

43. A nucleic acid detection device, comprising:

a detection chamber that comprises at least one high efficiency nucleic acid detection array on at least one surface of the chamber, wherein the chamber is configured to reduce signal background for signals detected from the array;

a thermo-regulatory module operably coupled to the detection chamber, which module regulates temperature within the chamber during operation of the device; and,

an optical train that detects a signal produced at the array during operation of the device.

44. The nucleic acid detection device of claim 43, wherein the device is less than about 500μm in depth in at least one dimension proximal to the array.

45. The nucleic acid detection device of claim 43, wherein the device is between about 10μm and about 200μm in depth in at least one dimension proximal to the array.

46. The nucleic acid detection device of claim 43, wherein the surface is composed of a ceramic, glass, quartz, or a polymer.

47. The nucleic acid detection device of claim 43, wherein capture nucleic acids are present in the array at a non-rate limiting density during operation of the device.

48. The nucleic acid detection device of claim 47, wherein the capture nucleic acids are coupled to a thermostable coating on the surface of the chamber.

49. The nucleic acid detection device of claim 48, wherein the coating comprises one or more of: a chemically reactive group, an electrophilic group, an NHS ester, a tetra- or pentafluorophenyl ester, a mono- or dinitrophenyl ester, a thioester, an isocyanate, an isothiocyanate, an acyl azide, an epoxide, an aziridine, an aldehyde, an α,β-unsaturated ketone or amide comprising a vinyl ketone or a maleimide, an acyl halide, a sulfonyl halide, an

imidate, a cyclic acid anhydride, a group active in a cycloaddition reaction, an alkene, a diene, an alkyne, an azide, or a combination thereof.

50. The nucleic acid detection device of claim 43, wherein the array comprises a plurality of capture nucleic acid types, wherein different types are localized to spatially distinct regions of the array.

51. The nucleic acid detection device of claim 43, wherein more than 5 different capture nucleic acid types are present on the array.

52. The nucleic acid detection device of claim 43, wherein between about 5 and about 100 different capture nucleic acid types are present on the array.

53. The nucleic acid detection device of claim 43, wherein the capture nucleic acids are arrayed at a density greater than 2000 fmoles/cm^2.

54. The nucleic acid detection device of claim 43, wherein the thermo-regulatory module comprises one or more of: a thermoelectric module, a Peltier device, a cooling fan, a heat sink, or a metal plate configured to mate with a portion of an outersurface of the chamber.

55. The nucleic acid detection device of claim 54, wherein the thermo regulatory module comprises a feedback enabled control system operably coupled to a computer.

56. The nucleic acid detection device of claim 43, wherein the optical train comprises or is operably coupled to an epifluorescent detection system.

57. The nucleic acid detection device of claim 43, wherein the optical train comprises one or more of: an excitation light source, an arc lamp, a mercury arc lamp, an LED, a lens, an optical filter, a prism, a camera, a photodetector, a CMOS camera, or a CCD array.

58. The nucleic acid detection device of claim 43, comprising an array reader module, which reader module correlates a position of the signal in the array to a nucleic acid to be detected.

59. The nucleic acid detection device of claim 43, wherein the device comprises or is operably coupled to system instructions embodied in a computer or computer readable medium that correlates one or more measurements of signal intensity and a number of amplification cycles performed by the thermo-regulatory module to determine a concentration of a target nucleic acid detected by the device.

60. A system comprising the device of claim 43, operably coupled to a computer, which computer comprises instructions that control the thermocycling by the thermo-regulatory module, and to specify when images are taken or viewed by the optical train, which computer further comprises instructions to convert image information into signal intensity curves as a function of time, and/or to determine concentration of a target nucleic acid analyzed by the device.

61. The system of claim 60, wherein the computer comprises instructions for detecting local background for one or more regions of the array, and for normalizing signal intensity measurements by correcting for said background.

62. The system of claim 60, wherein the computer comprises instructions for normalizing signal intensity by correcting for variability in array capture nucleic acid spotting, or uneven field of view of different regions of the array.

63. A nucleic acid detection consumable, comprising: a thin chamber less than about 500μm in depth, which chamber comprises an optically transparent window that comprises a high efficiency capture nucleic acid array disposed on an inner surface of the window, which chamber additionally comprises at least one reagent delivery port fluidly coupled to the

chamber, wherein the consumable is configured to permit thermocycling of fluid within the chamber.

64. The consumable of claim 63, wherein the nucleic acid array comprises a plurality of different capture nucleic acid types, which types are located in spatially distinct regions of the array.

65. The consumable of claim 63, wherein the chamber comprises a first upper surface comprising the reagent delivery port, and a bottom transparent surface comprising the window, wherein the top and bottom surface are joined by sidewalls comprising a pressure-sensitive adhesive material.

66. The consumable of claim 63, wherein the chamber comprises a first upper surface comprising the reagent delivery port, and a bottom transparent surface comprising the window, wherein the top and bottom surface are joined together by a gasket or shaped feature on the upper or lower surface, or both, wherein the gasket or feature is fused or adhered to a corresponding region of the upper or lower surface, or both.

67. The consumable of claim 66, wherein the upper and lower surfaces are ultrasonically fused together, wherein the gasket or feature delimits regions that are fused.

68. The consumable of claim 66, wherein the feature is a transparent region on either the upper or lower surface and a corresponding shaded region on a cognate upper or lower surface, wherein the upper and lower surfaces are laser welded together by directing laser light through the transparent region and onto the shaded region.

69. The consumable of claim 66, wherein the gasket or feature directs flow of a UV curable adhesive, which adhesive is flowed between the upper and lower surfaces and exposed to UV light, thereby joining the upper and lower surfaces.

70. The consumable of claim 65, wherein the capture nucleic acid array is coupled to a thermally stable coating on the window.

71. The consumable of claim 70, wherein the coating comprises a chemically reactive group, an electrophilic group, an NHS ester, a tetra- or pentafluorophenyl ester, a mono- or dinitrophenyl ester, a thioester, an isocyanate, an isothiocyanate, an acyl azide, an epoxide, an aziridine, an aldehyde, an α,β-unsaturated ketone or amide comprising a vinyl ketone or a maleimide, an acyl halide, a sulfonyl halide, an imidate, a cyclic acid anhydride, a group active in a cycloaddition reaction, an alkene, a diene, an alkyne, an azide, or a combination thereof.

72. The consumable of claim 65, wherein the capture nucleic acid array is arrayed at a density greater than 2000 fmoles/cm^2.

73. The consumable of claim 65, wherein the capture nucleic acid array is arrayed at a density greater than 2500 fmoles/cm^2.

74. The consumable of claim 70, wherein the window comprises glass, quartz, a ceramic, or a polymer.

75. The consumable of claim 63, wherein the chamber is between about 10μm and about 200μm in depth.

76. The consumable of claim 63, wherein the chamber is about 140 μm in depth or less.

77. The consumable of claim 63, wherein the chamber is about 100 μm in depth or less.

78. The consumable of claim 63, wherein the chamber is between about 1 mm and about 50 mm in average diameter.

79. The consumable of claim 63, wherein the chamber is between about 10 mm and about 20 mm in average diameter.

80. A kit comprising the consumable of claim 63, packaged in packaging material, the kit optionally comprising one or more control reagents.

81. A method of detecting the presence of a target nucleic acid sequence in a sample, comprising:

performing an amplification reaction on the sample with a polymerase enzyme that possesses nuclease activity, in the presence of a first labeled probe that comprises a first portion complementary to a first target nucleic acid sequence and a second labeled portion not complementary to the first target nucleic acid sequence, such that the second portion is cleaved from the first portion when the target nucleic acid sequence is amplified;

hybridizing the second labeled portion to a substrate that comprises a capture probe complementary to the second portion; and

detecting the presence of the second labeled portion hybridized to the capture probe on the substrate.

82. The method of claim 81, wherein the substrate comprises a planar substrate.

83. The method of claim 81, wherein the substrate comprises a bead.

84. The method of claim 82, further comprising providing a plurality of labeled probes, each of the plurality of labeled probes having a first portion complementary to a different target nucleic acid sequence, and a second labeled portion where each second labeled portion comprises a different sequence that is not complementary to any of the different target

nucleic acid sequences, such that the second labeled portion is cleaved from the first portion when the different target nucleic acid sequences is amplified;

hybridizing the second labeled portions cleaved during the amplification reaction to a plurality of different capture probes complementary to each different labeled second portion, wherein each different capture probe is disposed at a different known location on the planar substrate; and

identifying the presence of a target nucleic acid sequence in the sample from a location at which a labeled second portion hybridizes to the capture probe on the substrate.

85. The method of claim 83, further comprising providing a plurality of labeled probes, each of the plurality of labeled probes having a first portion complementary to a different target nucleic acid sequence, and a second labeled portion where each second labeled portion comprises a different sequence that is not complementary to any of the different target nucleic acid sequences, such that the second labeled portion is cleaved from the first portion when the different target nucleic acid sequences is amplified;

hybridizing the second labeled portions cleaved during the amplification reaction to a plurality of different capture probes complementary to each different labeled second portion, wherein each different capture probe is disposed on a different bead bearing a unique label; and

detecting the presence of a given target nucleic acid sequence by identifying the bead to which it binds.