"Click"	This method relies on functionalization of the antibody with an azide or alkyne group, depending on the specific catalyst and specific process.	Can be a chemically harsh process that limits use to "robust" antibodies. Since this method relies on another amine/carboxy conjugation method this can also suffer from a wide distribution of biomolecules/antibody
Sulfhydryl-maleimide	This method uses free sulfhydryl groups on the surface of an antibody (or protein) to react with a maleimide group typically synthetically attached to a biomolecule of interest.	The distribution of sulfhydryl groups over the surface of an antibody are well understood but this chemistry can lead to degraded performance of the antibody and requires post-conjugation purification.

[0002] Further, due do the potential harsh chemistries involved and the inherent "stickiness" of currently available dyes, purification of dyes following conjugation is a necessary step in current manufacturing of biomolecule conjugates.

SUMMARY

[0003] Provided for herein is a polynucleotide-modified binding molecule bioconjugate comprising a binding molecule linked to a conjugate component via a nucleic acid linker. Provided for herein is a polynucleotide-modified bioconjugate, comprising a substrate linked to an oligonucleotide-based fluorescent label via a nucleic acid linker; wherein the substrate comprises an at least partially single-stranded nucleic acid linker, and the oligonucleotide-based fluorescent label comprises an at least partially single-stranded nucleic acid linker; and wherein at least a portion of the sequence of the single-stranded nucleic acid linker of the substrate is complementary to a portion of the sequence of the single-stranded nucleic acid linker of the oligonucleotide-based fluorescent label, such that the nucleic acid linker of the substrate and the single-stranded nucleic acid linker of the oligonucleotide-based fluorescent label are annealed to form a double-stranded nucleic acid linker segment, said nucleic acid linker comprising the double-stranded nucleic acid linker segment.

[0004] Provided for herein is also a polynucleotide-modified bead bioconjugate comprising a bead linked to a conjugate component via a nucleic acid linker.

[0005] Provided for are methods of producing a polynucleotide-modified binding molecule bioconjugate of this disclosure or a polynucleotide-modified bead bioconjugate of this disclosure comprising: (i) contacting a polynucleotide-modified substrate comprising an at least partially single-stranded nucleic acid linker with a polynucleotide-modified conjugate component comprising an at least partially single-stranded nucleic acid linker, wherein the substrate is a binding molecule or a bead, wherein at least a portion of the single-stranded linker sequence of the substrate is complementary to a portion of the single-stranded linker sequence of the conjugate component and wherein when contacted, the nucleic acid linker of the substrate and the nucleic acid linker of the conjugate component anneal to form an at least partially double-

stranded linker linking the substrate to the conjugate component; (ii) contacting a substrate with a conjugate component, wherein the substrate is a binding molecule or a bead, and attaching a nucleic acid linker to the substrate and attaching the same nucleic acid linker to the conjugate component to form the polynucleotide-modified binding molecule bioconjugate, (iii) contacting a polynucleotide-modified conjugate component comprising a nucleic acid linker with a substrate, wherein the substrate is a binding molecule or a bead, and attaching the nucleic acid linker of the polynucleotide-modified conjugate component to the substrate to form the polynucleotide-modified binding molecule or bead bioconjugate, (iv) contacting a polynucleotide-modified substrate comprising a nucleic acid linker with a conjugate component, wherein the substrate is a binding molecule or a bead, and attaching the nucleic acid linker of the polynucleotide-modified substrate to the conjugate component to form the polynucleotide-modified binding molecule or bead bioconjugate; or (v) contacting (i) a polynucleotide-modified substrate comprising an at least partially single-stranded nucleic acid linker, wherein the substrate is a binding molecule or a bead, (ii) a polynucleotide-modified conjugate component comprising an at least partially single-stranded nucleic acid linker, and (iii) a further nucleic acid linker segment that is not the nucleic acid linker of (i) or (ii), wherein at least a portion of the single-stranded linker sequence of the substrate is complementary to a single-stranded portion of the further nucleic acid linker segment (iii) and/or wherein at least a portion of the single-stranded linker sequence of the conjugate component is complementary to a single-stranded portion of the further nucleic acid linker segment (iii), and wherein when contacted, the nucleic acid linker of the substrate, the nucleic acid linker of the conjugate component, and the further nucleic acid linker segment anneal to form an at least partially double-stranded linker linking the substrate to the conjugate component. In one aspect, provided herein is a process of making a polynucleotide-modified bioconjugate, comprising contacting in solution: a substrate comprising an at least partially single-stranded nucleic acid linker with an oligonucleotide-based fluorescent label comprising an at least partially single-stranded nucleic acid linker; wherein at least a portion of the sequence of the single-stranded nucleic acid linker of the substrate is complementary to a portion of the sequence of the single-stranded nucleic acid linker of the oligonucleotide-based fluorescent label, such that the nucleic acid linkers anneal and form a double-stranded nucleic acid linker segment linking the substrate to the oligonucleotide-based fluorescent label.

[0006] Provided for herein is a high-rate method of producing a labeled binding molecule for detection, wherein separate binding-molecule molecules of the same binding molecule are labeled

with different conjugate components, the method comprising: (a) attaching an at least partially single-stranded nucleic acid linker to at least two separate binding-molecule molecules of the same binding molecule to produce a plurality of polynucleotide-modified binding-molecule molecules; and (b) contacting at least one polynucleotide-modified binding-molecule molecule of the plurality with a first polynucleotide-modified conjugate component comprising an at least partially single-stranded nucleic acid linker and contacting at least one different polynucleotide-modified binding-molecule molecule of the plurality with a second polynucleotide-modified conjugate component comprising an at least partially single-stranded

CLAIMS

~~What is claimed is:~~

~~1. A polynucleotide-modified binding molecule bioconjugate comprising a binding molecule linked to a conjugate component via a nucleic acid linker;~~

~~optionally, wherein the nucleic acid linker comprises a double-stranded segment;~~

~~optionally, wherein the nucleic acid linker is entirely double-stranded.~~

~~2. The polynucleotide-modified binding molecule bioconjugate of claim 1, wherein the conjugate component comprises a nucleic acid and the nucleic acid linker comprises an extension of a nucleic acid strand of the conjugate component;~~

~~optionally, wherein the nucleic acid of the conjugate component has a length of at least 10, 15, 20, 25, 30, 35, 40, 50, 55, 60, 65, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 175, 200, 300, or 400, nucleotides, or any range in between, not including the nucleic acid linker;~~

~~optionally, wherein the nucleic acid of the conjugate component has a tertiary and/or a quaternary structure.~~

~~3. The polynucleotide-modified binding molecule bioconjugate of claim 1 or 2, wherein the binding molecule is an antibody or an antigen-binding fragment, variant, or derivative thereof, a peptides, recombinant, natural, or engineered receptor/ligand proteins, aptamers, tetramers (folded MHC proteins with peptides used for detecting T cell receptors), non-antibody proteins or antibody mimetics, e.g., affilins, affimers, affitins, alphabodies, avimers, fynomers, Kunitz domain peptides, nanoCLAMPS, Designed Ankyrin Repeat Proteins (DARPins), monobodies, nanobodies, anticalins, affibodies, and SOMAmers;~~

optionally, wherein the binding molecule is an antibody or an antigen-binding fragment, variant, or derivative thereof;

optionally, wherein the binding molecule is a receptor ligand.

4. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 3, wherein the nucleic acid linker is from any of about 10, 15, 20, 25, 30, 35, 40, or 50 nucleotides in length to any of about 15, 20, 25, 30, 35, 40, 50, or 75 nucleotides in length;

optionally, wherein the conjugate component comprises a nucleic acid and the length of the nucleic acid linker is determined from the edge of the conjugate component, and wherein the edge of the conjugate component is an end of any single-stranded segment longer than four nucleotides.

5. The polynucleotide-modified binding molecule bioconjugate of claim 4, wherein the double-stranded segment of the nucleic acid linker is from any of about 10, 15, 20, 25, 30, 35, 40, or 50 nucleotides in length to any of about 15, 20, 25, 30, 35, 40, 50, or 75 nucleotides in length.

6. The polynucleotide-modified binding molecule bioconjugate of claim 5, wherein the double-stranded segment comprises from any of about 10, 15, 20, 25, 30, 35, 40, or 50 complementary base pairs to any of about 15, 20, 25, 30, 35, 40, 50, or 75 complementary base pairs;

optionally, wherein at least 85%, 90%, 95%, or 98% of the double-stranded segment is complementary base paired or wherein the double-stranded segment has no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mismatched base pairs;

optionally, wherein the double-stranded segment comprises at least about 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 consecutive complementary base pairs or from any of about 7,

~~8, 9, 10, 15, 20, 25, 30, 35, 40, or 50 consecutive complementary base pairs to any of about 8, 9, 10, 15, 20, 25, 30, 35, 40, 50, 55, 60, 65, 70, or 75 consecutive complementary base pairs;~~

~~optionally, wherein 100% of the double-stranded segment is complementary base paired.~~

~~7. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 6:~~

~~wherein the double-stranded segment of the nucleic acid linker comprises a polyadenosine sequence (polyA) in one strand and a polythymidine sequence (polyT) in the other strand;~~

~~wherein the double-stranded segment of the nucleic acid linker comprises a polycytosine sequence (polyC) in one strand and a polyguanidine sequence (polyG) in the other strand;~~

~~wherein the double-stranded segment of the nucleic acid linker comprises polyA and polyC sequences in one strand and polyT and polyG sequences in the other strand; or~~

~~wherein the double-stranded segment of the nucleic acid linker comprises polyA and polyG sequences in one strand and polyT and polyC sequences in the other strand;~~

~~optionally, wherein the double-stranded segment of the nucleic acid linker consists of a polyadenosine sequence (polyA) in one strand and a polythymidine sequence (polyT) in the other strand; or~~

~~optionally, wherein the double-stranded segment of the nucleic acid linker consists of a polycytosine sequence (polyC) in one strand and a polyguanidine sequence (polyG) in the other strand.~~

~~8. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 7, wherein the conjugate component is an antibody or an antigen-binding fragment, variant, or derivative thereof, a nucleic acid, an aptamer, a protein, a dye or label, a small molecule, a~~

~~therapeutic peptide, a receptor ligand, a pharmaceutically active agent, or an oligonucleotide-based fluorescent label.~~

~~9. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 7, wherein the conjugate component is an oligonucleotide-based fluorescent label.~~

~~10. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 9,~~

~~wherein the degree-of-labeling (DoL) of the binding molecule is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11, or any range in between inclusive of the endpoints;~~

~~wherein the degree-of-labeling (DoL) of the binding molecule is controlled stoichiometrically via the availability of the nucleic acid; and/or~~

~~wherein the degree-of-labeling (DoL) of the nucleic acids on a polynucleotide-modified binding molecule is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11, or any range in between inclusive of the endpoints and is independent of the DoL of the conjugate component.~~

~~11. The polynucleotide-modified binding molecule bioconjugate of any one of claim 1 to 10, wherein the bioconjugate can be used to specifically label a cell, tissue, and/or organ for one or more of flow cytometry, antibody screening, ELISA or other sandwich assays, immune monitoring, biomarker assays, lateral flow, point-of-care/rapid diagnostics, imaging, microscopy, molecular diagnostics, next generation sequencing, long read sequencing, *in situ* sequencing, polymerase chain reaction, microarrays, nucleic acid sequencing, amino acid sequencing, digital pathology, Southern blotting, Northern blotting, Western blotting, or prophylactic and/or therapeutic purposes.~~

~~12. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 11, wherein the nucleic acid linker comprises a unique identifying sequence;~~

~~optionally, wherein the double-stranded segment of the nucleic acid linker comprises a unique identifying sequence.~~

~~13. The polynucleotide-modified binding molecule bioconjugate of claim 12, wherein the unique identifying sequence can be used for nucleic acid amplification and/or next-generation sequencing.~~

~~14. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 13,~~

~~wherein the nucleic acid linker comprises a sequence enabling it to be filtered out in downstream sequencing applications;~~

~~wherein the nucleic acid linker comprises a sequence for specific binding by a third biomolecule and/or for targeted gene editing through enzymatic cleavage (e.g., CRISPR, Zinc-finger nucleases, restriction enzymes);~~

~~wherein the nucleic acid linker comprises two or more unique sequences enabling enzymatic or binding activity; and/or~~

~~wherein a unique sequence enabling enzymatic or binding activity is present in the double-stranded segment.~~

~~15. The polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 14, wherein the nucleic acid linker comprises (i) a portion attached to the binding molecule, (ii) a portion attached to or an extension of the conjugate component, and (iii) at least one additional portion that is not (i) or (ii);~~

~~optionally, wherein (iii) could also be a second portion attached to or an extension of the conjugate component or attached to or an extension of an additional conjugate component.~~

~~16. A polynucleotide-modified bead bioconjugate comprising a bead linked to a conjugate component via a nucleic acid linker;~~

~~optionally, wherein the nucleic acid linker comprises a double-stranded segment;~~

~~optionally, wherein the nucleic acid linker is entirely double-stranded.~~

~~17. The polynucleotide-modified bead bioconjugate of claim 16, wherein the conjugate component comprises a nucleic acid and the nucleic acid linker comprises an extension of a nucleic acid strand of the conjugate component;~~

~~optionally, wherein the nucleic acid of the conjugate component has a length of at least 10, 15, 20, 25, 30, 35, 40, 50, 55, 60, 65, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 175, 200, 300, or 400, nucleotides, or any range in between, not including the nucleic acid linker;~~

~~optionally, wherein the nucleic acid of the conjugate component has a tertiary and/or a quaternary structure.~~

~~18. The polynucleotide-modified bead bioconjugate of claim 16 or 17, wherein the nucleic acid linker is from any of about 10, 15, 20, 25, 30, 35, 40, or 50 nucleotides in length to any of about 15, 20, 25, 30, 35, 40, 50, or 75 nucleotides in length;~~

~~optionally, wherein the conjugate component comprises a nucleic acid and the length of the nucleic acid linker is determined from the edge of the conjugate component, and wherein the edge of the conjugate component is an end of any single-stranded segment longer than four nucleotides.~~

~~19. The polynucleotide-modified bead bioconjugate of claim 18, wherein the double-stranded segment of the nucleic acid linker is from any of about 10, 15, 20, 25, 30, 35, 40, or 50 nucleotides in length to any of about 15, 20, 25, 30, 35, 40, 50, or 75 nucleotides in length.~~

~~20. The polynucleotide-modified bead bioconjugate of claim 19, wherein the double-stranded segment comprises from any of about 10, 15, 20, 25, 30, 35, 40, or 50 complementary base pairs to any of about 15, 20, 25, 30, 35, 40, 50, or 75 complementary base pairs;~~

~~optionally, wherein at least 85%, 90%, 95%, or 98% of the double-stranded segment is complementary base paired or wherein the double-stranded segment has no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mismatched base pairs;~~

~~optionally, wherein the double-stranded segment comprises at least about 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 consecutive complementary base pairs or from any of about 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, or 50 consecutive complementary base pairs to any of about 8, 9, 10, 15, 20, 25, 30, 35, 40, 50, 55, 60, 65, 70, or 75 consecutive complementary base pairs;~~

~~optionally, wherein 100% of the double-stranded segment is complementary base paired.~~

~~21. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 20:~~

~~wherein the double-stranded segment of the nucleic acid linker comprises a polyadenosine sequence (polyA) in one strand and a polythymidine sequence (polyT) in the other strand;~~

~~wherein the double-stranded segment of the nucleic acid linker comprises a polycytosine sequence (polyC) in one strand and a polyguanidine sequence (polyG) in the other strand;~~

~~wherein the double-stranded segment of the nucleic acid linker comprises polyA and polyC sequences in one strand and polyT and polyG sequences in the other strand; or~~

~~wherein the double-stranded segment of the nucleic acid linker comprises polyA and polyG sequences in one strand and polyT and polyC sequences in the other strand;~~

~~optionally, wherein the double-stranded segment of the nucleic acid linker consists of a polyadenosine sequence (polyA) in one strand and a polythymidine sequence (polyT) in the other strand; or~~

~~optionally, wherein the double-stranded segment of the nucleic acid linker consists of a polycytosine sequence (polyC) in one strand and a polyguanidine sequence (polyG) in the other strand.~~

~~22. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 21, wherein the conjugate component is an antibody or an antigen-binding fragment, variant, or derivative thereof, a nucleic acid, an aptamer, a protein, a dye or label, a small molecule, a therapeutic peptide, a receptor ligand, a pharmaceutically active agent, or an oligonucleotide-based fluorescent label.~~

~~23. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 21, wherein the conjugate component is an oligonucleotide-based fluorescent label.~~

~~24. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 23,~~

~~wherein the DoL of the bead is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11, or any range in between inclusive of the endpoints;~~

~~wherein the DoL of the bead is 100, 1,000, 10,000, 100,000, or 1,000,000, or any range in between inclusive of the endpoints; and/or~~

~~wherein the degree-of-labeling (DoL) of the bead is controlled stoichiometrically via the availability of the nucleic acid.~~

~~wherein the degree of labeling (DoL) of the nucleic acids on a polynucleotide-modified bead is independent of the DoL of the conjugate component.~~

~~25. The polynucleotide-modified bead bioconjugate of any one of claim 16 to 24, wherein the bioconjugate can be used to label a cell, tissue, and/or organ for one or more of flow cytometry, antibody screening, ELISA or other sandwich assays, immune monitoring, biomarker assays, lateral flow, point-of-care/rapid diagnostics, imaging, microscopy, molecular diagnostics, next generation sequencing, long read sequencing, *in situ* sequencing, polymerase chain reaction, microarrays, nucleic acid sequencing, amino acid sequencing, digital pathology, Southern blotting, Northern blotting, Western blotting, as a reference sample such as a control or for calibration of an instrument, assay, or system, or prophylactic and/or therapeutic purposes.~~

~~26. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 25, wherein the nucleic acid linker comprises a unique identifying sequence;~~

~~optionally, wherein the double-stranded segment of the nucleic acid linker comprises a unique identifying sequence.~~

~~27. The polynucleotide-modified bead bioconjugate of claim 26, wherein the unique identifying sequence can be used for nucleic acid amplification and/or next-generation sequencing.~~

~~28. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 27,~~

~~wherein the nucleic acid linker comprises a sequence enabling it to be filtered out in downstream sequencing applications;~~

~~wherein the nucleic acid linker comprises a sequence for specific binding by a third biomolecule and/or for targeted gene editing through enzymatic cleavage (e.g., CRISPR, Zinc-finger nucleases, restriction enzymes);~~

~~wherein the nucleic acid linker comprises two or more unique sequences enabling enzymatic or binding activity; and/or~~

~~wherein a unique sequence enabling enzymatic or binding activity is present in the double-stranded segment.~~

~~29. The polynucleotide-modified bead bioconjugate of any one of claims 16 to 28, wherein the nucleic acid linker comprises (i) a portion attached to the bead, (ii) a portion attached to or an extension of the conjugate component, and (iii) at least one additional portion that is not (i) or (ii);~~

~~optionally, wherein (iii) could also be a second portion attached to or an extension of the conjugate component or attached to or an extension of an additional conjugate component.~~

1. A ~~method~~ process of ~~producing~~ making ~~the~~ a polynucleotide-modified ~~binding molecule~~ bioconjugate ~~of any one of claims 1 to 15 or the polynucleotide-modified bead bioconjugate of any one of claims 16 to 29~~, ~~the method~~ comprising contacting in solution:

~~(i) contacting~~ a ~~polynucleotide-modified~~ substrate comprising an at least partially single-stranded nucleic acid linker with an oligonucleotide-based fluorescent label ~~a polynucleotide-modified conjugate component~~ comprising an at least partially single-stranded nucleic acid linker~~, wherein the substrate is a binding molecule or a bead~~;~~,~~

wherein at least a portion of the ~~single-stranded linker~~ sequence of the single-stranded nucleic acid linker of the substrate is complementary to a portion of the sequence of the single-

stranded nucleic acid linker of the oligonucleotide-based fluorescent label, ~~sequence of the conjugate component and wherein when contacted, the nucleic acid linker of the substrate and the nucleic acid linker of the conjugate component~~ such that the nucleic acid linkers anneal ~~to~~ and form ~~an at least partially~~a double-stranded nucleic acid linker segment linking the substrate to the oligonucleotide-based fluorescent label.~~conjugate component~~;

~~optionally, wherein prior to contacting the polynucleotide-modified substrate and the polynucleotide-modified conjugate component, the method comprises the step of attaching the at least partially single-stranded nucleic acid linker to the substrate to form the polynucleotide-modified substrate; and/or~~

~~optionally, wherein prior to contacting the polynucleotide-modified substrate and the polynucleotide-modified conjugate component, the method comprises the step of attaching the at least partially single-stranded nucleic acid linker to the conjugate component to form the polynucleotide-modified conjugate component;~~

~~(ii) contacting a substrate with a conjugate component, wherein the substrate is a binding molecule or a bead, and attaching a nucleic acid linker to the substrate and attaching the same nucleic acid linker to the conjugate component to form the polynucleotide-modified bioconjugate,~~

~~optionally, wherein the nucleic acid linker comprises a double-stranded segment or wherein the nucleic acid linker is entirely double-stranded and the method comprises hybridizing nucleic acid strands to form an at least partially double-stranded nucleic acid linker prior to attaching to the substrate and to the conjugate component;~~

~~(iii) contacting a polynucleotide-modified conjugate component comprising a nucleic acid linker with a substrate, wherein the substrate is a binding molecule or a bead, and attaching the~~

~~nucleic acid linker of the polynucleotide-modified conjugate component to the substrate to form the polynucleotide-modified bioconjugate,~~

~~optionally, wherein the nucleic acid linker comprises a double-stranded segment or wherein the nucleic acid linker is entirely double-stranded and the method comprises hybridizing nucleic acid strands to form an at least partially double-stranded nucleic acid linker on the polynucleotide-modified conjugate component prior to attaching the nucleic acid linker of the polynucleotide-modified conjugate component to the substrate to form the polynucleotide-modified bioconjugate;~~

~~(iv) contacting a polynucleotide-modified substrate comprising a nucleic acid linker with a conjugate component, wherein the substrate is a binding molecule or a bead, and attaching the nucleic acid linker of the polynucleotide-modified substrate to the conjugate component to form the polynucleotide-modified bioconjugate,~~

~~optionally, wherein the nucleic acid linker comprises a double-stranded segment or wherein the nucleic acid linker is entirely double-stranded and the method comprises hybridizing nucleic acid strands to form an at least partially double-stranded nucleic acid linker on the polynucleotide-modified substrate prior to attaching the nucleic acid linker of the polynucleotide-modified substrate to the conjugate component to form the polynucleotide-modified bioconjugate; or~~

~~(v) contacting (i) a polynucleotide-modified substrate comprising an at least partially single-stranded nucleic acid linker, wherein the substrate is a binding molecule or a bead, (ii) a polynucleotide-modified conjugate component comprising an at least partially single-stranded nucleic acid linker, and (iii) a further at least partially single-stranded nucleic acid linker segment that is not the nucleic acid linker of (i) or (ii),~~

~~wherein at least a portion of the single-stranded linker sequence of the substrate is complementary to a single-stranded portion of the further nucleic acid linker segment (iii) and/or wherein at least a portion of the single-stranded linker sequence of the conjugate component is complementary to a single-stranded portion of the further nucleic acid linker segment (iii), and wherein when contacted, the nucleic acid linker of the substrate, the nucleic acid linker of the conjugate component, and the further nucleic acid linker segment anneal to form an at least partially double-stranded linker linking the substrate to the conjugate component.~~

2. The process of claim 1, wherein the substrate comprises a binding molecule or a bead.

3. The process of claim 2, wherein the binding molecule is an antibody, or antigen-binding fragment, variant, or derivative thereof.

4. The process of claim 2 or claim 3, wherein the degree-of-labeling (DoL) of the polynucleotide-modified binding molecule is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11, or any range in between inclusive of the endpoints.

5. The process of any of claims 2 to 4, wherein the degree-of-labeling (DoL) of the binding molecule is controlled stoichiometrically via the availability of the at least partially single-stranded nucleic acid linker of the substrate.

6. The process of any preceding claim, wherein the double-stranded nucleic acid linker segment comprises at least about 10 complementary base pairs.

7. The process of any preceding claim, wherein the double-stranded nucleic acid linker segment comprises from at least about 10 complementary base pairs to at least about 75 complementary base pairs; optionally from at least about 60 complementary base pairs to at least about 75 complementary base pairs.

8. The process of any preceding claim, wherein the oligonucleotide-based fluorescent label is an oligonucleotide-based nanoparticle.

9. A polynucleotide-modified bioconjugate obtainable by the method of any of claims 1 to 8.

10. A polynucleotide-modified bioconjugate, comprising a substrate linked to an oligonucleotide-based fluorescent label via a nucleic acid linker;

wherein the substrate comprises an at least partially single-stranded nucleic acid linker, and the oligonucleotide-based fluorescent label comprises an at least partially single-stranded nucleic acid linker; and

wherein at least a portion of the sequence of the single-stranded nucleic acid linker of the substrate is complementary to a portion of the sequence of the single-stranded nucleic acid linker of the oligonucleotide-based fluorescent label, such that the nucleic acid linker of the substrate and the single-stranded nucleic acid linker of the oligonucleotide-based fluorescent label are annealed to form a double-stranded nucleic acid linker segment, said nucleic acid linker comprising the double-stranded nucleic acid linker segment.

11. The polynucleotide-modified bioconjugate of claim 10, wherein the bioconjugate further comprises the features of any of claims 2 to 8.

~~31. The method of claim 30:~~

~~wherein the single-stranded nucleic acid linker of the polynucleotide-modified substrate comprises a polyA sequence and the single-stranded nucleic acid linker of the polynucleotide-modified conjugate component comprises a polyT sequence; or~~

~~wherein the single-stranded nucleic acid linker of the polynucleotide-modified substrate comprises a polyT sequence and the single-stranded nucleic acid linker of the polynucleotide-modified conjugate component comprises a polyA sequence; or~~

~~wherein the single-stranded nucleic acid linker of the polynucleotide-modified substrate comprises a polyC sequence and the single-stranded nucleic acid linker of the polynucleotide-modified conjugate component comprises a polyG sequence; or~~

~~wherein the single-stranded nucleic acid linker of the polynucleotide-modified substrate comprises a polyG sequence and the single-stranded nucleic acid linker of the polynucleotide-modified conjugate component comprises a polyC sequence; or~~

~~wherein the single-stranded nucleic acid linker of the polynucleotide-modified substrate comprises a polyC sequence and a polyA and/or polyT sequence and the single-stranded nucleic acid linker of the polynucleotide-modified conjugate component comprises a polyG sequence and a polyA and/or polyT sequence; or~~

~~wherein the single-stranded nucleic acid linker of the polynucleotide-modified substrate comprises a polyG sequence and a polyA and/or polyT sequence and the single-stranded nucleic acid linker of the polynucleotide-modified conjugate component comprises a polyC sequence and a polyA and/or polyT sequence.~~

~~32. A high-rate method of producing a labeled binding molecule for detection, wherein separate binding-molecule molecules of the same binding molecule are labeled with different conjugate components, the method comprising:~~

~~(a) attaching an at least partially single-stranded nucleic acid linker to at least two separate binding-molecule molecules of the same binding molecule to produce a plurality of polynucleotide-modified binding-molecule molecules; and~~

~~(b) contacting at least one polynucleotide-modified binding-molecule molecule of the plurality with a first polynucleotide-modified conjugate component comprising an at least partially single-stranded nucleic acid linker and contacting at least one different polynucleotide-modified binding-molecule molecule of the plurality with a second polynucleotide-modified conjugate component comprising an at least partially single-stranded nucleic acid linker, wherein the first and second polynucleotide-modified conjugate components comprise detection labels and differ at least in their detection labels,~~

~~wherein at least a portion of the single-stranded sequence of the nucleic acid linker of the binding-molecule molecules is complementary to a single-stranded sequence of the nucleic acid linker of the first and/or second conjugate components, and wherein when contacted, the nucleic acid linkers anneal to form a double-stranded linker linking the binding-molecule molecules to the conjugate components;~~

~~optionally, wherein one or more additional polynucleotide-modified binding-molecule molecules of the plurality are contacted with one or more additional polynucleotide-modified conjugate components having different detection labels;~~

~~optionally, wherein at least three, four, five, six, seven, eight, nine, or ten of the polynucleotide-modified binding-molecule molecules of the plurality are each contacted with a polynucleotide-modified conjugate component having a different detection label from the others;~~

~~optionally, wherein the binding molecule is an antibody or an antigen-binding fragment, variant, or derivative thereof; or~~

~~wherein the high-rate method of producing a labeled binding molecule for detection is performed by directly attaching a nucleic acid linker to a binding molecule, a conjugate component, or both a binding molecule and a conjugate component as in claim 30 and/or wherein the high-rate of producing a labeled binding molecule for detection is performed using an additional nucleic acid linker segment as in claim 30,~~

~~wherein separate binding-molecule molecules of the same binding molecule are labeled with different conjugate components;~~

~~optionally, wherein at least three, four, five, six, seven, eight, nine, or ten separate binding-molecule molecules are each labeled with a conjugate component having a different detection label from the others;~~

~~optionally, wherein the binding molecule is an antibody or an antigen-binding fragment, variant, or derivative thereof.~~

~~33. The method of claim 32, comprising aliquoting polynucleotide-modified binding-molecule molecules of the plurality into separate compartments for contacting with a uniquely labeled polynucleotide-modified conjugate components in each compartment, thus producing differently-labeled binding-molecule molecules of the same binding molecule.~~

~~34. The method of claim 32 or 33, wherein the at least partially single-stranded nucleic acid linker of the plurality of the binding-molecule molecules is the same for all of the polynucleotide-modified binding-molecule molecules and wherein the at least partially single-stranded nucleic acid linker of the conjugate component is the same for all the polynucleotide-modified conjugate components.~~

~~35. A high-rate method of producing labeled binding molecules for detection, wherein different binding molecules are labeled with the same conjugate component, the method comprising:~~

~~(a) attaching an at least partially single-stranded nucleic acid linker to at least two different binding molecules to produce at least two different polynucleotide-modified binding molecules; and~~

~~(b) contacting the at least two different polynucleotide-modified binding molecules with a polynucleotide-modified conjugate component comprising a detection label and comprising an at least partially single-stranded nucleic acid linker,~~

~~wherein at least a portion of the single-stranded sequence of the nucleic acid linker of the binding molecules is complementary to a single-stranded sequence of the nucleic acid linker of the conjugate component and wherein when contacted the nucleic acid linkers anneal to form a double-stranded linker linking the binding molecules to the conjugate component;~~

~~optionally, wherein one, two, three, four, five, six, seven, eight, nine, ten, or more additional polynucleotide-modified binding molecules are contacted with the polynucleotide-modified conjugate component;~~

~~optionally, wherein one or more of the binding molecules is an antibody or an antigen-binding fragment, variant, or derivative thereof; or~~

~~wherein the high-rate method of producing a labeled binding molecule for detection is performed by directly attaching a nucleic acid linker to a binding molecule, a conjugate component, or both a binding molecule and a conjugate component as in claim 30 and/or wherein the high-rate of producing a labeled binding molecule for detection is performed by incorporating an additional nucleic acid linker segment as in claim 30;~~

optionally, wherein one, two, three, four, five, six, seven, eight, nine, ten, or more additional polynucleotide-modified binding molecules are contacted with the polynucleotide-modified conjugate component;

optionally, wherein the binding molecule is an antibody or an antigen-binding fragment, variant, or derivative thereof.

36. The method of claim 35, comprising aliquoting the different polynucleotide-modified binding molecules into a separate compartment for each type of binding molecule for contacting with the polynucleotide-modified conjugate component in each compartment thus producing different binding molecules labeled with the same label.

37. The method of claim 35 or 36, wherein the at least partially single-stranded nucleic acid linker of the different binding molecules is the same for all the polynucleotide-modified binding molecules and a single at least partially single-stranded nucleic acid sequence is used as the nucleic acid linker of the polynucleotide-modified conjugate component.

38. A high-rate method of producing a labeled binding molecule or binding molecules for detection, the method comprising combining the methods of any one of claims 32 to 34 and the methods any one of claims 35 to 37.

39. A composition comprising:

(i)(a) a substrate comprising an at least partially single-stranded nucleic acid linker, wherein the substrate is a binding molecule or a bead, and

(i)(b) a conjugate component comprising an at least partially single-stranded nucleic acid linker,

~~wherein at least a sufficient portion of the single-stranded sequence of the nucleic acid linker of the substrate is complementary to a portion of the single-stranded sequence of the nucleic acid linker of the conjugate component to allow for the linkers to anneal and form an at least partially double-stranded linker linking the substrate to the conjugate component;~~

~~(ii)(a) a substrate comprising a nucleic acid linker, wherein the substrate is a binding molecule or a bead, and~~

~~(ii)(b) a conjugate component capable of attachment to the nucleic acid linker to link the substrate to the conjugate component;~~

~~(iii)(a) a conjugate component comprising a nucleic acid linker,~~

~~(iii)(b) a substrate capable of attachment to the nucleic acid linker to link the conjugate component to the substrate;~~

~~(iv)(a) a substrate capable of attachment to a nucleic acid linker, wherein the substrate is a binding molecule or a bead, and a conjugate component capable of attachment to a nucleic acid linker, and~~

~~(iv)(b) a nucleic acid linker, wherein the nucleic acid linker is single-stranded, comprises a double-stranded segment, or wherein the nucleic acid linker is entirely double stranded; or~~

~~(v)(a) a substrate comprising an at least partially single-stranded nucleic acid linker, wherein the substrate is a binding molecule or a bead,~~

~~(v)(b) a conjugate component comprising an at least partially single-stranded nucleic acid linker; and~~

~~(v)(c) a further nucleic acid linker segment,~~

~~wherein (v)(a), (v)(b), and (v)(c) can anneal to form an at least partially double-stranded nucleic acid linker comprising (v)(a), (v)(b), and (v)(c) and linking (v)(a) to (v)(b).~~

~~40. The composition of claim 39, wherein the composition is capable of producing the polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 15 or the polynucleotide-modified bead bioconjugate of any one of claims 16 to 29.~~

~~41~~12. An *ex vivo* method of labeling a cell, tissue, ~~and/~~or organ, the method comprising:

contacting the cell, tissue, ~~and/~~or organ with the fluorescently labeled bioconjugate of any of claims 9 to 11, ~~a polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 15~~ wherein the ~~binding molecule portion of the bioconjugate binds to an antigen, epitope, and/or hapten of the cell, tissue, and/or organ and wherein the conjugate component portion of the bioconjugate comprises a detectable label;~~

~~optionally, wherein the binding molecule~~ substrate portion of the bioconjugate comprises a binding molecule that ~~specifically recognizes and specifically~~ binds to an antigen, epitope, ~~and/~~or hapten of the cell, tissue, ~~and/~~or organ~~;~~

~~optionally, wherein the label is a label for visual detection,~~

~~optionally, wherein the labeled cell can be used for one or more of flow cytometry, antibody screening, ELISA or other sandwich assays, immune monitoring, biomarker assays, lateral flow, point-of-care/rapid diagnostics, imaging, microscopy, molecular diagnostics, next generation sequencing, long read sequencing, *in situ* sequencing, polymerase chain reaction, microarrays, nucleic acid sequencing, amino acid sequencing, digital pathology, Southern blotting, Northern blotting, Western blotting, as a reference sample such as a control or for calibration of an instrument, assay, or system, or prophylactic and/or therapeutic purposes;~~

~~optionally, wherein the label is a label for cellular membranes,~~

~~optionally, wherein the label is a label for cellular viability, or~~

~~optionally, wherein the label is a specific label targeting genomic material~~.

~~42~~13. The method of claim ~~41~~12, further comprising use of the labeled cell in one or more of ~~wherein the labeled cell is used in~~ flow cytometry, antibody screening, sandwich assays, immune monitoring, biomarker assays, lateral flow, point-of-care/rapid diagnostics, imaging, microscopy, molecular diagnostics, next generation sequencing, long read sequencing, in situ sequencing, polymerase chain reaction, microarrays, nucleic acid sequencing, amino acid sequencing, digital pathology, Southern blotting, Northern blotting, or Western blotting.

14. The method of claim 12 or claim 13, further comprising use of the labeled cell in flow cytometry.

~~43. A method of quantitatively measuring a signal from a labeled cell, tissue, and/or organ, the method comprising:~~

~~(a) contacting the cell, tissue, and/or organ with a polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 15 wherein the binding molecule portion of the bioconjugate binds to an antigen, epitope, membrane, genomic material, and/or hapten of the cell, tissue, and/or organ and the conjugate component portion of the bioconjugate comprises a detectable label; and~~

~~(b) measuring the presence of the polynucleotide-modified binding molecule bioconjugate wherein the DoL of the binding molecule is known, thus allowing a quantitative measurement to be made;~~

~~optionally, wherein the degree of labeling (DoL) of the binding molecule is controlled stoichiometrically via the availability of the nucleic acid;~~

~~optionally, wherein the DoL of the binding molecule is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 or any range in between inclusive of the endpoints;~~

~~optionally, wherein the degree of labeling (DoL) of the nucleic acids on a polynucleotide-modified binding molecule is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11, or any range inbetween inclusive of the endpoints and is independent of the DoL of the conjugate component; and/or~~

~~optionally, wherein the degree of labeling (DoL) of the nucleic acids on a polynucleotide-modified binding molecule is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11, or any range in between inclusive of the endpoints and is independent of the DoL of the conjugate component.~~

~~44~~15. A kit comprising: ~~one or more components necessary to produce the polynucleotide-modified binding molecule bioconjugate of any one of claims 1 to 15, to produce the~~

(a) a polynucleotide-modified ~~bead~~ bioconjugate of any ~~one~~ of claims ~~16 to 29~~9-11;~~,~~ and ~~to produce the composition of claim 39 or 40, or to perform any of the methods of the preceding claims;~~

~~optionally, wherein the kit further comprises~~

(b) instructions ~~either printed and/or on an electronic storage medium~~for use, and/or buffers and/or additional reagents, and/or packaging materials.