embodiments, the gel bead comprises the magnetic bead. In some embodiments, the method further comprises degrading the gel bead. In some embodiments, the plurality of nucleic acid barcode molecules and the second plurality of nucleic acid barcode molecules are attached to a bead, and wherein the partition further comprises the bead. In some embodiments, the barcoded nucleic acid fragment and the barcoded cDNA molecule is released from the partition. In some embodiments, the method further comprises sequencing the barcoded nucleic acid fragment or a derivative thereof and the barcoded cDNA molecule or a derivative thereof.

[0036] In some embodiments, the method further comprises (a) lysing a plurality of cells in the presence of a cell lysis agent and a blocking agent; and (b) separating a plurality of nuclei from the plurality of lysed cells to generate the plurality of biological particles, wherein the blocking agent reduces the fraction of sequencing reads corresponding to a mitochondrial genome compared to sequencing reads obtained in the absence of the blocking agent. In some embodiments, the blocking agent is bovine serum albumin (BSA).

[0037] In some embodiments, the method further comprises cleaving one or more mitochondrial nucleic acid molecules or derivatives thereof, using (i) one or more guide ribonucleic acid molecules (gRNAs) targeted to the one or more mitochondrial nucleic acid fragments; and (ii) a clustered regularly interspaced short palindromic (CRISPR) associated (Cas) nuclease. In some embodiments, the Cas nuclease is Cas9. In some embodiments, the mitochondrial nucleic acid molecules are cleaved prior to (c). In some embodiments, the mitochondrial nucleic acid molecules are cleaved in the partition. In some embodiments, the partition comprises the Cas nuclease. In some embodiments, the partition further comprises the one or more gRNAs. In some embodiments, the mitochondrial nucleic acid molecules are cleaved subsequent to (d).

[0037a] In one aspect, the present disclosure provides a method of nucleic acid processing, comprising:

(a) providing a plurality of cells or cell nuclei comprising chromatin;

(b) in said plurality of cells or cell nuclei, generating a plurality of nucleic acid fragments of said chromatin using a plurality of transposase-nucleic acid complexes;

(c) partitioning said plurality of cells or cell nuclei to provide a plurality of partitions, each comprising (i) a cell or a cell nucleus of said plurality of cells or cell nuclei, said cell or said cell nucleus comprising a nucleic acid fragment of said plurality of nucleic acid fragments, and (ii) a bead having attached thereto a plurality of barcode oligonucleotide molecules each comprising a barcode sequence; and

(d) in each of said plurality of partitions, generating a barcoded nucleic acid fragment using at least (i) said nucleic acid fragment, and (ii) a barcode oligonucleotide molecule of said plurality of barcode oligonucleotide molecules.

[0038] Additional aspects and advantages of the present disclosure will become readily apparent to those skilled in this art from the following detailed description, wherein only illustrative embodiments of the present disclosure are shown and described. As will be realized, the present disclosure is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, all without departing from the disclosure. Accordingly, the drawings and description are to be regarded as illustrative in nature, and not as restrictive.

INCORPORATION BY REFERENCE

[0039] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference. To

WHAT IS CLAIMED IS:

1. A method of nucleic acid processing, comprising:

(a) providing a plurality of cells or cell nuclei comprising chromatin;

(b) in said plurality of cells or cell nuclei, generating a plurality of nucleic acid fragments of said chromatin using a plurality of transposase-nucleic acid complexes;

(c) partitioning said plurality of cells or cell nuclei to provide a plurality of partitions, each comprising (i) a cell or a cell nucleus of said plurality of cells or cell nuclei, said cell or said cell nucleus comprising a nucleic acid fragment of said plurality of nucleic acid fragments, and (ii) a bead having attached thereto a plurality of barcode oligonucleotide molecules each comprising a barcode sequence; and

(d) in each of said plurality of partitions, generating a barcoded nucleic acid fragment using at least (i) said nucleic acid fragment, and (ii) a barcode oligonucleotide molecule of said plurality of barcode oligonucleotide molecules.

2. The method of claim 1, wherein said bead is a gel bead.

3. The method of claim 1, wherein said plurality of barcode oligonucleotide molecules is releasable from said bead upon application of a stimulus.

4. The method of claim 3, further comprising using said stimulus to release said plurality of barcode oligonucleotide molecules from said bead.

5. The method of claim 2, wherein said partition further comprises a chemical agent to depolymerize or degrade said gel bead.

6. The method of claim 5, wherein said chemical agent comprises a reducing agent.

7. The method of claim 1, wherein said plurality of partitions comprises a plurality of droplets.

8. The method of claim 1, wherein said plurality of partitions comprises 1,000 wells.

9. The method of claim 1, further comprising amplifying said barcoded nucleic acid fragment, or a derivative generated from said barcoded nucleic acid fragment, by nucleic acid amplification.

10. The method of claim 9, wherein said nucleic acid amplification is performed in said partition.

11. The method of claim 1, further comprising sequencing said barcoded nucleic acid fragment, or a derivative generated from said barcoded nucleic acid fragment.

12. The method of claim 1, wherein the transposase-nucleic acid complexes of said plurality of transposase-nucleic acid complexes comprise (i) a first nucleic acid molecule comprising a first adapter sequence; and (ii) a second nucleic acid molecule comprising a second adapter sequence.

13. The method of claim 1, wherein a transposase-nucleic acid complex of said plurality of transposase-nucleic acid complexes comprises:

(i) a first partially double-stranded nucleic acid molecule comprising: (1) a first strand comprising a first adapter sequence and a first transposon end sequence and (2) a second strand comprising a sequence complementary to said first transposon end sequence; and

(ii) a second partially double-stranded nucleic acid molecule comprising a third strand comprising a second adapter sequence and a second transposon end sequence and a second strand comprising a first sequence complementary to said second transposon end sequence.

14. The method of claim 13, wherein said barcode oligonucleotide molecules of said plurality of barcode oligonucleotide molecules comprise a third adapter sequence, said barcode sequence, and a primer sequence complementary to said first adapter sequence.

15. The method of claim 13, wherein said barcode oligonucleotide molecules of said plurality of barcode oligonucleotide molecules are partially double-stranded molecules comprising: (i) a

fourth strand comprising: a third adapter sequence, said barcode sequence, and a second sequence complementary to said first adapter sequence; and (ii) a fifth strand comprising a sequence complementary to said third adapter sequence and a third sequence complementary to said barcode sequence.

16. The method of claim 15, wherein said barcoded nucleic acid fragment is generated by ligation of said barcode oligonucleotide molecule with said nucleic acid fragment or a derivative generated from said nucleic acid fragment.

17. The method of claim 16, wherein subsequent to said ligation, said nucleic acid fragment is subjected to a gap-filling reaction to generate a gap-filled, nucleic acid fragment.

18. The method of claim 14, wherein said barcoded nucleic acid fragment is generated by amplification of said nucleic acid fragment, or a derivative generated from said nucleic acid fragment, using said primer sequence of said barcode oligonucleotide molecule.

19. The method of claim 18, wherein said barcode oligonucleotide molecules of said plurality of barcode oligonucleotide molecules are single-stranded.

20. The method of claim 1, wherein said barcoded nucleic acid fragment is indicative of a region of accessible chromatin of said cell or said cell nucleus.

21. The method of claim 12, wherein said first adapter sequence and said second adapter sequence are the same.

22. The method of claim 12, wherein said first adapter sequence and said second adapter sequence are different.

23. The method of claim 1, wherein said barcode oligonucleotide molecules of said plurality of barcode oligonucleotide molecules are releasably attached to said bead through a labile bond.

24. The method of claim 23, wherein said labile bond is selected from the group consisting of: a thermally cleavable bond, a chemically labile bond, an enzymatically-labile bond, and a photo-sensitive bond.

25. The method of claim 23, wherein said labile bond comprises a linkage selected from the group consisting of: an ester linkage, a vicinal diol linkage, a Diels-Alder linkage, a sulfone linkage, a silyl ester linkage, a glycosidic linkage, a peptide linkage, and a phosphodiester linkage.

26. The method of claim 1, wherein said partition comprises at most a single cell or at most a single cell nucleus of said plurality of cells or cell nuclei.

27. The method of claim 6, wherein said reducing agent is selected from the group consisting of: beta-mercaptoethanol dithiobutylamine (DTBA), tris(2-carboxyethyl) phosphine (TCEP), and dithiothreitol (DTT).

28. The method of claim 14, wherein said third adapter sequence comprises a sequencer specific flow cell attachment sequence.

29. The method of claim 1, further comprising, prior to (b), permeabilizing one or more cells or cell nuclei of said plurality of cells or cell nuclei.

30. The method of claim 1, wherein each of said plurality of partitions comprises a unique barcode.