CLAIMS

1. A method, comprising:

exposing a sample to a plurality of nucleic acid probes;

for each of the nucleic acid probes, simultaneously capturing fluorescent images of the sample using at least four detector banks, each detector bank being configured to image a respective one of at least four different color channels associated with each of four different readout probes for identifying the nucleic acid probes, the detectors of each respective detector bank being focused on at least four different focal planes within the sample;

determining binding of the nucleic acid probes within the sample using the fluorescent images; and

determining an abundance and/or a spatial distribution of nucleic acids within the sample corresponding to the binding of the plurality of nucleic acid probes.

2. The method of claim 1, comprising capturing images of the sample using at least 8 detector banks focused on different focal planes within the sample.

3. The method of any one of claims 1-2, comprising capturing images of the sample using at least 16 detector banks focused on different focal planes within the sample.

4. The method of any one of claims 1-3, comprising capturing images of the sample using at least 32 detector banks focused on different focal planes within the sample.

5. The method of any one of claims 1-4, wherein each of the different focal planes is focused at no more than 1000 nm from a neighboring focal plane.

6. The method of any one of claims 1-5, comprising passing light from the sample through a plurality of beamsplitters to the at least 4 detector banks.

7. The method of any one of claims 1-6, wherein at least some of the detectors are cameras.

8. The method of any one of claims 1-7, wherein at least some of the detectors are point detectors.

9. The method of any one of claims 1-8, wherein at least some of the detectors are photodetectors.

10. The method of any one of claims 1-9, wherein at least some of the detectors are avalanche photodiodes.

11. The method of any one of claims 1-10, wherein at least some of the detectors are one dimensional arrays.

12. The method of any one of claims 1-11, wherein at least some of the detectors are line detectors.

13. The method of any one of claims 1-12, comprising determining z positions of at least some of the nucleic acid probes in the sample at a resolution better than 300 nm.

14. The method of any one of claims 1-13, comprising exposing the nucleic acid probes to primary amplifier nucleic acids able to bind to the nucleic acid probes, wherein a maximum number of primary amplifier nucleic acids is able to bind to a nucleic acid probe; and

exposing the primary amplifier nucleic acids to secondary amplifier nucleic acids able to bind to the primary amplifier nucleic acids, wherein a maximum number of secondary amplifier nucleic acids is able to bind to the primary amplifier nucleic acids.

15. The method of claim 14, comprising exposing the primary amplifier nucleic acids to secondary amplifier nucleic acids able to bind to the primary amplifier nucleic acids, wherein the binding of primary amplifier nucleic acids and secondary amplifier nucleic acids to a target is saturable.

16. The method of any one of claims 14 or 15, comprising exposing the primary amplifier nucleic acids to secondary amplifier nucleic acids able to bind to the primary

amplifier nucleic acids, wherein the secondary amplifier nucleic acids bind to the primary amplifier nucleic acids within a fixed distance.

17. The method of any one of claims 14-16, further comprising exposing the primary amplifier nucleic acids to secondary amplifier nucleic acids able to bind to the primary amplifier nucleic acids,.

18. The method of claim 17, wherein the secondary amplifier nucleic acids comprise a fluorescent signaling entity.

19. The method of any one of claims 1-18, further comprising:

creating codewords binding of the nucleic acid probes within the sample; and

for at least some of the codewords, matching the codeword to a valid codeword optionally wherein, if no match is found, applying error correction to the codeword to form a valid codeword.

20. The method of any one of claims 1-19, comprising exposing the sample to at least 5 different nucleic acid probes.

21. The method of any one of claims 1-19, comprising sequentially exposing the sample to the plurality of nucleic acid probes.

22. The method of any one of claims 1-19, wherein the plurality of nucleic acid probes comprises a combinatorial combination of nucleic acid probes with different sequences.

23. The method of any one of claims 1-19, wherein the plurality of nucleic acid probes have an average length of between 10 and 300 nucleotides.

24. The method of any one of claims 1-23, wherein at least some of the plurality of nucleic acid probes comprises a target sequence and one or more read sequences.

25. The method of claim 24, wherein the target sequence of the plurality of nucleic acid probes has an average length of between 10 and 200 nucleotides.

26. The method of any one of claims 24 or 25, wherein the target sequence binds to a target via specific binding.

27. The method of any one of claims 24-26, wherein the plurality of read sequences are distributed on the plurality of nucleic acid probes so as to define an error-correcting code.

28. The method of any one of claims 1-27, wherein the plurality of nucleic acid probes defines a code space with a Hamming distance of at least 2.

29. The method of any one of claims 1-28, comprising determining binding of the nucleic acid probes using fluorescence imaging.

30. The method of any one of claims 1-29, comprising determining binding of the nucleic acid probes using multi-color fluorescence imaging.

31. The method of any one of claims 1-30, comprising determining binding of the nucleic acid probes using a super-resolution fluorescence imaging technique.

32. The method of claim 31, comprising determining binding of the nucleic acid probes using stochastic optical reconstruction microscopy (STORM).

33. The method of any one of claims 1-32, wherein the sample comprises a cell.

34. The method of claim 33, wherein the cell is a human cell.

35. The method of any one of claims 33 or 34, wherein the cell is fixed.