

CLAIMS

WHAT IS CLAIMED IS:

1. A method for processing a nucleic acid molecule, comprising:
 - (a) providing a partition comprising:
 - (i) a biological particle comprising: (I) a tagmented fragment of a deoxyribonucleic acid (DNA) molecule, and (II) a ribonucleic acid (RNA) molecule,
 - (ii) a first nucleic acid barcode molecule comprising a first barcode sequence,
 - (iii) a second nucleic acid barcode molecule comprising a second barcode sequence, and
 - (iv) a splint molecule, wherein said first nucleic acid barcode molecule comprises an overhang sequence, and wherein said splint molecule comprises a first sequence complementary to a sequence of said tagmented fragment and a second sequence complementary to said overhang sequence; and
 - (b) within said partition:
 - (i) hybridizing said sequence of said tagmented fragment to said splint molecule, and hybridizing said overhang sequence of, said first nucleic acid barcode molecule to said splint molecule to generate a first barcoded nucleic acid product comprising: (I) said first barcode sequence or a complement thereof and (II) a sequence of said DNA molecule; and
 - (ii) using said RNA molecule and said second nucleic acid barcode molecule to generate a second barcoded nucleic acid product comprising: (I) said second barcode sequence or a complement thereof and (II) a complementary DNA (cDNA) sequence of said RNA molecule, wherein said second nucleic acid barcode molecule comprises a capture sequence complementary to said RNA molecule and wherein (b)(ii) comprises hybridizing said capture sequence to said RNA molecule and reverse transcribing said RNA molecule to generate said second barcoded nucleic acid product.
2. The method of claim 1, wherein said biological particle is a cell, a cell bead, or a cell nucleus.
3. The method of claim 1, further comprising lysing or permeabilizing said biological particle within said partition to provide access to said tagmented fragment and said RNA molecule.

4. The method of any one of claims 1-3, further comprising, prior to (a), contacting an open chromatin structure of said biological particle with a transposase-nucleic acid complex to yield said biological particle comprising said tagmented fragment.
5. The method of claim 4, wherein said transposase-nucleic acid complex comprises a first transposon end oligonucleotide molecule and a second transposon end oligonucleotide molecule and wherein said tagmented fragment comprises a sequence of said DNA molecule flanked by said first transposon end oligonucleotide molecule and said second transposon end oligonucleotide molecule.
6. The method of claim 5, wherein (b)(i) comprises hybridizing said splint molecule to (A) said first transposon end oligonucleotide molecule or said second transposon end oligonucleotide molecule of said tagmented fragment and (B) said first nucleic acid barcode molecule, and ligating said first nucleic acid barcode molecule to said tagmented fragment to generate said first barcoded nucleic acid product.
7. The method of claim 5, wherein said first transposon end oligonucleotide molecule comprises a first transposon end sequence and a first primer sequence and wherein said second transposon end oligonucleotide molecule comprises a second transposon end sequence and a second primer sequence.
8. The method of claim 7, wherein (b)(i) comprises:
hybridizing said splint molecule to (A) said first primer sequence or said second primer sequence of said tagmented fragment and (B) said first nucleic acid barcode molecule, and ligating said first nucleic acid barcode molecule to said tagmented fragment to generate said first barcoded nucleic acid product.
9. The method of claim 8, further comprising, prior to said ligating, using a kinase to phosphorylate said tagmented fragment.
10. The method of claim 1, further comprising subjecting said first barcoded nucleic acid product to one or more nucleic acid extension reactions.
11. The method of claim 10, further comprising attaching, to said first barcoded nucleic acid product, one or more flow cell adapter sequences, one or more sequencing primer sequences, one or more sequencing primer binding sequences, or one or more sample index sequences.
12. The method of claim 1, wherein said capture sequence comprises a poly-thymine (poly-T) sequence.
13. The method of claim 1, further comprising use of an enzyme with terminal transferase activity to facilitate a template switching reaction that adds a polynucleotide sequence to said first barcoded nucleic acid product.

14. The method of claim 13, wherein said polynucleotide sequence comprises a polycytosine (polyC) sequence.
15. The method of claim 1, wherein said partition is a droplet.
16. The method of claim 1, wherein said partition is a well.
17. The method of claim 1, wherein said first barcode sequence and said second barcode sequence are the same.
18. The method of claim 1, wherein said first barcode sequence and said second barcode sequence are different.
19. The method of claim 1, wherein said tagmented fragment comprises a 5' phosphate.
20. The method of any one of claims 1-19, wherein said first nucleic acid barcode molecule and said second nucleic acid barcode molecule are coupled to a bead.
21. The method of claim 20, wherein said bead is a gel bead.
22. The method of claim 20 or 21, wherein said first nucleic acid barcode molecule and said second nucleic acid barcode molecule are releasable from said bead upon application of a stimulus.
23. The method of claim 20, wherein said first nucleic acid barcode molecule and said second nucleic acid barcode molecule are each coupled to said bead via a labile bond.