## 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 2, wherein:~~

~~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.~~

~~4. The method of claim 3, wherein the interfering agent interferes with hybridization of two or more second probes to the corresponding second target nucleic acid sequences.~~

3~~5~~. The method of ~~any of~~ claim~~s~~ 1 or claim 2~~-4~~, 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.

~~6. The method of any of claims 1-5, wherein the sample comprising the first and second target nucleic acid sequence is contacted with the interfering agent to form a second target nucleic acid /interfering agent hybridization complex.~~

~~7. The method of any of claims 1-6, wherein the contacting in (a) comprises contacting the sample with a plurality of interfering agents.~~

~~8. The method of any of claims 5-7, wherein the plurality of interfering agents comprise interfering agents that interfere with hybridization of second probes to the same corresponding second target nucleic acid sequences.~~

~~9. The method of any of claims 5-8, wherein interfering agents of the plurality interfere with hybridization of different second probes to the corresponding second target nucleic acid sequences.~~

~~10. The method of claim 9, wherein the different second probes share a binding sequence that hybridizes to the second target nucleic acid sequence but comprise different binding sequences for different detectably labelled detection oligonucleotides.~~

~~11. The method of any of claims 5-10, wherein the plurality of interfering agents comprise an interfering agent that interferes with hybridization of two or more second probes to the corresponding second target nucleic acid sequences.~~

~~12. The method of any of claims 1-11, wherein the interfering agent comprises a sequence complementary to a sequence of the second probe, or a sequence complementary to a sequence of the second target nucleic acid sequence.~~

4~~13~~. The method of any one of claims 1-3~~12~~, wherein the interfering agent hybridizes to the second probe but not to the first probe.

~~14. The method of claim 13, wherein the interfering agent prevents the second probe from hybridizing to the second target nucleic acid sequence.~~

~~15. The method of claim 13 or 14, wherein the interfering agent displaces the second probe which is hybridized to the second target nucleic acid sequence.~~

~~16. The method of any of claims 1-12, wherein the interfering agent hybridizes to the second target nucleic acid sequence but not to the first target nucleic acid sequence.~~

~~17. The method of claim 16, wherein the interfering agent prevents the second probe from hybridizing to the second target nucleic acid sequence, optionally~~

~~18. The method of claim 16 or 17, wherein the interfering agent hybridizes to a sequence adjacent to the second target nucleic acid sequence, thereby initiating a strand displacement reaction and displacing the second probe which is hybridized to the second target nucleic acid sequence.~~

~~19. The method of any of claims 1-18, wherein the first probe and/or the second probe are detectably labelled.~~

~~20. The method of any of claims 1-19, wherein the first probe and/or the second probe are covalently or noncovalently coupled to a fluorescent label.~~

5~~21~~. The method of any one of claims 1-~~419~~, wherein the first probe and/or the second probe directly or indirectly bind to a detectably labelled detection probe.

6~~22~~. The method of claim 5~~20 or 21~~, 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~~23~~. The method of claim 6~~22~~, wherein at least one of the one or more overhangs is capable of hybridizing to a detectably labelled detection probe.

8~~24~~. The method of claim 6~~22~~ or claim 7~~23~~, wherein the second probe comprises an overhang that is capable of hybridizing to a sequence of the interfering agent.

9~~25~~. The method of claim 8~~24~~, 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~~26~~. The method of any one of claims 1-9~~25~~, 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.

~~27. The method of claim 26, wherein the first and/or second analytes are DNA (e.g., genomic DNA or cDNA), RNA (e.g., mRNA), or protein.~~

~~28. The method of claim 26 or 27, wherein the first analyte is less abundant than the second analyte in the sample.~~

~~29. The method of claim 28, wherein the number of molecules comprising the second analyte is at least 2, 5, 10, 20, 50, 100, 200, 500, or 1,000 times of the number of molecules comprising the first analyte.~~

1130. The method of ~~any of~~ claim~~s~~ 1026-29, 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.

1231. The method of claim 1130, wherein the signal indicative of the hybridization of the first probe to the first target nucleic acid sequence overlaps with the reference signal.

~~32. The method of any of claims 26-31, wherein the first and/or second analytes are selected prior to the contacting step.~~

~~33. The method of claim 32, further comprising selecting the first and second probes corresponding to the first and second analytes, respectively.~~

~~34. The method of claim 33, further comprising selecting the interfering agent which hybridizes to the second probe but does not hybridize to the first probe.~~

~~35. The method of claim 33, further comprising selecting the interfering agent which hybridizes to the second target nucleic acid sequence but does not hybridize to the first target nucleic acid sequence.~~

~~36. The method of any of claims 1-35, further comprising removing the first probe hybridized to the first target nucleic acid sequence in the sample.~~

~~37. The method of claim 36, further comprising contacting the sample with the second probe but not the interfering agent, and detecting a signal indicative of the hybridization of the second probe to the second target nucleic acid sequence in the sample, thereby detecting the second target nucleic acid sequence in the sample.~~

~~38. The method of any of claims 1-37, further comprising prior to the contacting step, contacting the sample with the first and second probes but not with the interfering agent, wherein a signal indicative of the hybridization of the first probe to the first target nucleic acid sequence in the sample is crowded out by the reference signal which is indicative of the hybridization of~~

~~the second probe to the second target nucleic acid sequence in the sample without the interfering agent.~~

~~39. The method of any of claims 1-38, wherein the first and/or second target nucleic acid sequences are comprised in nucleic acid analytes in the sample.~~

~~40. The method of claim 39, wherein the first and/or second probes are circular or circularizable (e.g., padlock) probes and the interfering agent does not facilitate circularization of the circularizable probes.~~

~~41. The method of any of claims 1-38, wherein the first and/or second target nucleic acid sequences are comprised in a product of a nucleic acid analyte in the sample, or a product of a labelling agent or a polynucleotide probe that directly or indirectly binds to an analyte in the sample.~~

~~42. The method of claim 41, wherein the product is a hybridization product, a ligation product, an extension product, a replication product, a transcription/reverse transcription product, and/or an amplification product.~~

~~43. The method of claim 41 or 42 wherein the product is a rolling circle amplification product.~~

~~44. The method of any one of claims 41-43, wherein the labelling agent comprises a reporter oligonucleotide comprising one or more barcode sequences, and the amplification product comprises multiple copies of the one or more barcode sequences.~~

13~~45~~. The method any one of claims 1-12~~43~~, 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.

~~46. The method of claim 45, wherein the RCA products of a plurality of different mRNA and/or cDNA analytes are analyzed, a barcode sequence in a particular circular or circularizable probe corresponds to a particular mRNA or cDNA analyte, and the particular circular or~~

~~circularizable probe further comprises an anchor sequence that is common among circular or circularizable probes for a subset of the plurality of different mRNA and/or cDNA analytes.~~

~~47. The method of claim 44, wherein the labelling agent directly or indirectly binds to a non-nucleic acid analyte in the sample.~~

~~48. The method of claim 47, wherein the labelling agent comprises a reporter oligonucleotide conjugated to an antibody or antigen binding fragment thereof that binds to a protein analyte, and the first and/or second target nucleic acid sequences are comprised in an RCA product of a circular or circularizable probe that hybridizes to the reporter oligonucleotide.~~

~~49. The method of any of claims 1-48, wherein molecules comprising the first and/or second target nucleic acid sequences are immobilized in the sample.~~

~~50. The method of any of claims 1-49, wherein molecules comprising the first and/or second target nucleic acid sequences are crosslinked to one or more other molecules in the sample, a matrix such as a hydrogel, and/or one or more functional groups on a substrate.~~

14~~51~~. The method of any one of claims 1-13~~50~~, wherein the first and/or second target nucleic acid sequences are detected *in situ* in the sample.

15~~52~~. The method of any one of claims 1-14~~51~~, 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.

~~53. The method of claim 52, wherein the barcode sequence in each first or second target nucleic acid sequence corresponds to a unique signal code sequence.~~

16~~54~~. The method of claim 15~~53~~, 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~~55~~. The method of claim 16~~54~~, 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~~56~~. The method of claim 17~~55~~, 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~~57~~. The method of claim 18~~56~~, 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~~58~~. The method of claim 19~~57~~, 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.

~~59. The method of any of claims 54-58, wherein $n$ sets of probes are used to decode signal code sequences for target nucleic acid sequences T1, …, T$k$, …, T$n$, in $m$ cycles, and~~

~~Probe Set 1 comprises P11, …, P1$j$, …, and P1$m$,~~

~~Probe Set $k$ comprises P$k$1, …, P$kj$, …, and P$km$,~~

~~Probe Set $n$ comprises P$n$1, …, P$nj$, …, and P$nm$,~~

~~$j$, $k$, $m$, and $n$ are integers, $2 \leq j \leq m$, and $2 \leq k \leq n$,~~

~~wherein the sample is contacted with Probe Library P11, …, P$k$1, …, and P$n$1 in Cycle 1, with Probe Library P1$j$, …, P$kj$, …, and P$nj$ in Cycle $j$, and Probe Library P1$m$, …, P$km$, …, and P$nm$ in Cycle $m$,~~

~~wherein each probe is detectable by a fluorescently labelled reporter probe, and the fluorescent signals for different probes in each probe set or each probe library can be of the same or different colors, and~~

~~wherein in one or more of Cycle 1 through Cycle *m*, the sample is contacted with an interfering agent that hybridizes to a target nucleic acid sequence or the corresponding probe(s), and the interfering agent is not fluorescently labelled.~~

~~60. The method of claim 59, wherein the interfering agent hybridizes to the target nucleic acid sequence and prevents, competes with, and/or displaces probe(s) from hybridizing to the target nucleic acid sequence, wherein the interfering agent is provided at a higher concentration than probe(s) for the target nucleic acid sequence.~~

~~61. The method of claim 59, wherein the interfering agent hybridizes to probe(s) for the target nucleic acid sequence, thereby preventing, competing with, and/or displacing the target nucleic acid sequence from hybridizing to the probe(s).~~

~~62. The method of any of claims 59-61, wherein the probe library for one of Cycle 1 through Cycle *m*, and the interfering agent if used in that cycle, are removed prior to contacting the sample with the probe library for the next cycle and optionally another interfering agent.~~

~~63. The method of claim 62, wherein the interfering agent and the another interfering agent interfere with the hybridization of the same target nucleic acid sequence to the probes for that target nucleic acid sequence.~~

~~64. The method of any of claims 59-63, wherein target nucleic acid sequences T1, …, T*k*, …, T*n* comprise barcode sequences B1, …, B*k*, …, B*n*, respectively.~~

~~65. The method of claim 64, wherein each probe in Probe Set 1, …, Probe Set *k*, …, and Probe Set *n* comprises recognition sequences R1, …, R*k*, …, R*n*, respectively, that hybridizes to barcode sequences B1, …, B*k*, …, B*n*, respectively.~~

~~66. The method of claim 65, wherein in each of Cycle 1 through Cycle *m*, the sample is contacted with interfering agents that hybridize to one or more of the recognition sequences or~~

~~one or more of the barcode sequences, whereby fluorescent signals corresponding to the one or more target nucleic acid sequences are not detected or are detected at a lower level compared to a reference signal detected without the interfering agents in Cycle 1 through Cycle *m*.~~

~~67. The method of claim 65, wherein in each of Cycle 1 through Cycle *m*, the sample is contacted with the same interfering agents that hybridize to the recognition sequence(s) corresponding to one or more target nucleic acid sequences.~~

~~68. The method of claim 66, wherein in each of Cycle 1 through Cycle *m*, the sample is contacted with the same interfering agents that hybridize to the barcode sequence(s) of one or more target nucleic acid sequences.~~

~~69. The method of any of claims 66-68, further comprising contacting the sample, in a cycle other than Cycle 1 through Cycle *m*, with one or more probes that hybridize to the one or more target nucleic acid sequences in the absence of interfering agents, wherein the one or more probes are detected in the sample.~~

~~70. The method of any of claims 59-69, wherein the signal code sequence for each target nucleic acid sequence comprises signal codes corresponding to the fluorescent signals (or lack thereof) from probes in Cycle 1 through Cycle *m*.~~

~~71. The method of claim 70, wherein the lack of fluorescent signals in one or more cycles is due to the interfering agents.~~

~~72. The method of any of claims 1-71, wherein the first and second target nucleic acid sequences are barcodes sequences in rolling circle amplification products.~~

2173. 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)~~to the highly expressed/abundant analytes~~; 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.

~~74. The method of claim 73, wherein the selected interfering agents are interfering probes that hybridize to padlock probes that each hybridizes to a DNA or RNA sequence of the highly expressed/abundant analytes, thereby interfering with the ligation of the padlock probes and generation of rolling circle amplification products indicative of the highly expressed/abundant analytes.~~

~~75. The method of claim 73, wherein the selected interfering agents are interfering probes that hybridize to a DNA or RNA sequence of the highly expressed/abundant analytes, thereby interfering with the hybridization of padlocks probes to the DNA or RNA sequence, ligation of the padlock probes, and generation of rolling circle amplification products indicative of the highly expressed/abundant analytes.~~

22~~76~~. The method of claim 21~~73~~, 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~~77~~. The method of claim 22~~76~~, 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~~78~~. The method of claim 22~~76~~ or claim 23~~77~~, wherein the interfering probes are contacted with the hybridization probes prior to contacting with the sample.

25~~79~~. The method of claim 24~~78~~, 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~~, optionally wherein each hybridization probe comprises (i) a sequence that hybridizes to a barcode sequence in the corresponding rolling circle amplification product~~.

~~80. The method of claim 73, 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 detection probes from hybridizing to the hybridization probes for the highly expressed/abundant analytes in the sample, wherein the interfering probes do not interfere with hybridization of the hybridization probes to the rolling circle amplification products in the sample.~~

26~~81~~. 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.

~~82. The method of claim 81, wherein the first probe and second probe each comprise a detection hybridization region, which may be the same or different among the first probe and the second probe, which is specific for a detection probe comprising the detectable label.~~

~~83. The method of claim 81 or 82, wherein the sequence complementary to the hybridization region of the interfering agent corresponds to the second target nucleic acid.~~

2784. 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~~, or to a sequence within the target nucleic acid sequence of the selected hybridization probe~~, 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.

~~85. The kit of claim 84, wherein the plurality of hybridization probes are combined in the same composition.~~

~~86. The kit of claim 85, wherein the kit comprises a plurality of interfering agents, wherein each of the interfering agents is separate from the composition comprising the plurality of hybridization probes.~~

~~87. The kit of any of claims 85-86, wherein the kit comprises multiple pluralities of hybridization probes, wherein each plurality of hybridization probes corresponds to a single round of sequential decoding.~~

~~88. The kit of any of claims 85-87, wherein the kit further comprises one or more separate compositions comprising hybridization probes corresponding to one or more interfering agents of the kit.~~

~~89. The kit of any of claims 85-88, wherein each hybridization probe of the plurality comprises an overhang region comprising a detection hybridization region specific for one of a~~

~~set of detection probes, wherein each detection probe of the set corresponds to a different detectable label or the absence of a label.~~

~~90. The kit of claim 89, wherein each overhang region further comprises a specific sequence corresponding to the recognition sequence of the hybridization probe.~~

~~91. The kit of claim 90, wherein the interfering agent comprises a quencher moiety, and wherein the interfering agent is capable of hybridizing to the specific sequence of a selected hybridization probe.~~