(b) contacting said composition with a polymer-nucleotide conjugate under conditions sufficient to allow a multivalent binding complex to be formed between said polymer-nucleotide conjugate and said two or more copies of said target nucleic acid sequence in said composition of (a), wherein the polymer-nucleotide conjugate comprises two or more nucleotide moieties that are complementary to said nucleotide in said two or more copies of said target nucleic acid sequence; and

(c) detecting said multivalent binding complex, thereby determining the identity of said nucleotide in the target nucleic acid sequence.

[0004] Disclosed herein are methods of determining an identity of a nucleotide in a target nucleic acid sequence comprising: a. providing a composition comprising: i. two or more copies of said target nucleic acid sequence; ii. two or more primer nucleic acid molecules that are complementary to one or more regions of said target nucleic acid sequence; and iii. two or more polymerase molecules; b. contacting said composition with a polymer nucleotide conjugate under conditions sufficient to allow a multivalent binding complex to be formed between said polymer-nucleotide conjugate and said two or more copies of said target nucleic acid sequence in said composition of (a), wherein the polymer-nucleotide conjugate comprises two or more copies of a nucleotide moiety and

CLAIMS

WHAT IS CLAIMED IS:

1. A method of determining an identity of a nucleotide in a target nucleic acid sequence, comprising:

(a) providing a composition comprising:

(i) two or more copies of said target nucleic acid sequence;

(ii) two or more primer nucleic acid molecules that are complementary to one or more regions of said target nucleic acid sequence; and

(iii) two or more polymerase molecules;

(b) contacting said composition with a polymer-nucleotide conjugate under conditions sufficient to allow a multivalent binding complex to be formed between said polymer-nucleotide conjugate and said two or more copies of said target nucleic acid sequence in said composition of (a), wherein the polymer-nucleotide conjugate comprises two or more nucleotide moieties that are complementary to said nucleotide in said two or more copies of said target nucleic acid sequence; and

(c) detecting said multivalent binding complex, thereby determining the identity of said nucleotide in the target nucleic acid sequence.

2. The method of claim 1, wherein the target nucleic acid sequence is DNA.

3. The method of claim 1, wherein the detection of the binding complex is performed in the absence of unbound or solution-borne polymer nucleotide conjugates.

4. The method of claim 1, wherein the target nucleic acid sequence has been replicated or amplified or has been produced by replication or amplification.

5. The method of claim 1, wherein detecting the multivalent binding complex comprises a fluorescence measurement.

6. The method of claim 1, wherein the contacting comprises use of one type of polymer-nucleotide conjugate.

7. The method of claim 1, wherein the contacting comprises use of two or more types of polymer-nucleotide conjugate.

8. The method of claim 7, wherein each type of the two or more types of polymer-nucleotide conjugate comprises a different type of nucleotide moiety.

9. The method of claim 8, wherein the contacting comprises use of three types of polymer-nucleotide conjugate and wherein each type of the three types of polymer-nucleotide conjugate comprises a different type of nucleotide moiety.

10. The method of claim 1, wherein the polymer-nucleotide conjugate comprises a blocked nucleotide moiety.

11. The method of claim 10, wherein the blocked nucleotide is a 3'-O-azidomethyl, 3'-O-methyl, or 3'-O-alkyl hydroxylamine nucleotide.

12. The method of claim 1, wherein said contacting occurs in the presence of an ion that stabilizes said multivalent binding complex.

13. The method of claim 1, wherein the contacting is done in the presence of strontium ions, magnesium ions, calcium ions, or any combination thereof.

14. The method of claim 1, wherein the polymerase molecules are catalytically inactive.

15. The method of claim 1, wherein the polymerase molecules have been rendered catalytically inactive by mutation or chemical modification.

16. The method of claim 1, wherein the polymerase molecules have been rendered catalytically inactive by the absence of a necessary ion or cofactor.

17. The method of claim 1, wherein the polymerase molecules are catalytically active.

18. The method of claim 1, wherein the polymer-nucleotide conjugate does not comprise a blocked nucleotide moiety.

19. The method of claim 1, wherein the multivalent binding complex has a persistence time of greater than 2 seconds.

20. The method of claim 1, wherein the method is carried out at a temperature within a range of 25°C to 42°C.

21. The method of claim 1, wherein the polymer-nucleotide conjugate further comprises one or more fluorescent labels and the two or more copies of the target nucleic acid sequence are deposited on, attached to, or hybridized to a surface, wherein a fluorescence image of the multivalent binding complex on the surface has a contrast to noise ratio in the detecting step of greater than 20.

22. The method of claim 1, wherein the composition of (a) is deposited on a surface using a buffer that incorporates a polar aprotic solvent.

23. The method of claim 1, wherein the contacting is performed under a condition that stabilizes said multivalent binding complex when said nucleotide moiety is complementary to a next base of said target nucleic acid sequence and destabilizes said multivalent binding complex when said nucleotide moiety is not complementary to said next base of said target nucleic acid sequence.

24. The method of claim 1, wherein said polymer-nucleotide conjugate comprises a polymer having a plurality of branches and said two or more nucleotide moieties are attached to said branches.

25. The method of claim 24, wherein said first polymer has a star, comb, cross-linked, bottle brush, or dendrimer configuration.

26. The method of claim 1, wherein said polymer-nucleotide conjugate comprises one or more binding groups selected from the group consisting of an avidin, a biotin, an affinity tag, and combinations thereof.

27. The method of claim 1, further comprising a dissociation step that destabilizes said multivalent binding complex formed between the composition of (a) and the polymer-nucleotide conjugate, said dissociation step enabling removal of said polymer-nucleotide conjugate.

28. The method of claim 27, further comprising an extension step to incorporate a nucleotide that is complementary to a next base of the target nucleic acid sequence into said two or more primer nucleic acid molecules.

29. The method of claim 28, wherein the extension step occurs concurrently with or after said dissociation step.

30. The method of claim 1, wherein said polymer-nucleotide conjugate comprises one or more detectable labels.