What is claimed is:

1. A method of detecting a plurality of target nucleic acids comprising:

(A) contacting a sample comprising a cell comprising a plurality of nucleic acids with a plurality of target probe sets, wherein each target probe set comprises a pair of target probes that specifically hybridize to a target nucleic acid;

(B) contacting the sample with a set of pre-amplifiers, wherein the set of pre-amplifiers comprises a plurality of pre-amplifiers, wherein the plurality of pre-amplifiers comprises a pre-amplifier specific for each target probe set, wherein each pre-amplifier comprises binding sites for the pair of target probes of one of the target probe sets and a plurality of binding sites for an amplifier;

(C) contacting the sample with a set of amplifiers, wherein the set of amplifiers comprises a plurality of subsets of amplifiers specific for each pre-amplifier, wherein each subset of amplifiers comprises a plurality of amplifiers, wherein the amplifiers of a subset of amplifiers comprise a binding site for one of the pre-amplifiers specific for a target probe set and a plurality of binding sites for a label probe;

(D) contacting the sample with a first set of label probes, wherein the first set of label probes comprises a plurality of first subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes in each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each first subset of label probes are distinguishable between the first subsets of label probes and wherein the labels are cleavable, and wherein the first set of label probes specifically label a first subset of target nucleic acids hybridized to the plurality of target probe sets;

(E) detecting the label probes of the first set of label probes bound to the target nucleic acids, thereby detecting the first subset of target nucleic acids;

(F) cleaving the labels from the first set of label probes bound to the first subset of target nucleic acids;

(G) contacting the sample with a second set of label probes, wherein the second set of label probes comprises a plurality of second subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the second subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each second subset of label probes are distinguishable between the second subsets of label probes and wherein the labels are cleavable, and wherein the second set of label probes specifically label a second subset of target nucleic acids hybridized to the plurality of target probe sets that is different than the first subset of target nucleic acids; and

(H) detecting the label probes of the second set of label probes bound to the target nucleic acids, thereby detecting the second subset of target nucleic acids;

wherein a plurality of target nucleic acids are detected.

2. The method of claim 1, wherein the method further comprises:

(I) cleaving the labels from the second set of label probes bound to the second set of target nucleic acids;

(J) contacting the sample with a third set of label probes, wherein the third set of label probes comprises a plurality of third subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the third subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first and second subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each third subset of label probes are distinguishable between the third subsets of label probes and wherein the labels are cleavable, and wherein the third set of label

probes specifically label a third subset of target nucleic acids hybridized to the plurality of target probe sets that is different than the first and second subsets of target nucleic acids; and

(K) detecting the label probes of the third set of label probes bound to the target nucleic acids, thereby detecting the third subset of target nucleic acids.

3. The method of claim 2, comprising repeating steps (I) through (K) one or more times.

4. The method of any one of claims 1-3, wherein each target probe set comprises two or more pairs of target probes that specifically hybridize to the same target nucleic acid.

5. The method of any one of claims 1-4, wherein the target nucleic acids are independently DNA or RNA.

6. The method of claim 5, wherein the target nucleic acids that are RNA are independently selected from the group consisting of messenger RNA (mRNA), micro RNA (miRNA), ribosomal RNA (rRNA), mitochondrial RNA, and non-coding RNA.

7. The method of any one of claims 1-6, wherein the sample is a tissue specimen or is derived from a tissue specimen.

8. The method of any one of claims 1-6, wherein the sample is a blood sample or is derived from a blood sample.

9. The method of any one of claims 1-6, wherein the sample is a cytological sample or is derived from a cytological sample.

10. A sample of fixed and/or permeabilized cells, comprising:

(A) at least one fixed and/or permeabilized cell containing a plurality of target nucleic acids;

(B) a plurality of target probe sets, wherein each target probe set comprises a pair of target probes specifically hybridized to target nucleic acids;

(C) a set of pre-amplifiers, wherein the set of pre-amplifiers comprises a plurality of pre-amplifiers, wherein the plurality of pre-amplifiers comprises a pre-amplifier specific for each target probe set, wherein each pre-amplifier comprises binding sites for the pair of target probes of one of the target probe sets and a plurality of binding sites for an amplifier, wherein the pre-amplifiers are hybridized to the respective specific target probe pairs;

(D) a set of amplifiers, wherein the set of amplifiers comprises a plurality of subsets of amplifiers specific for each pre-amplifier, wherein each subset of amplifiers comprises a plurality of amplifiers, wherein the amplifiers of a subset of amplifiers comprise a binding site for one of the pre-amplifiers specific for a target probe set and a plurality of binding sites for a label probe, wherein the amplifiers are hybridized to the respective pre-amplifiers specific for the target probe sets;

(E) a first set of label probes, wherein the first set of label probes comprises a plurality of first subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes in each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each first subset of label probes are distinguishable between the first subsets of label probes and wherein the labels are cleavable, and wherein the first set of label probes are hybridized to the respective amplifiers and specifically label a first subset of target nucleic acids hybridized to the plurality of target probe sets;

wherein the hybridizations provide a detectable label on the first subset of target nucleic acids.

11. The sample of claim 10, wherein the labels of the first set of label probes bound to the first subset of target nucleic acids are cleaved.

12. The sample of claim 11, comprising a second set of label probes, wherein the second set of label probes comprises a plurality of second subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the second subsets of label probes are specific for amplifiers of different subsets of

amplifiers than the first subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each second subset of label probes are distinguishable between the second subsets of label probes and wherein the labels are cleavable, and wherein the second set of label probes are hybridized to the respective amplifiers and specifically label a second subset of target nucleic acids hybridized to the plurality of target probe sets that is different than the first subset of target nucleic acids,

wherein the hybridizations provide a detectable label on the second subset of target nucleic acids.

13. The sample of claim 12, wherein the labels from the second set of label probes bound to the second subset of target nucleic acids are cleaved.

14. The sample of claim 13, comprising a third set of label probes, wherein the third set of label probes comprises a plurality of third subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the third subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first and second subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each third subset of label probes are distinguishable between the third subsets of label probes and wherein the labels are cleavable, and wherein the third set of label probes are hybridized to the respective amplifiers and specifically label a third subset of target nucleic acids hybridized to the plurality of target probe sets that is different than the first and second subsets of target nucleic acids,

wherein the hybridizations provide a detectable label on the third subset of target nucleic acids.

15. The sample of any one of claims 10-14, wherein each target probe set comprises two or more pairs of target probes that specifically hybridize to the same target nucleic acid.

16. The sample of any one of claims 10-15, wherein the target nucleic acids are independently DNA or RNA.

17. The sample of claim 16, wherein the target nucleic acids that are RNA are independently selected from the group consisting of messenger RNA (mRNA), micro RNA (miRNA), ribosomal RNA (rRNA), mitochondrial RNA, and non-coding RNA.

18. The sample of any one of claims 10-17, wherein the sample is a tissue specimen or is derived from a tissue specimen.

19. The sample of any one of claims 10-17, wherein the sample is a blood sample or is derived from a blood sample.

20. The sample of any one of claims 10-17, wherein the sample is a cytological sample or is derived from a cytological sample.

21. A slide comprising:

(A) a slide having immobilized thereon a plurality of fixed and/or permeabilized cells comprising at least one fixed and/or permeabilized cell containing target nucleic acids;

(B) a plurality of target probe sets, wherein each target probe set comprises a pair of target probes specifically hybridized to target nucleic acids;

(C) a set of pre-amplifiers, wherein the set of pre-amplifiers comprises a plurality of pre-amplifiers, wherein the plurality of pre-amplifiers comprises a pre-amplifier specific for each target probe set, wherein each pre-amplifier comprises binding sites for the pair of target probes of one of the target probe sets and a plurality of binding sites for an amplifier, wherein the pre-amplifiers are hybridized to the respective specific target probe pairs;

(D) a set of amplifiers, wherein the set of amplifiers comprises a plurality of subsets of amplifiers specific for each pre-amplifier, wherein each subset of amplifiers comprises a plurality of amplifiers, wherein the amplifiers of a subset of amplifiers comprise a binding site for one of the pre-amplifiers specific for a target probe set and a plurality of binding sites for a

label probe, wherein the amplifiers are hybridized to the respective pre-amplifiers specific for the target probe sets;

(E) a first set of label probes, wherein the first set of label probes comprises a plurality of first subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes in each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each first subset of label probes are distinguishable between the first subsets of label probes and wherein the labels are cleavable, and wherein the first set of label probes are hybridized to the respective amplifiers and specifically label a first subset of target nucleic acids hybridized to the plurality of target probe sets;

wherein the hybridizations provide a detectable label on the first subset of target nucleic acids.

22. The slide of claim 21, wherein the labels of the first set of label probes bound to the first subset of target nucleic acids are cleaved.

23. The slide of claim 22, comprising a second set of label probes, wherein the second set of label probes comprises a plurality of second subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the second subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each second subset of label probes are distinguishable between the second subsets of label probes and wherein the labels are cleavable, and wherein the second set of label probes are hybridized to the respective amplifiers and specifically label a second subset of target nucleic acids hybridized to the plurality of target probe sets that is different than the first subset of target nucleic acids,

wherein the hybridizations provide a detectable label on the second subset of target nucleic acids.

24. The slide of claim 23, wherein the labels from the second set of label probes bound to the second subset of target nucleic acids are cleaved.

25. The slide of claim 24, comprising a third set of label probes, wherein the third set of label probes comprises a plurality of third subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the third subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first and second subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each third subset of label probes are distinguishable between the third subsets of label probes and wherein the labels are cleavable, and wherein the third set of label probes are hybridized to the respective amplifiers and specifically label a third subset of target nucleic acids hybridized to the plurality of target probe sets that is different than the first and second subsets of target nucleic acids,

wherein the hybridizations provide a detectable label on the third subset of target nucleic acids.

26. The slide of any one of claims 21-25, wherein each target probe set comprises two or more pairs of target probes that specifically hybridize to the same target nucleic acid.

27. The slide of any one of claims 21-26, wherein the target nucleic acids are independently DNA or RNA.

28. The slide of claim 27, wherein the target nucleic acids that are RNA are independently selected from the group consisting of messenger RNA (mRNA), micro RNA (miRNA), ribosomal RNA (rRNA), mitochondrial RNA, and non-coding RNA.

29. The slide of any one of claims 21-28, wherein the sample is a tissue specimen or is derived from a tissue specimen.

30. The slide of any one of claims 21-28, wherein the sample is a blood sample or is derived from a blood sample.

31. The slide of any one of claims 21-28, wherein the sample is a cytological sample or is derived from a cytological sample.

32. A kit for *in situ* detection of target nucleic acids, comprising:

(A) a set of pre-amplifiers, wherein the set of pre-amplifiers comprises a plurality of pre-amplifiers, wherein the plurality of pre-amplifiers comprises a pre-amplifier specific for each target probe set, wherein each pre-amplifier comprises binding sites for the pair of target probes of one of the target probe sets and a plurality of binding sites for an amplifier;

(B) a set of amplifiers, wherein the set of amplifiers comprises a plurality of subsets of amplifiers specific for each pre-amplifier, wherein each subset of amplifiers comprises a plurality of amplifiers, wherein the amplifiers of a subset of amplifiers comprise a binding site for one of the pre-amplifiers specific for a target probe set and a plurality of binding sites for a label probe;

(C) a first set of label probes, wherein the first set of label probes comprises a plurality of first subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes in each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each first subset of label probes are distinguishable between the first subsets of label probes and wherein the labels are cleavable, and wherein the first set of label probes can specifically label a first subset of target nucleic acids;

(D) a second set of label probes, wherein the second set of label probes comprises a plurality of second subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the second subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the

amplifiers of one of the subsets of amplifiers, wherein the labels in each second subset of label probes are distinguishable between the second subsets of label probes and wherein the labels are cleavable, and wherein the second set of label probes can specifically label a second subset of target nucleic acids that is different than the first subset of target nucleic acids.

33. The kit of claim 32, further comprising a third set of label probes, wherein the third set of label probes comprises a plurality of third subsets of label probes, wherein each subset of label probes is specific for the amplifiers of one of the subsets of amplifiers, wherein the third subsets of label probes are specific for amplifiers of different subsets of amplifiers than the first and second subsets of label probes, wherein each subset of label probes comprises a plurality of label probes, wherein the label probes of each of the subsets of label probes comprise a label and a binding site for the amplifiers of one of the subsets of amplifiers, wherein the labels in each third subset of label probes are distinguishable between the third subsets of label probes and wherein the labels are cleavable, and wherein the third set of label probes can specifically label a third subset of target nucleic acids that is different than the first and second subsets of target nucleic acids.

34. The kit of claim 32 or 33, wherein the kit comprises one or more target probe sets, wherein each target probe set comprises a pair of target probes that specifically hybridize to a target nucleic acid.

35. The kit of claim 34, wherein each target probe set comprises two or more pairs of target probes that can specifically hybridize to the same target nucleic acid.

36. The kit of any one of claims 32-35, wherein the kit comprises a cleaving agent to cleave the cleavable labels from the label probes.

37. The kit of any one of claims 32-36, wherein the kit comprises at least one reagent for permeabilizing cells.