CLAIMS

1. A method for nucleic acid sequence detection, comprising:

(a) in any suitable order, contacting a sample comprising a first target nucleic acid sequence and a second target nucleic acid sequence, a first probe capable of hybridizing to the first target nucleic acid sequence, a second probe capable of hybridizing to the second target nucleic acid sequence, and an interfering agent, wherein:

the first and second target nucleic acid sequences are different, and

hybridization of the first probe to the first target nucleic acid sequence is not interfered by the interfering agent, whereas hybridization of the second probe to the second target nucleic acid sequence is interfered by the interfering agent, wherein the interfering agent prevents the second probe from hybridizing to the second target nucleic acid sequence; and

(b) detecting a signal indicative of the hybridization of the first probe to the first target nucleic acid sequence in the sample, whereas a signal indicative of the hybridization of the second probe to the second target nucleic acid sequence in the sample is not detected or is detected at a lower level compared to a reference signal detected without the interfering agent interfering with hybridization,

thereby detecting the first target nucleic acid sequence in the sample.

2. The method of claim 1, wherein:

i) the sample comprises a plurality of first target nucleic acid sequences that are different from each other, and

the contacting step comprises contacting the sample with a plurality of first probes each capable of hybridizing to one of the plurality of first target nucleic acid sequences; and/or

ii) the sample comprises a plurality of second target nucleic acid sequences that are different from each other and different from the first target nucleic acid sequence(s), and the contacting step comprises contacting the sample with a plurality of second probes each capable of hybridizing to one of the plurality of second target nucleic acid sequences.

3. The method of claim 1 or claim 2, wherein the first and second probes are contacted with the interfering agent to form a second probe/interfering agent hybridization complex, before the sample is contacted with the first and second probes and the interfering agent.

4. The method of any one of claims 1-3, wherein the interfering agent hybridizes to the second probe but not to the first probe.

5. The method of any one of claims 1-4, wherein the first probe and/or the second probe directly or indirectly bind to a detectably labelled detection probe.

6. The method of claim 5, wherein the first probe and/or the second probe comprise one or more overhangs that do not hybridize to the first and second target nucleic acid sequences, respectively.

7. The method of claim 6, wherein at least one of the one or more overhangs is capable of hybridizing to a detectably labelled detection probe.

8. The method of claim 6 or claim 7, wherein the second probe comprises an overhang that is capable of hybridizing to a sequence of the interfering agent.

9. The method of claim 8, wherein hybridization of the interfering agent to the overhang of the second probe initiates a strand displacement reaction whereby the interfering agent hybridizes to the second probe and displaces it from the second target nucleic acid sequence.

10. The method of any one of claims 1-9, wherein the first and second target nucleic acid sequences correspond to a first analyte and a second analyte, respectively, in the sample, optionally wherein the first and/or second analytes are DNA (e.g., genomic DNA or cDNA), RNA (e.g., mRNA), or protein.

11. The method of claim 10, wherein the signals in step (b) are optical (e.g., fluorescent) signals, and the signal indicative of the hybridization of the first probe to the first target nucleic acid sequence does not overlap with the signal indicative of the hybridization of the second probe to the second target nucleic acid, if detected.

12. The method of claim 11, wherein the signal indicative of the hybridization of the first probe to the first target nucleic acid sequence overlaps with the reference signal.

13. The method any one of claims 1-12, wherein the first and/or second target nucleic acid sequences are comprised in an RCA product of a circular or padlock probe that hybridizes to a DNA or RNA analyte in the sample.

14. The method of any one of claims 1-13, wherein the first and/or second target nucleic acid sequences are detected *in situ* in the sample.

15. The method of any one of claims 1-14, wherein the first and/or second target nucleic acid sequences comprise a barcode sequence, and the barcode sequence in each first or second target nucleic acid sequence corresponds to a unique signal code sequence.

16. The method of claim 15, wherein a set of probes is provided for decoding of each signal code sequence for each target nucleic acid sequence,

wherein each probe in a set comprises the same recognition sequence that hybridizes to the target nucleic acid sequence and a detection hybridization region or the absence of a detection hybridization region,

wherein the detection hybridization region or the absence thereof may be the same or different among probes in the set, wherein the detection hybridization region, if present, is specific for a detection probe comprising a detectable label or lacking a detectable label, and

wherein the probes of the set are used sequentially in multiple cycles of decoding in a pre-determined sequence which corresponds to the signal code sequence.

17. The method of claim 16, wherein a given cycle of decoding comprises contacting the sample with a probe library comprising a probe of each set of probes, wherein the probe of each set corresponds to the given cycle of decoding.

18. The method of claim 17, wherein the method comprises contacting the sample with an interfering agent or a set of interfering agents in multiple cycles of decoding, wherein the same

interfering agent or set of interfering agents is used with the probe library in each cycle of decoding.

19. The method of claim 18, wherein the interfering agent or an interfering agent of the set of interfering agents interferes with hybridization of different second probes to the same corresponding second target nucleic acid sequences in different cycles of decoding.

20. The method of claim 19, wherein the different second probes share a binding sequence that hybridizes to the same second target nucleic acid sequence but comprise different binding sequences for different detectably labelled detection oligonucleotides.

21. A method for detecting multiple analytes, comprising:

a) determining highly expressed/abundant analytes in a sample;

b) select interfering agents to the highly expressed/abundant analytes;

c) contacting the sample with the interfering agents selected in b); and

d) detecting signals in the sample,

wherein signals indicative of the highly expressed/abundant analytes in the sample are not detected or are detected at a lower level compared to a reference signal detected without the interfering agents.

22. The method of claim 21, wherein the selected interfering agents are interfering probes that hybridize to hybridization probes that each hybridizes to a rolling circle amplification product indicative of a highly expressed/abundant analyte, thereby preventing the hybridization probes for the highly expressed/abundant analytes from hybridizing to the corresponding rolling circle amplification products in the sample.

23. The method of claim 22, wherein each hybridization probe comprises (i) a sequence that hybridizes to a barcode sequence in the corresponding rolling circle amplification product and (ii) a non-hybridizing overhang.

24. The method of claim 22 or claim 23, wherein the interfering probes are contacted with the hybridization probes prior to contacting with the sample.

25. The method of claim 24, wherein the selected interfering agents are interfering probes that hybridize to rolling circle amplification products indicative of the highly expressed/abundant analytes, thereby preventing the rolling circle amplification products from hybridizing to the hybridization probes for the highly expressed/abundant analytes in the sample.

26. A method for nucleic acid sequence detection, comprising:

(a) in any suitable order, contacting a sample, a first probe capable of hybridizing to a first target nucleic acid sequence, a second probe capable of hybridizing to a second target nucleic acid sequence, and an interfering agent, wherein:

the first and second target nucleic acid sequences are different,

the first probe and the second probe are each associated with a detectable label, which may be the same or different among the first and second probe,

the interfering agent is a probe comprising a hybridization region and a quencher moiety,

the second probe, but not the first probe, comprises a sequence complementary to the hybridization region of the interfering agent, wherein the interfering agent hybridizes to the sequence of the second probe and quenches the detectable label associated with the second probe; and

(b) detecting a signal indicative of the hybridization of the first probe to the first target nucleic acid sequence in the sample, whereas a signal indicative of the hybridization of the second probe to the second target nucleic acid sequence in the sample is inhibited,

thereby detecting the first target nucleic acid sequence in the sample.

27. A kit for nucleic acid sequence detection, the kit comprising:

(a) a plurality of hybridization probes comprising different hybridization probes each specific for a different target nucleic acid sequence, wherein each hybridization probe has a recognition sequence complementary to a sequence within its target nucleic acid sequence, and is capable of generating a signal by means of which it can be detected; and

(b) an interfering agent comprising a sequence capable of hybridizing to a sequence within a selected hybridization probe of the plurality of hybridization probes, wherein hybridization of the interfering agent to the selected hybridization probe or corresponding target

nucleic acid sequence interferes with hybridization of the selected hybridization probe and/or generation of the signal by the selected hybridization probe.