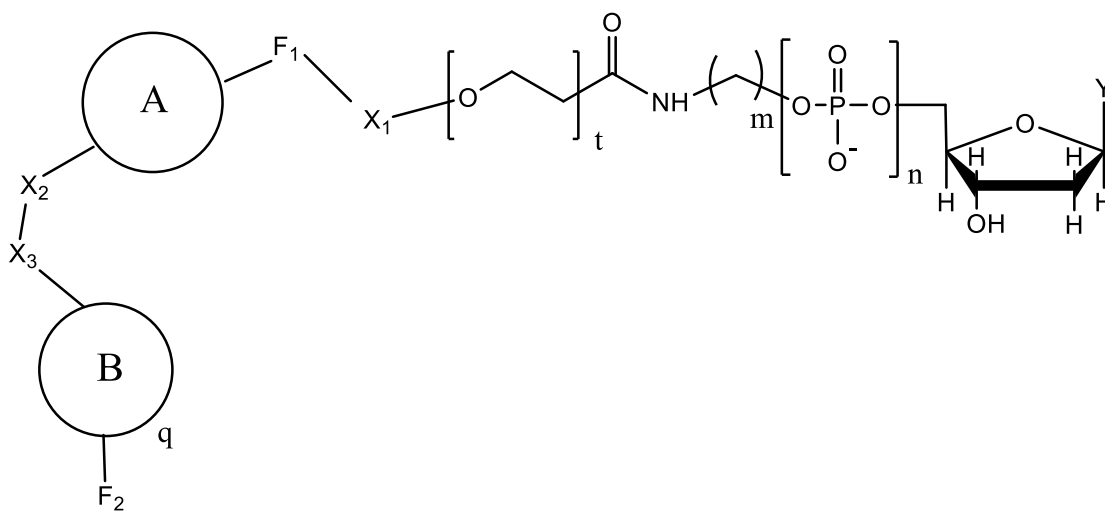


Claims

1. A method comprising:
 - detecting an incorporation of a labelled nucleotide into a nascent polynucleotide strand complementary to a template polynucleotide strand by a polymerase, wherein the polymerase is tethered to a solid support conductive channel by a tether,
 - the labelled nucleotide is a compound of Formula I
- [Formula I]



wherein n is an integer from 3 to 10,

m is an integer from 1 to 10,

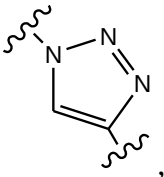
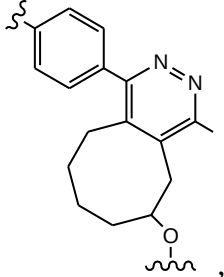
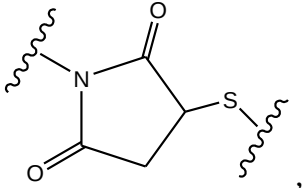
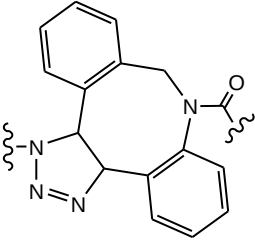
t is an integer from 0 to 50,

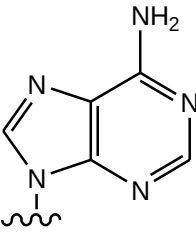
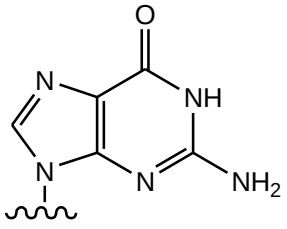
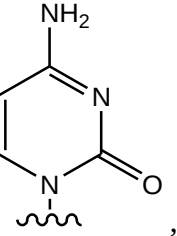
X₁ is a direct bond, a C₁-C₁₀ alkyl, a C₁-C₁₀ oxaalkyl, a C₁-C₁₀ thiaalkyl, or a C₁-C₁₀ azaalkyl,

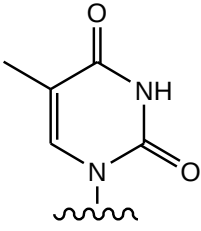
X₂ is C₁-C₂₀ alkyl wherein optionally one or more individual CH₂ residue is replaced with one or more of a peptide bond and (-O-CH₂-CH₂-)_a wherein a is an integer from 1 to 24,

X₃ is a direct bond or an oligonucleotide wherein the oligonucleotide hybridizes to an acceptor region of the tether when the label is in proximity to the conductive channel,

F₁ is selected from a fluorophore and a direct bond and F₂ is absent or a fluorophore,

A is: , , , , or an amide bond,

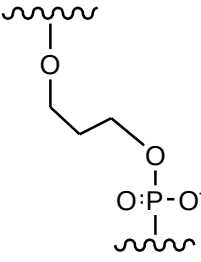
Y is: , , ,

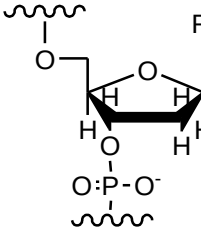
or ,

and wherein

B is: a) an amino acid or comprises an amino acid,

b) a nucleotide,

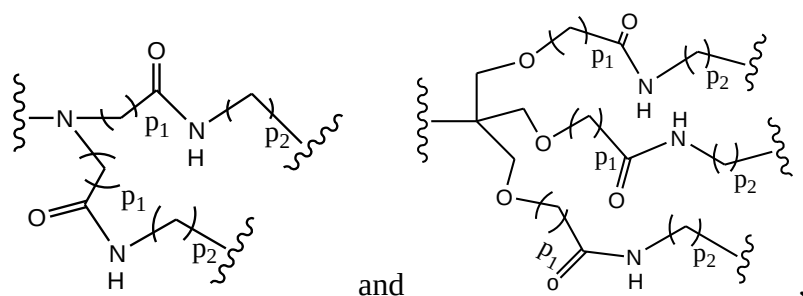
c) , or

d)  wherein R is Y or hydrogen,

and wherein q is an integer from 1 to 100 and the conductive channel is to detect the labelled nucleotide during the incorporation; optionally wherein the q number of B has a charge and a charge density;

or

B is a dendron of z generations comprising one or more constitutional repeating unit and a plurality of end units, wherein z is an integer from 1 to 6, the constitutional end units are selected from:



wherein

p_1 is an integer from 1 to 3, wherein any one or more of the p_1 -CH₂- groups is optionally replaced with from 1 to 3 -O-CH₂-CH₂- groups,

p_2 is an integer from 1 to 3, wherein any one or more of the p_2 -CH₂- groups is optionally replaced with from 1 to 3 -O-CH₂-CH₂- groups, and

the end groups are selected from carboxylic acid, sulfonic acid, phosphonic acid, sperminyl group, amino group, and quaternary ammonium group, B has a charge and a charge density, q is 1 and the charge sensor is to detect the labelled nucleotide during the incorporation, optionally wherein the conductive channel is to detect the labelled nucleotide during the incorporation.

2. A method as claimed in claim 1, wherein the charge is between -100e and +100e.
3. A method as claimed in claim 2, wherein the charge density is between -100e per cubic nanometer and +100e per cubic nanometer.
4. A method as claimed in claim 1, wherein the charge is between -200e and +200e.
5. A method as claimed in claim 4, wherein the charge density is between -200e per cubic nanometer and +200e per cubic nanometer.
6. A method as claimed in claim 1, wherein the q number of B comprises a polynucleotide.
7. A method as claimed in claim 6, wherein the polynucleotide is selected from a branched polynucleotide and one or more hairpin loops.
8. A method as claimed in claim 7, wherein the polynucleotide comprises between two and five hairpin loops.
9. A method as claimed in claim 1, wherein the q number of B comprises a polypeptide.
10. A method as claimed in claim 9, wherein the polypeptide is selected from a branched polypeptide, coiled polypeptide, and coiled-coil polypeptide.

11. A method as claimed in claim 1, wherein B comprises an amino acid, and one or more of the q number of B comprise methyllysine, dimethyllysine, or trimethyllysine.
12. A method as claimed in claim 1, wherein A was formed by a reaction comprising a linking reaction and the linking reaction is selecting from an azide-alkyne copper-assisted click reaction, a tetrazine-trans-cyclooctene ligation, an azide-dibenzocyclooctyne group copper-free click reaction, and a thiol-maleimide conjugation.
13. A method as claimed in any one of claims 1 to 12, further comprising successively incorporating a plurality of labelled nucleotides wherein the charge of each of the plurality of labelled nucleotides differs from the charge of any other of the plurality of labelled nucleotides when the Y of the each and the Y of the any other differ from each other; optionally further comprising identifying the Y of one or more labelled polynucleotide incorporated into the nascent polynucleotide strand based on the charge detected by the conductive channel.
14. A method as claimed in claim 1, wherein X_2 is $(-O-CH_2-CH_2-)_a$ wherein a is an integer from 1 to 24, optionally wherein a is 4, 8, 12, 16 or 24.