

FIG. 1

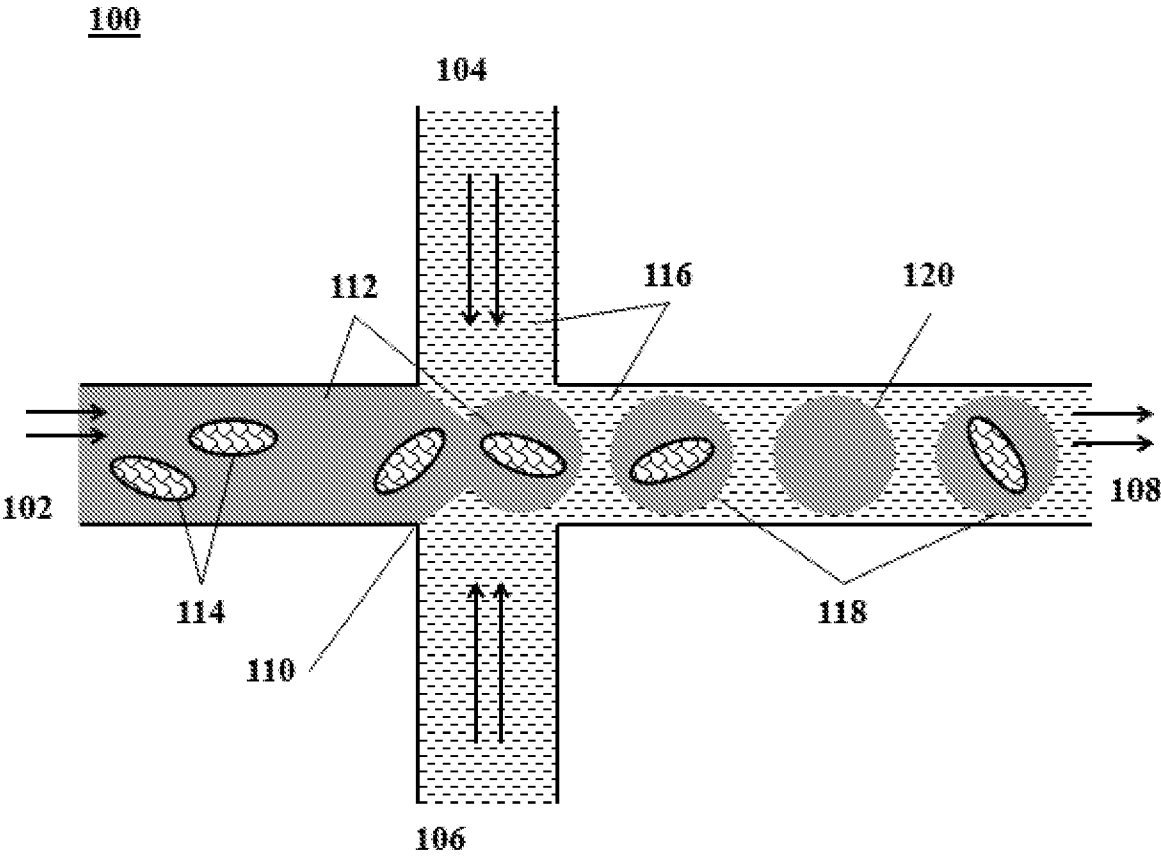


FIG. 2

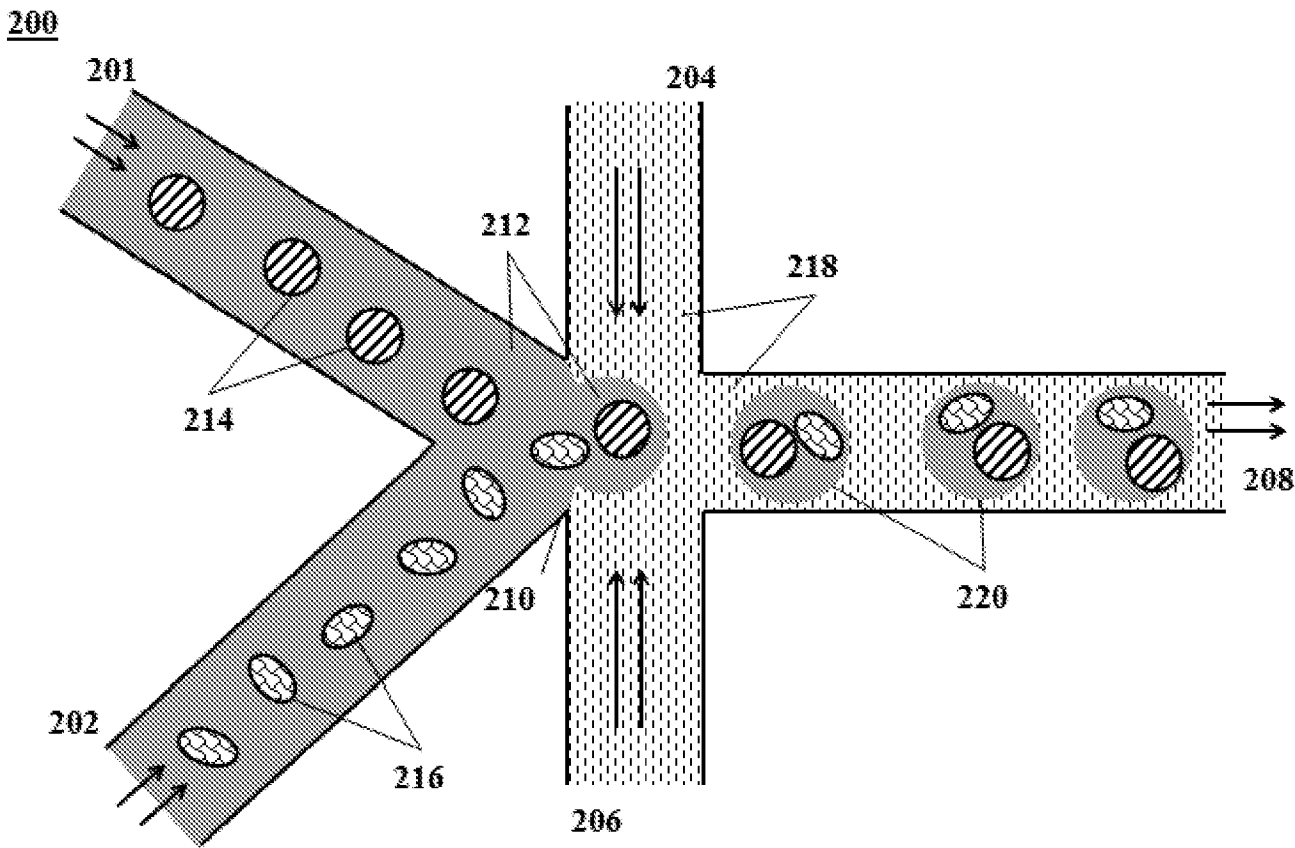


FIG. 3

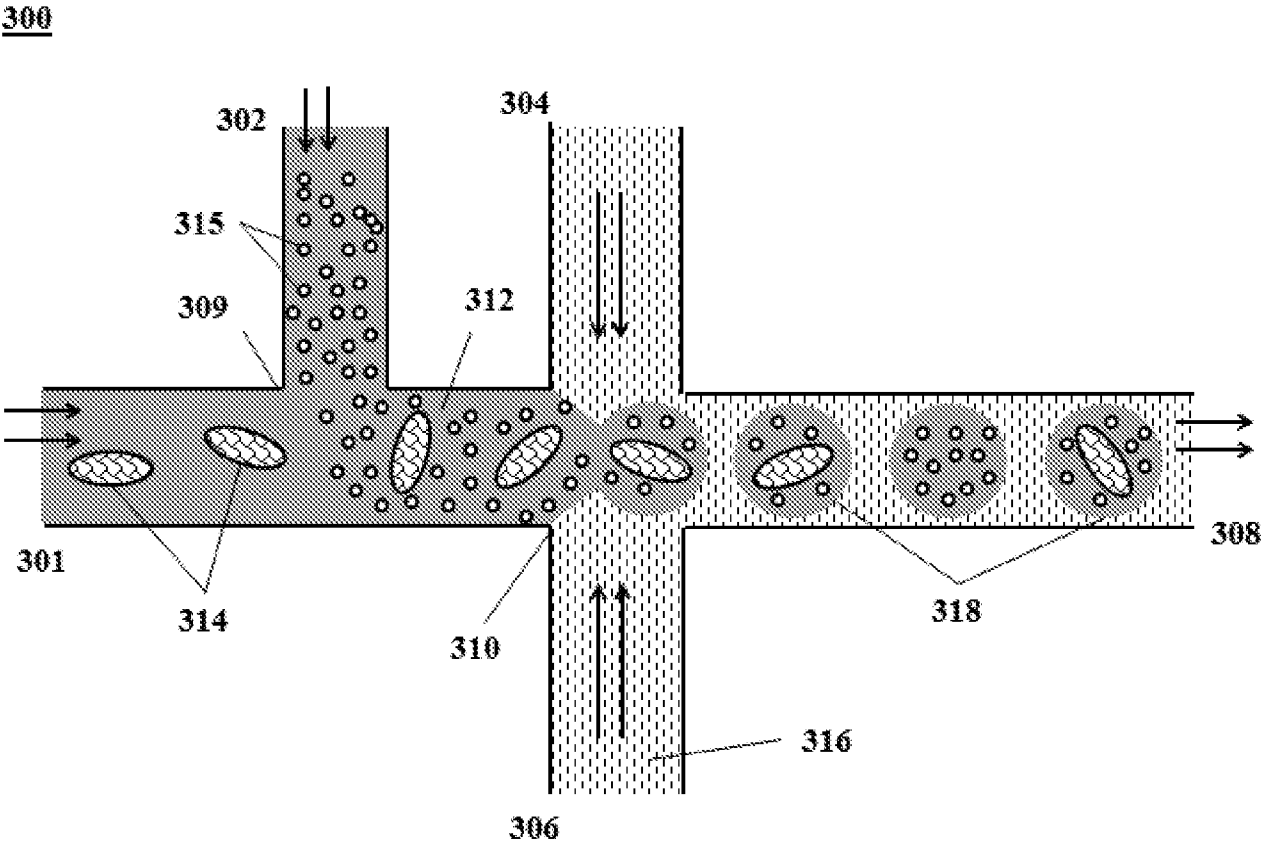


FIG. 4

400

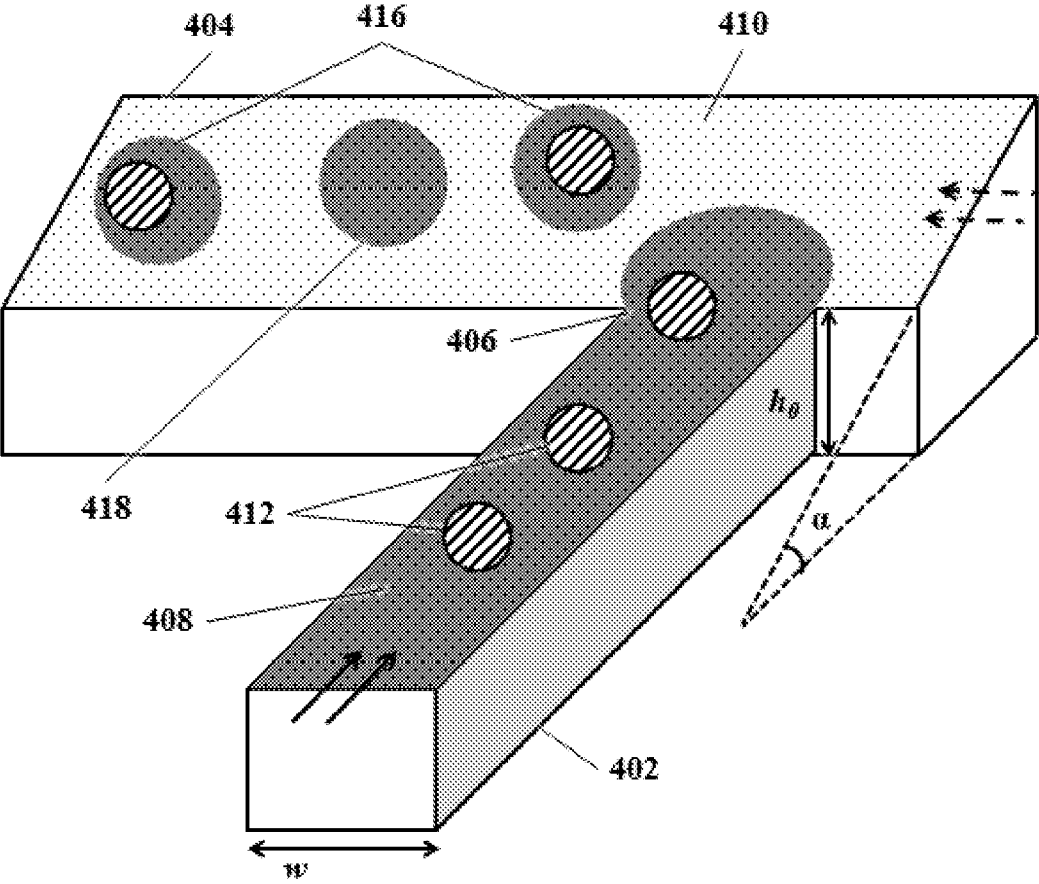


FIG. 5

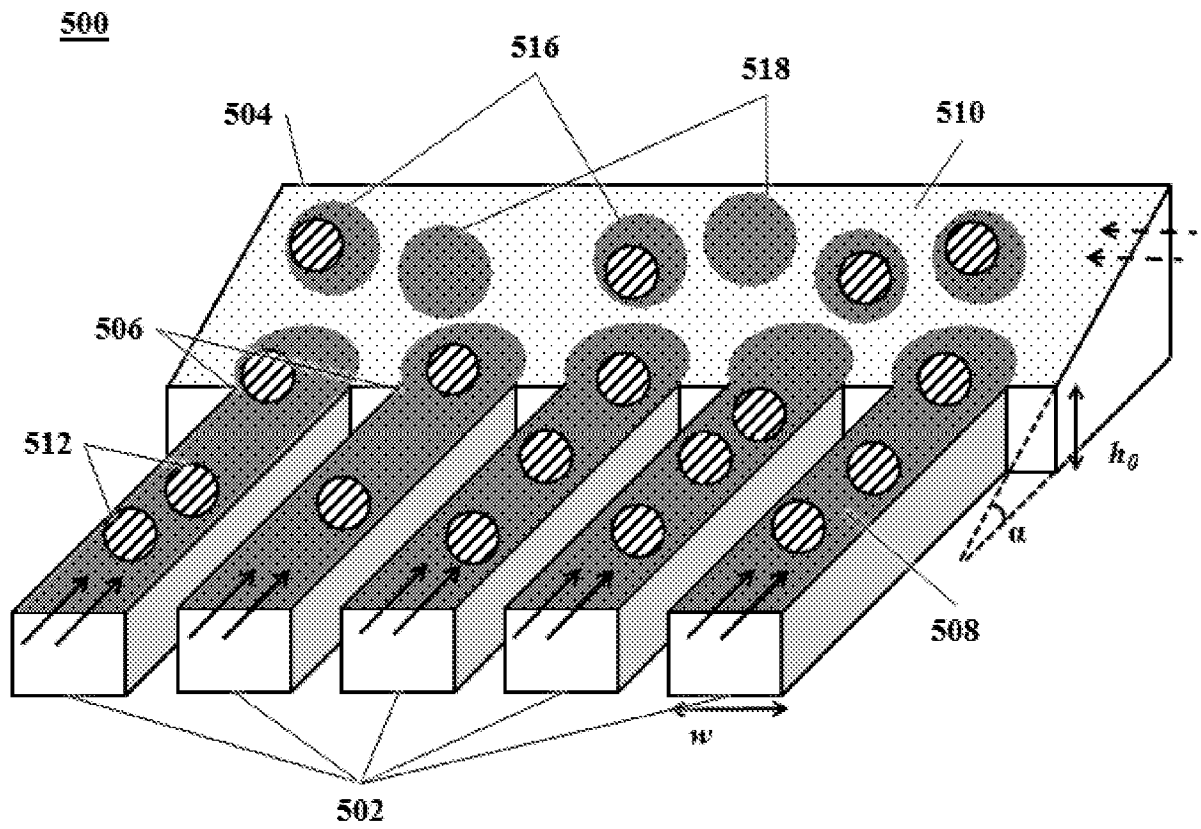


FIG. 6

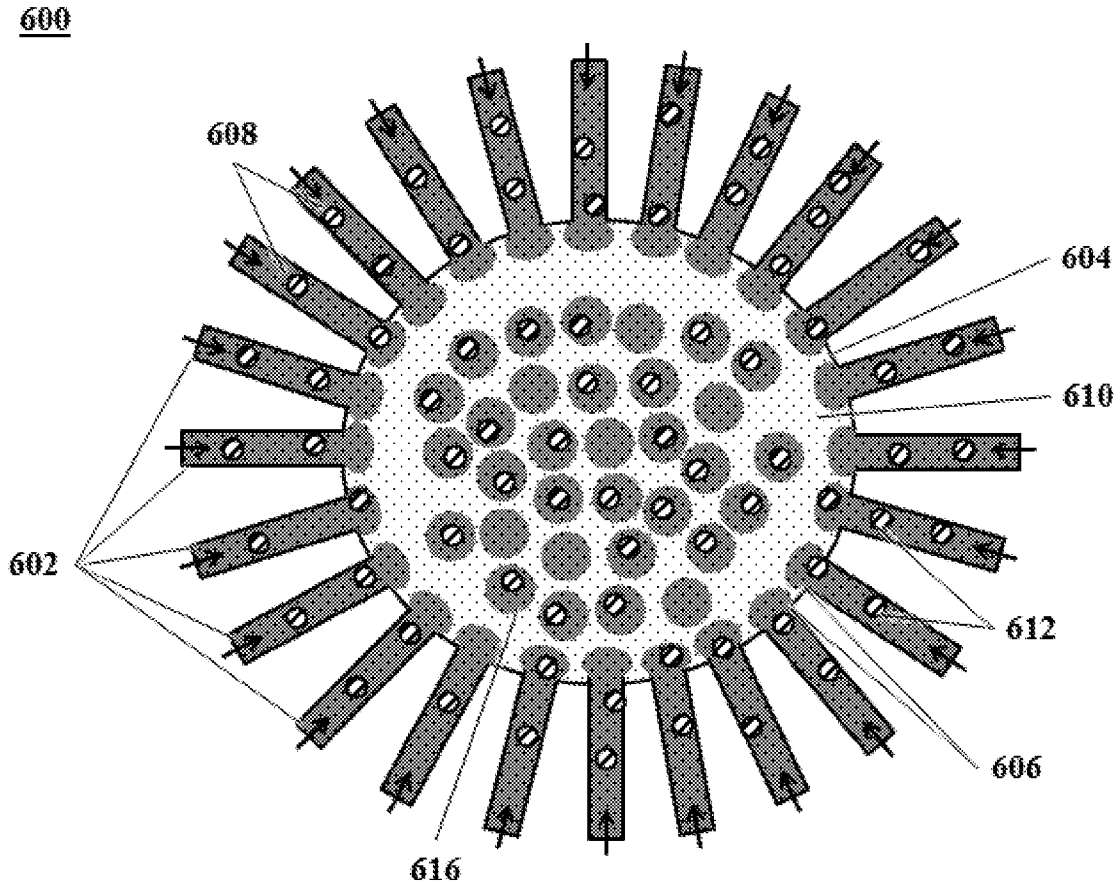


FIG. 7

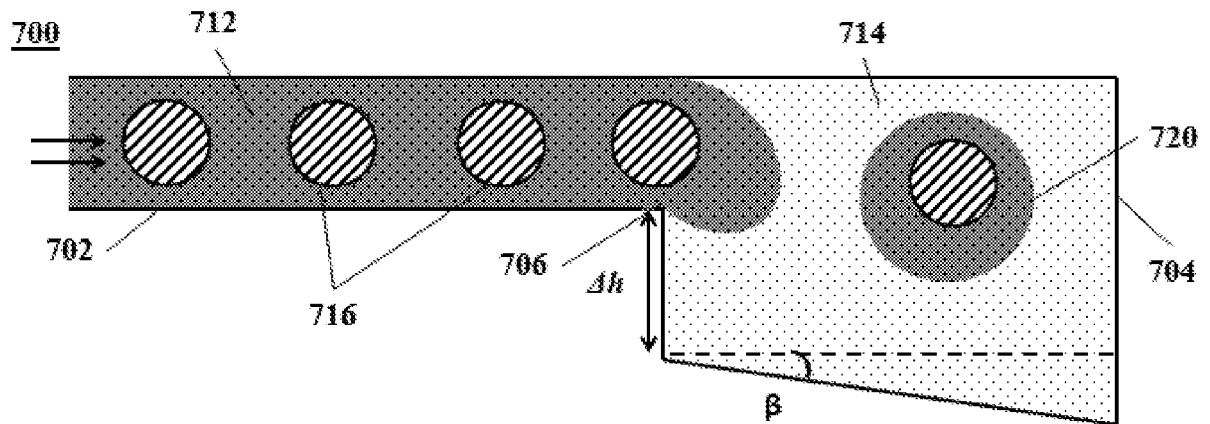


FIG. 74

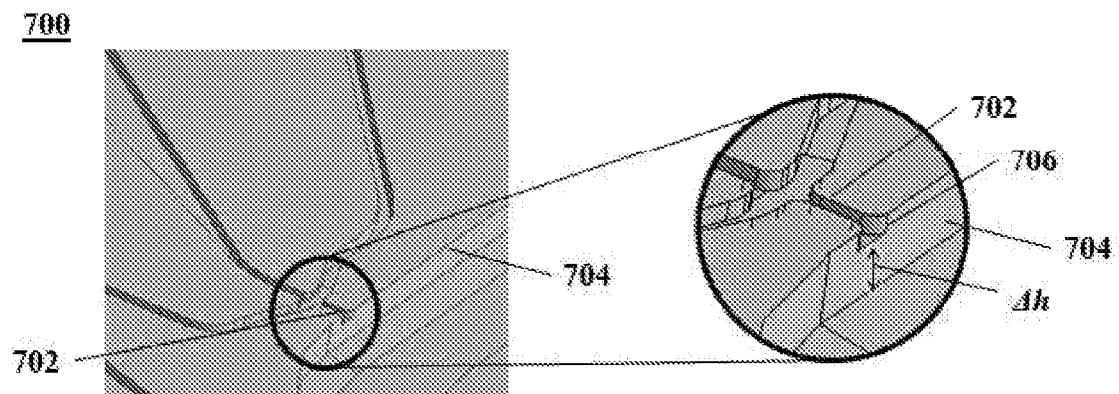


FIG. 7B

FIG. 8

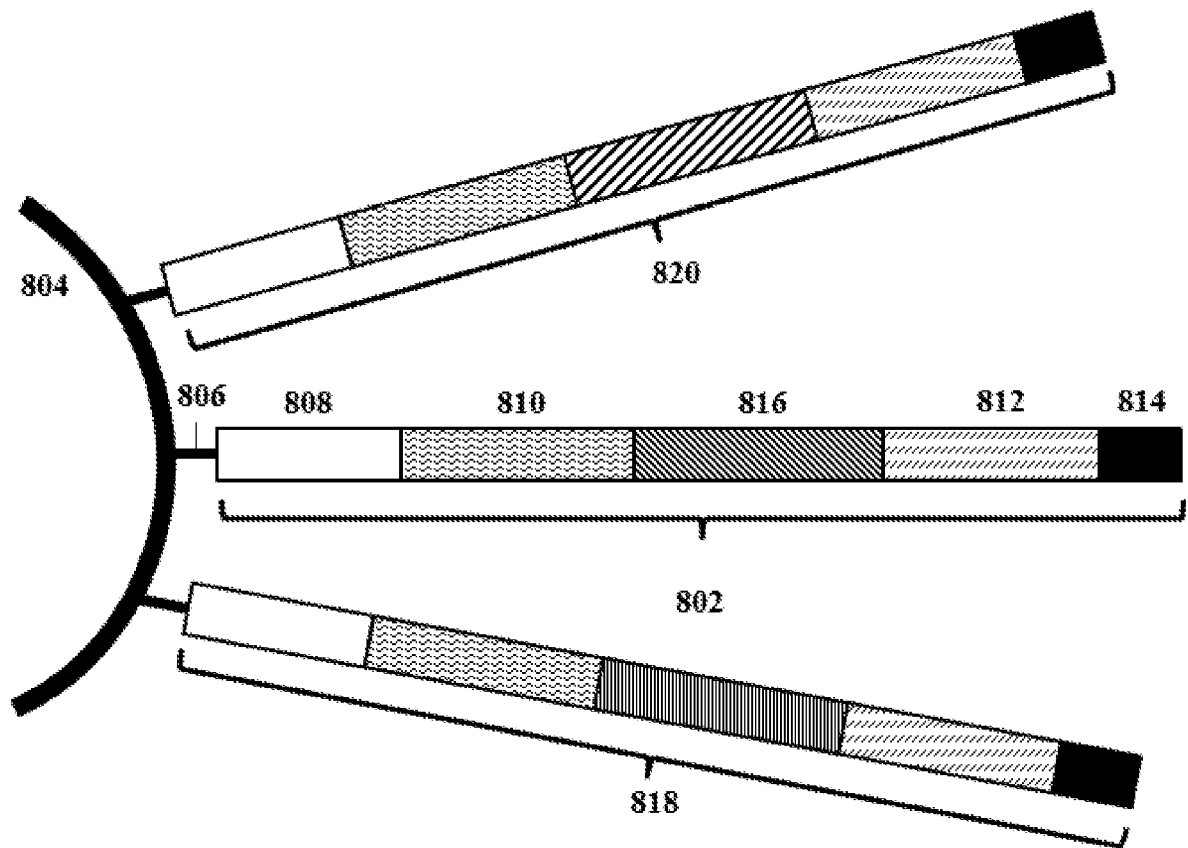
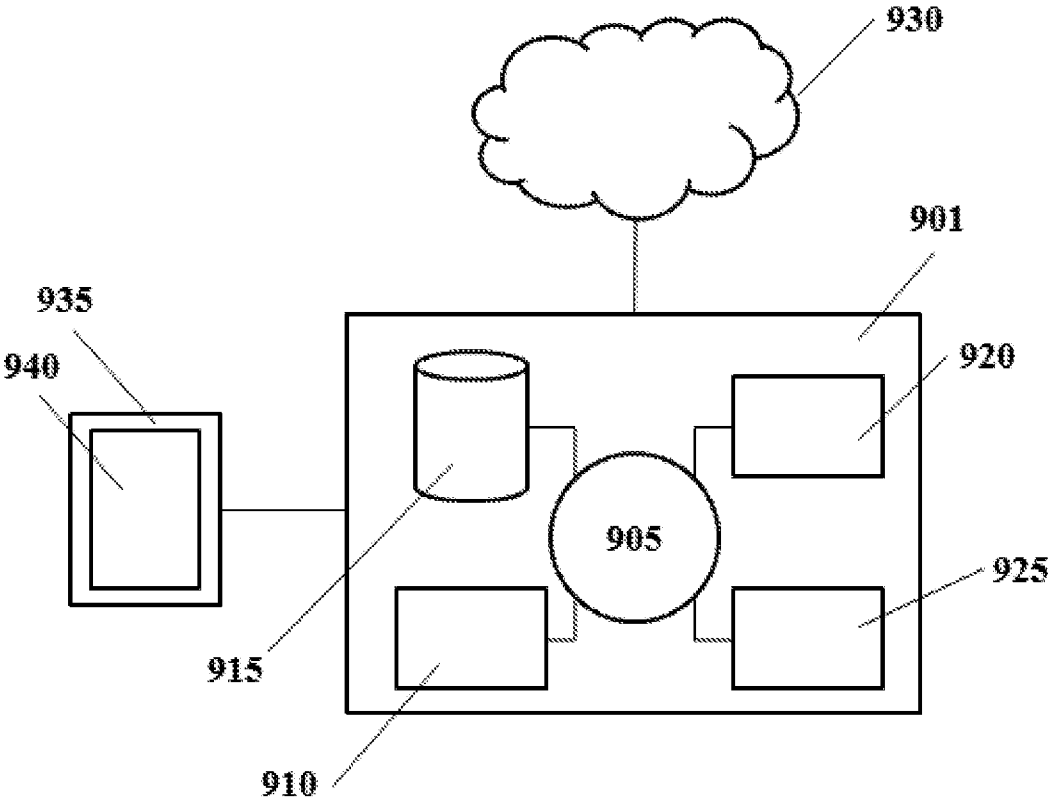


FIG. 9



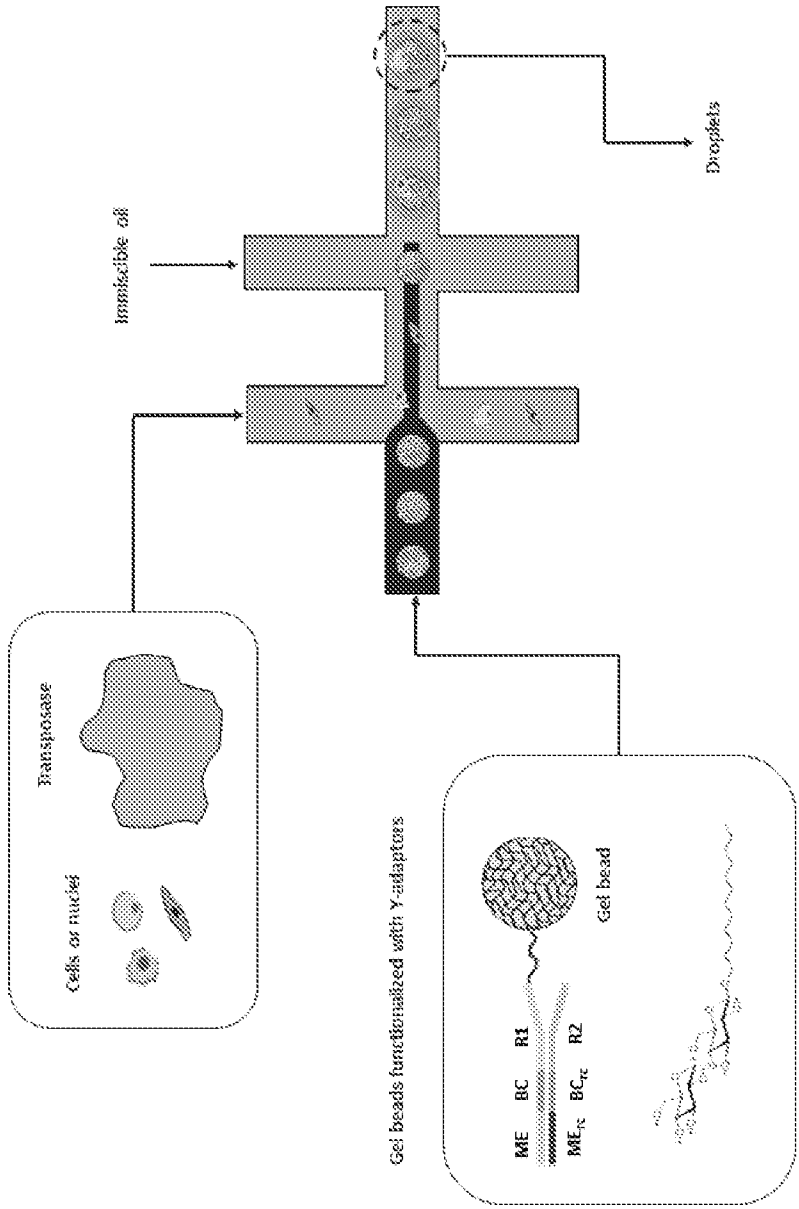


FIG. 10

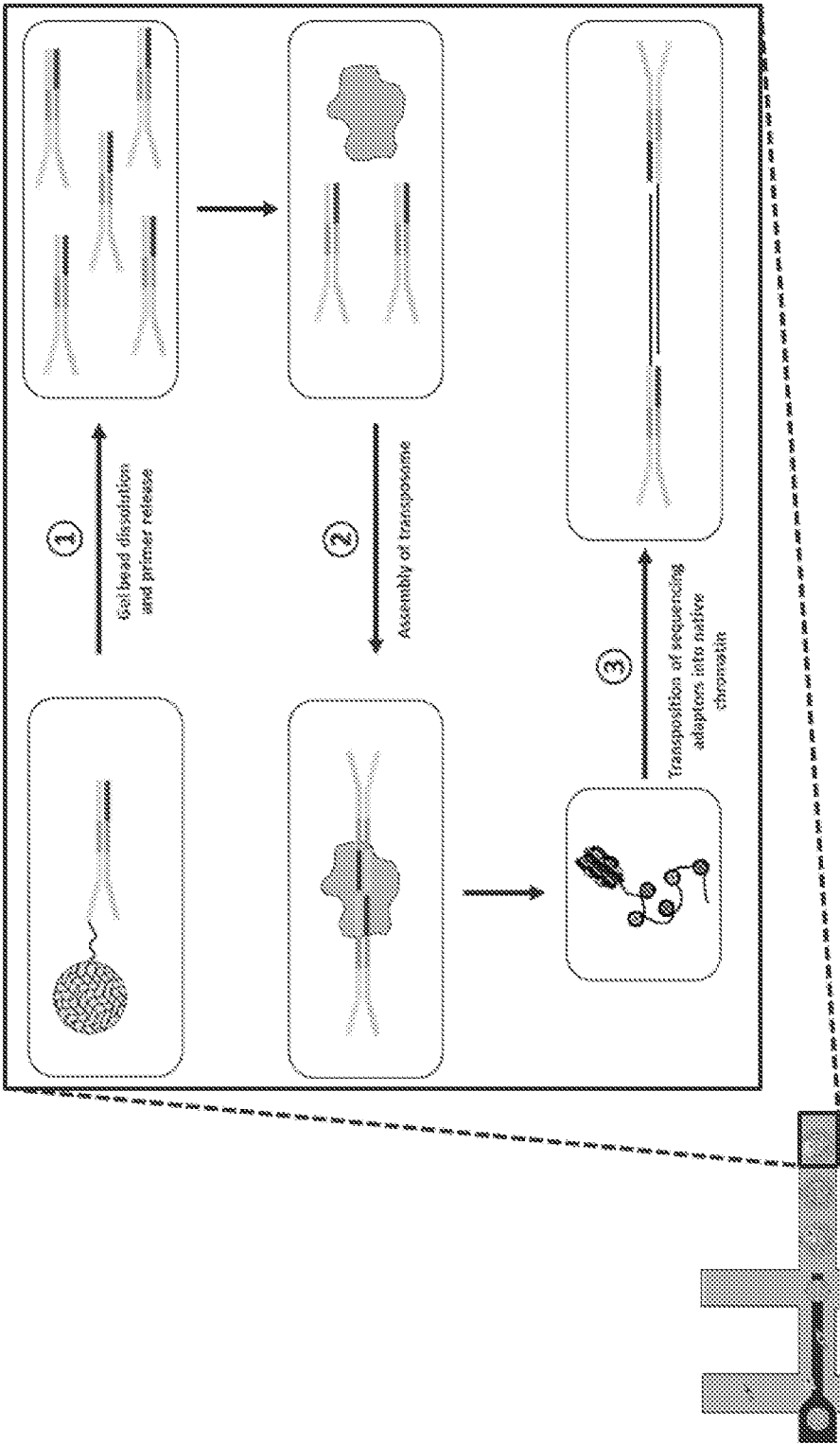
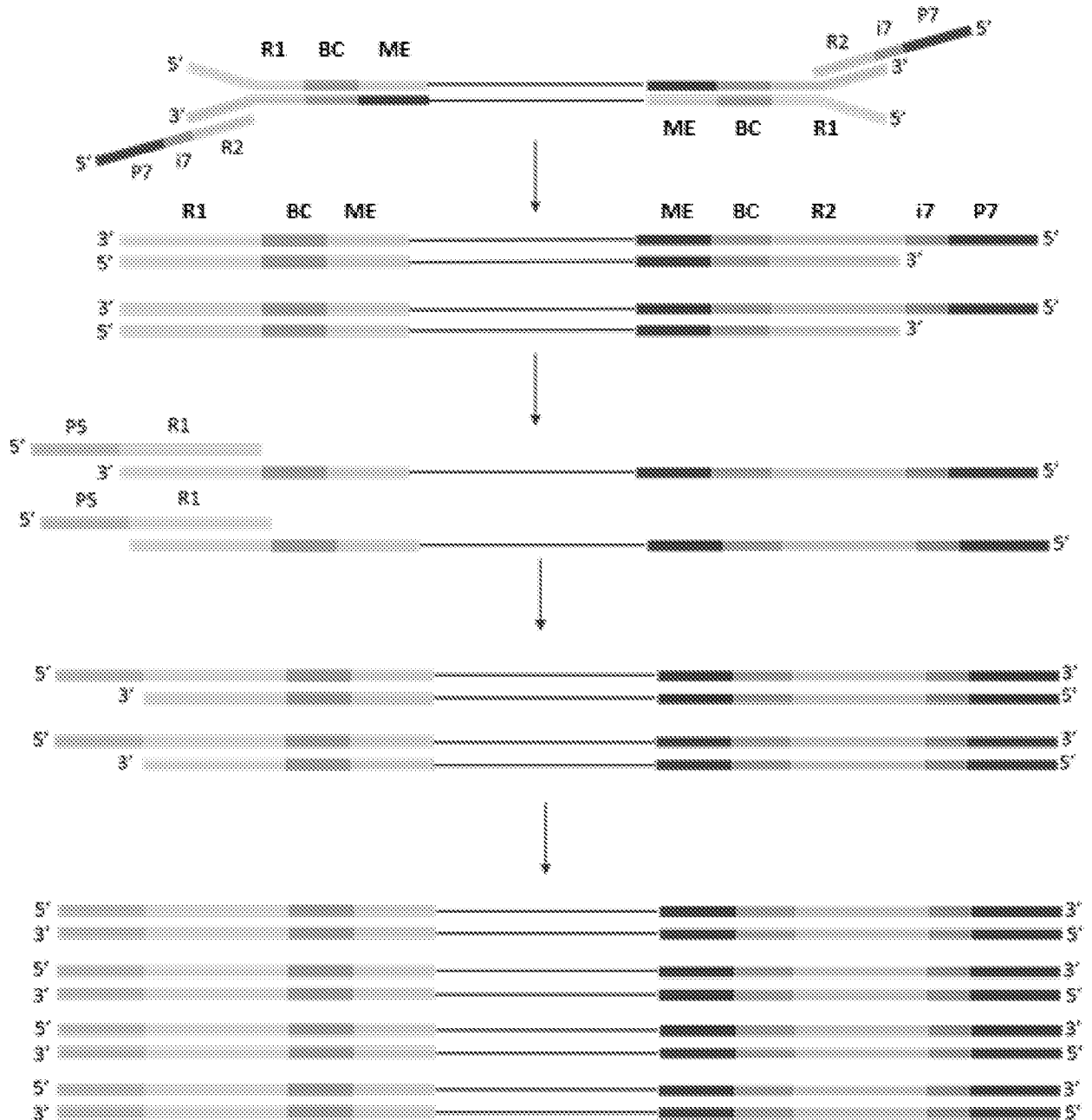


FIG. 11A

FIG. 11B



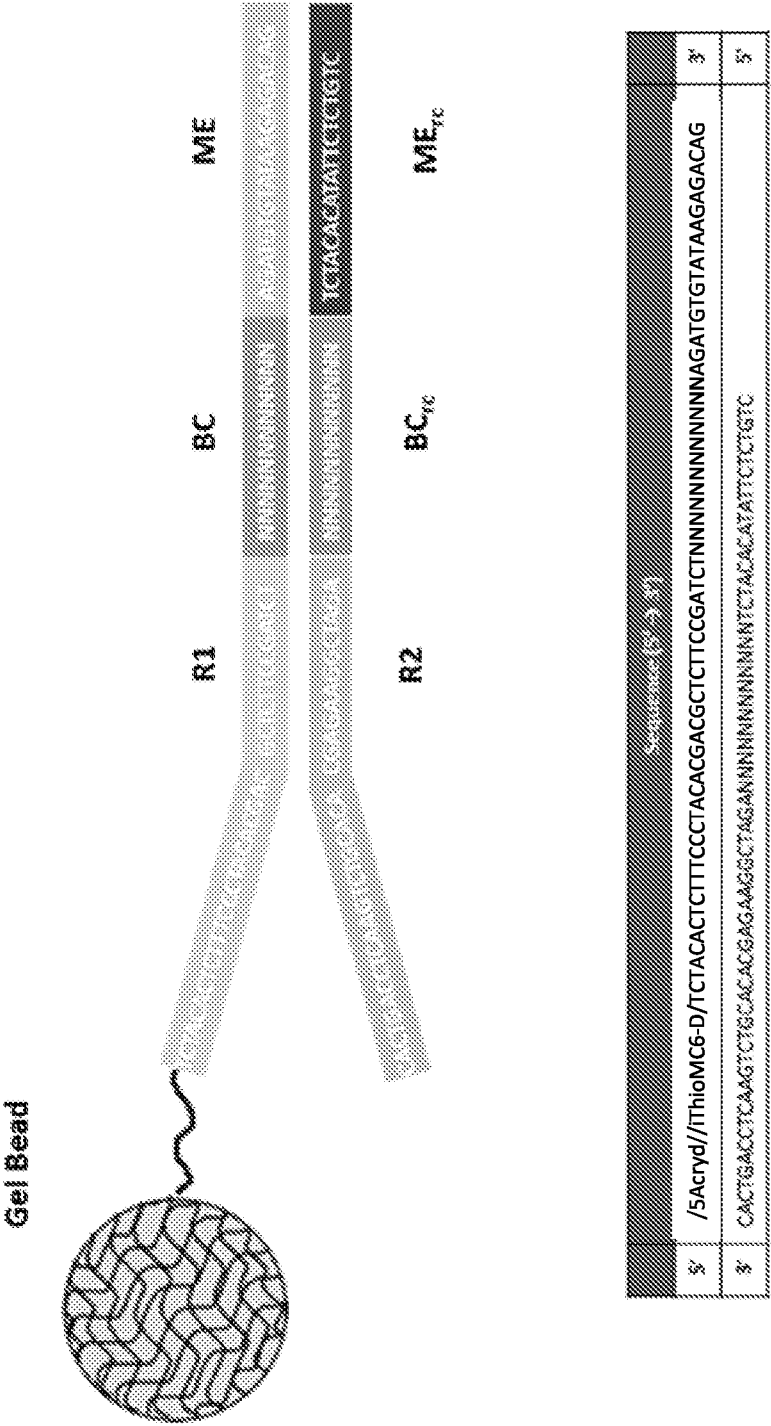


FIG. 12A

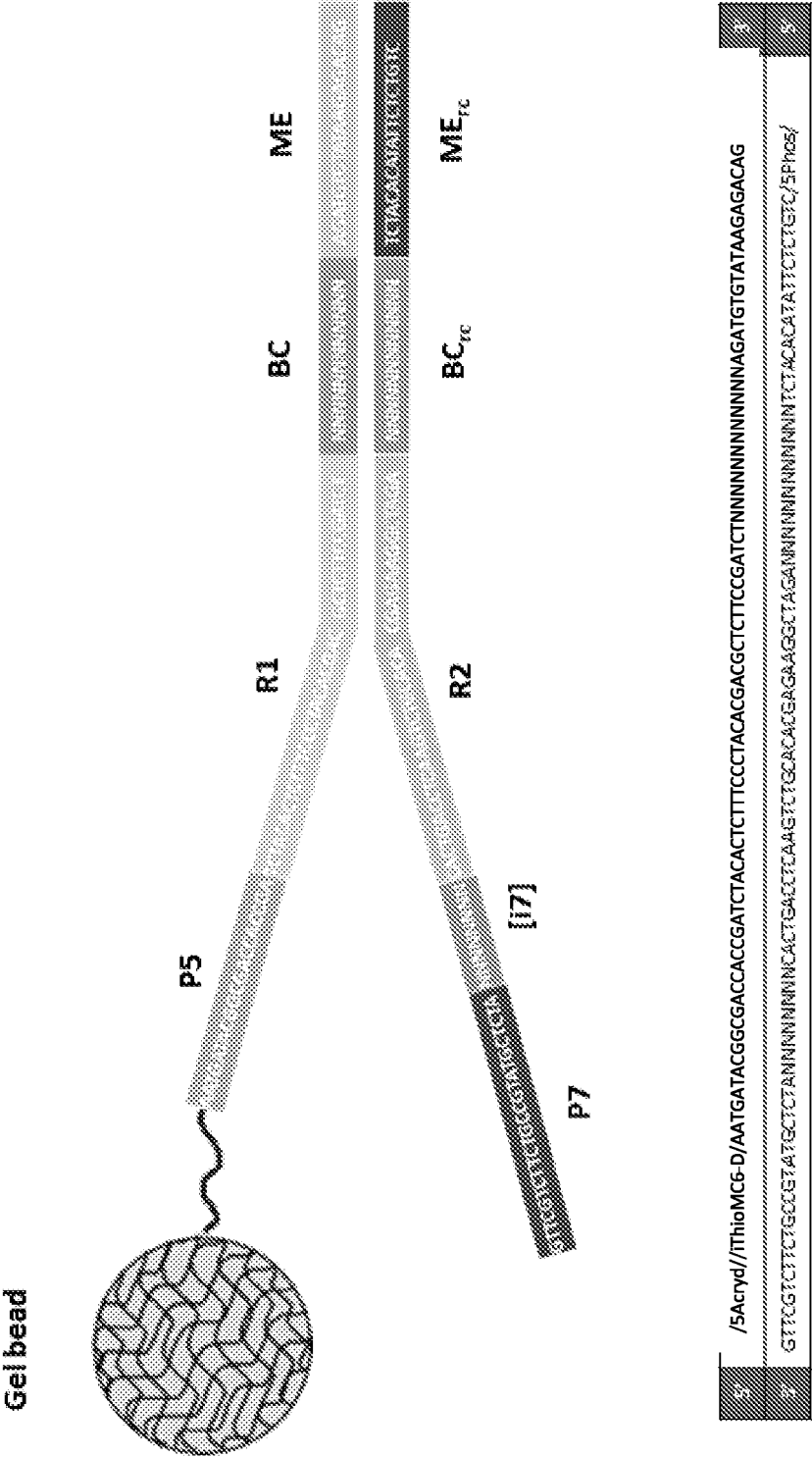


FIG. 12B

FIG. 13

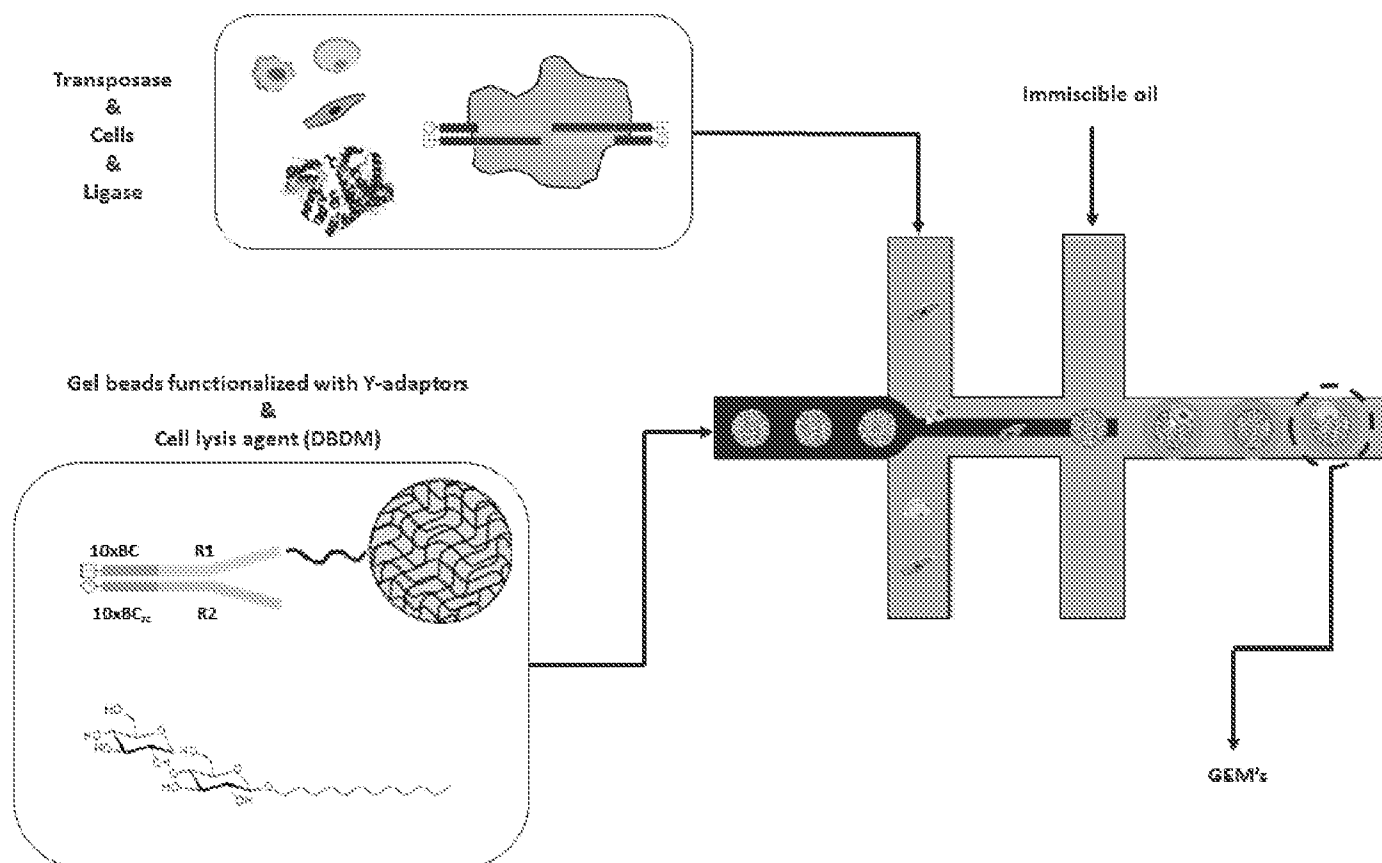


FIG. 14A

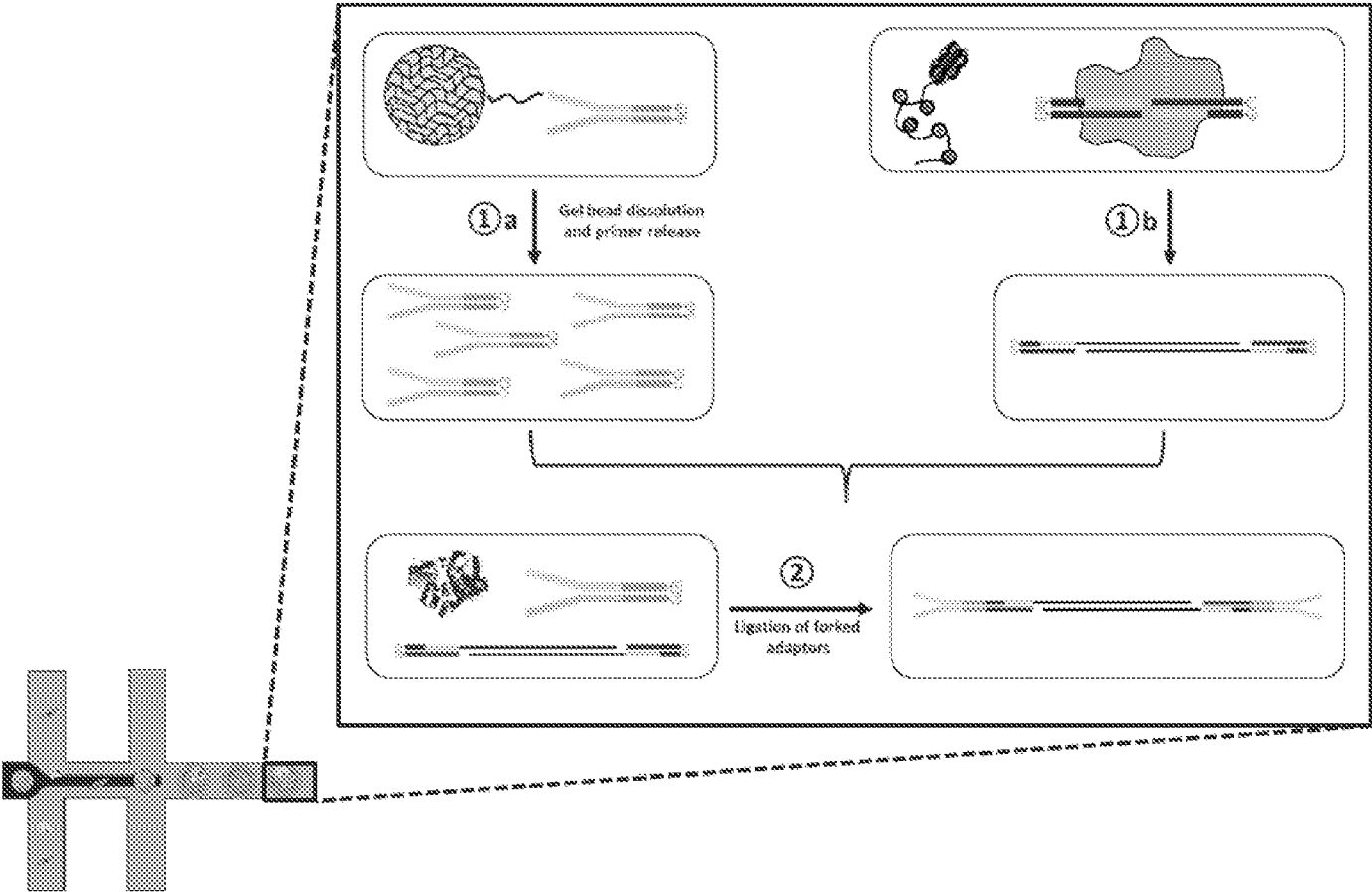
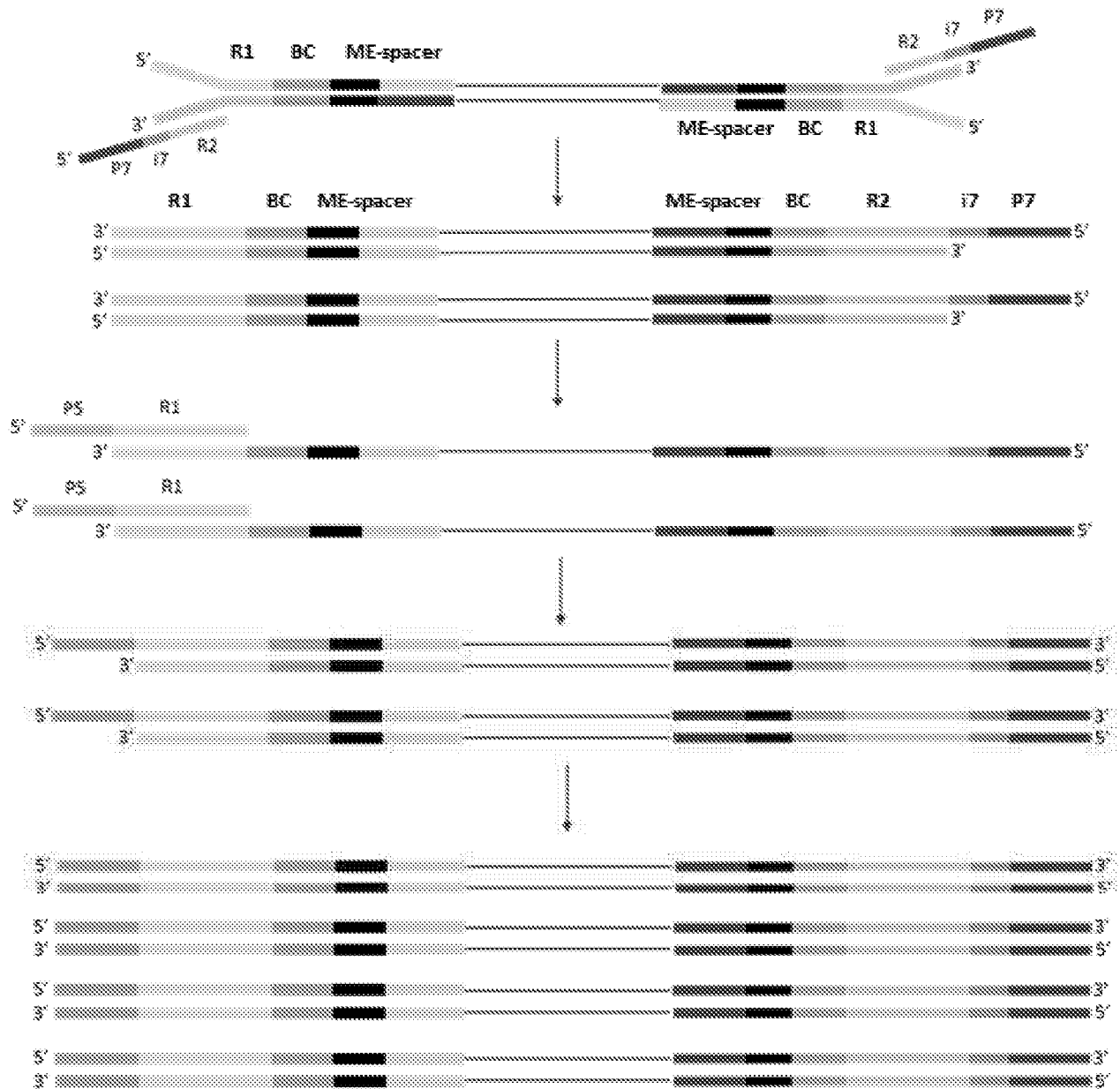


FIG. 14B



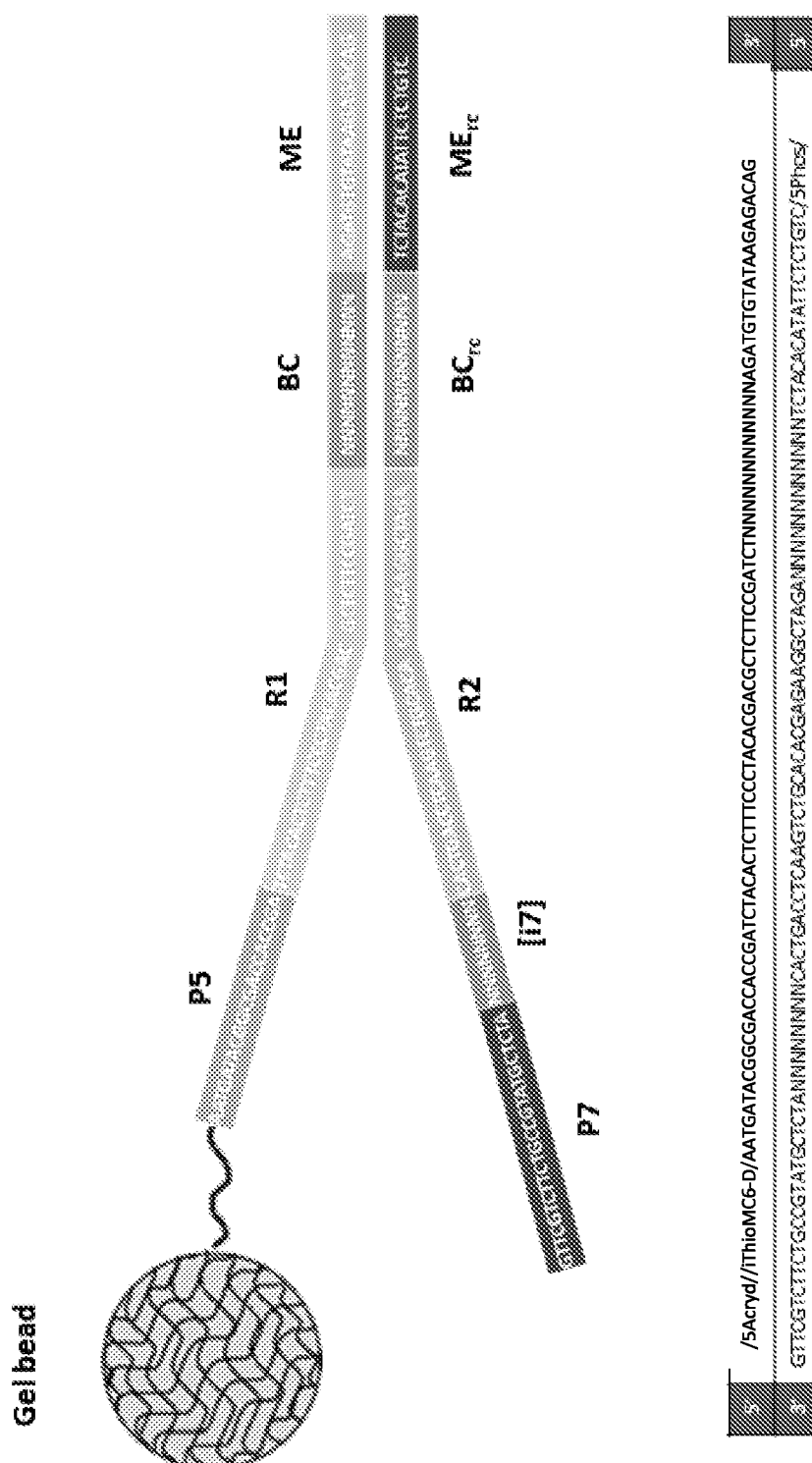


FIG. 15A

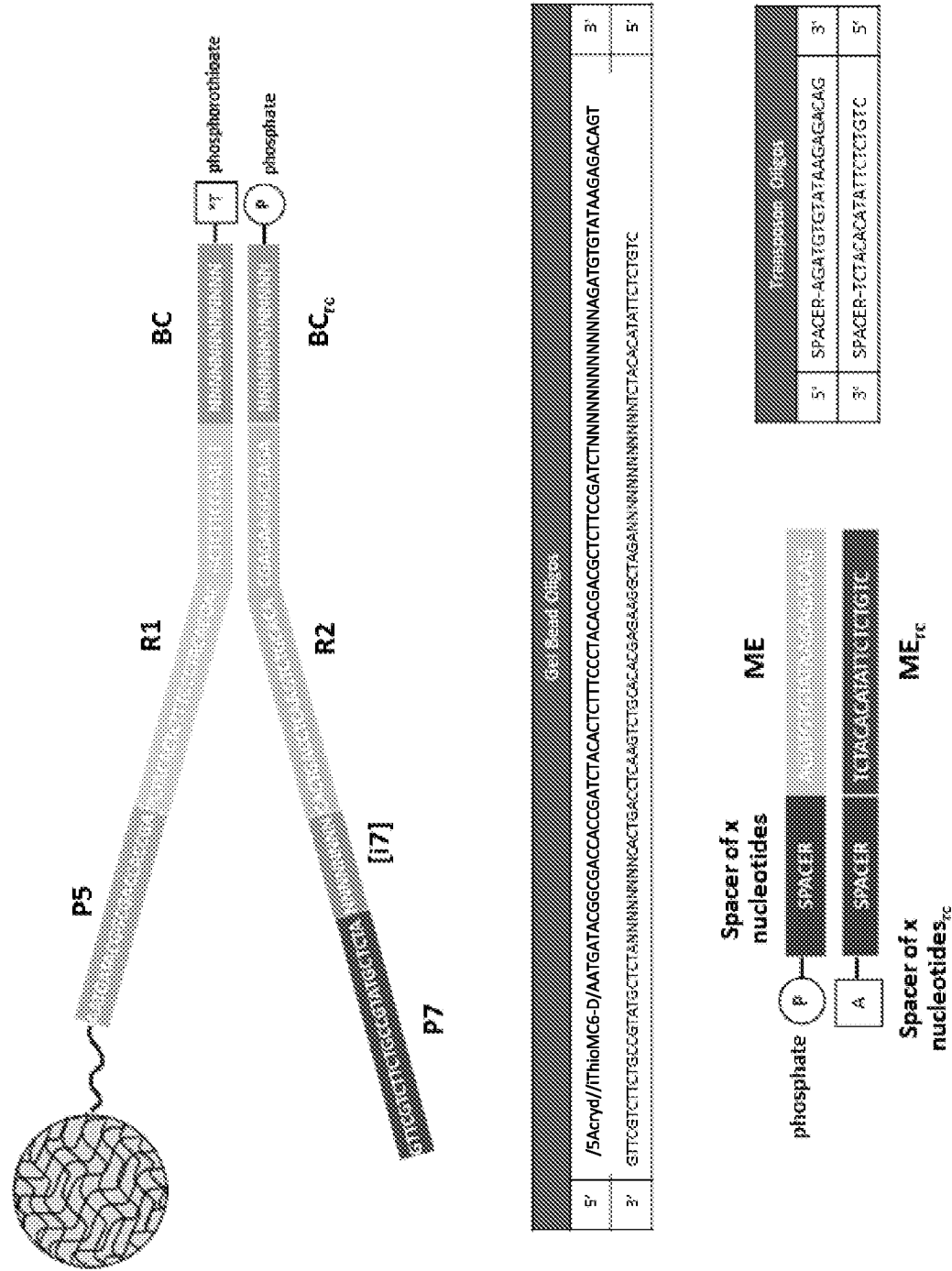


FIG. 15B

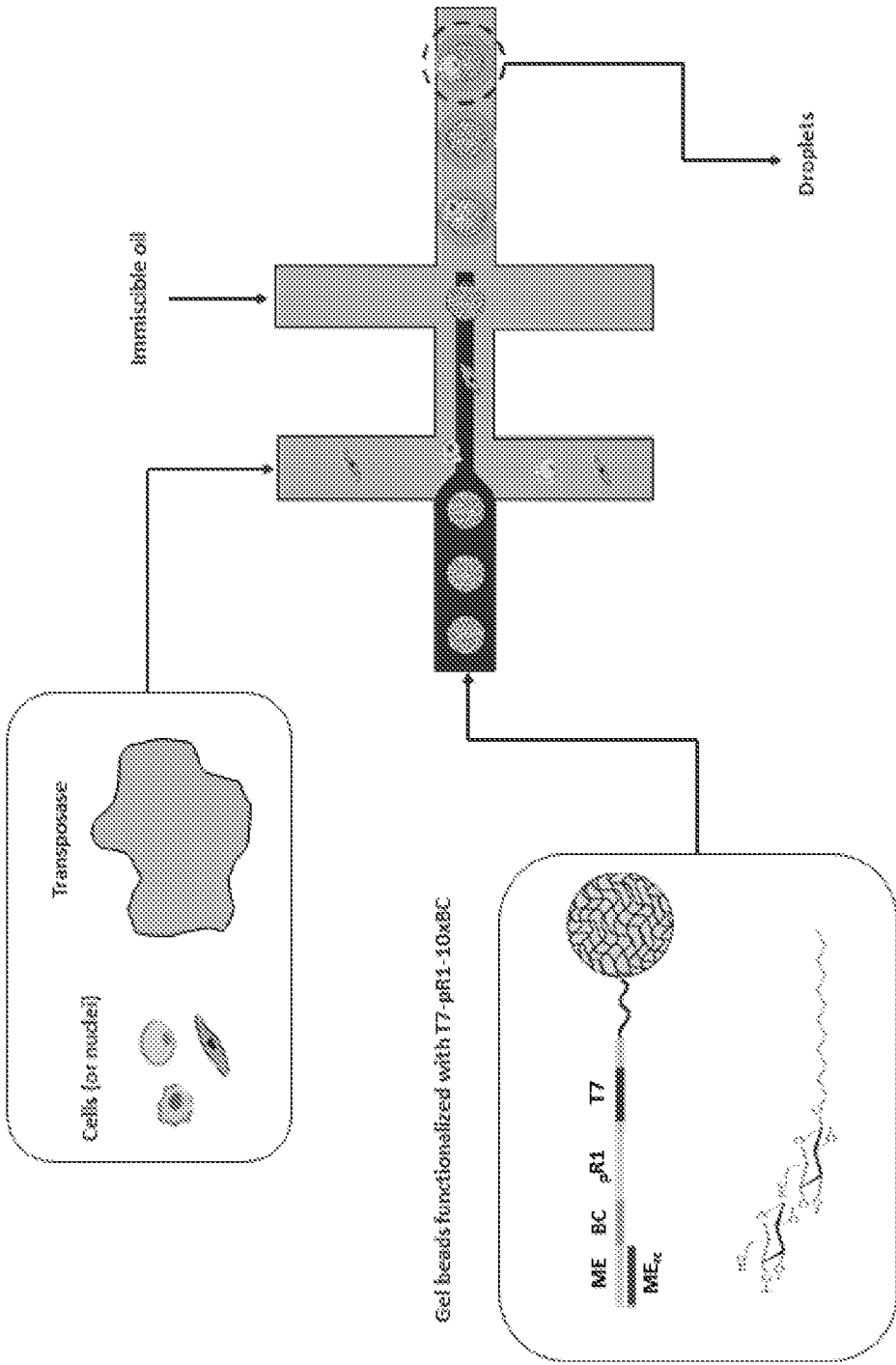


FIG. 16

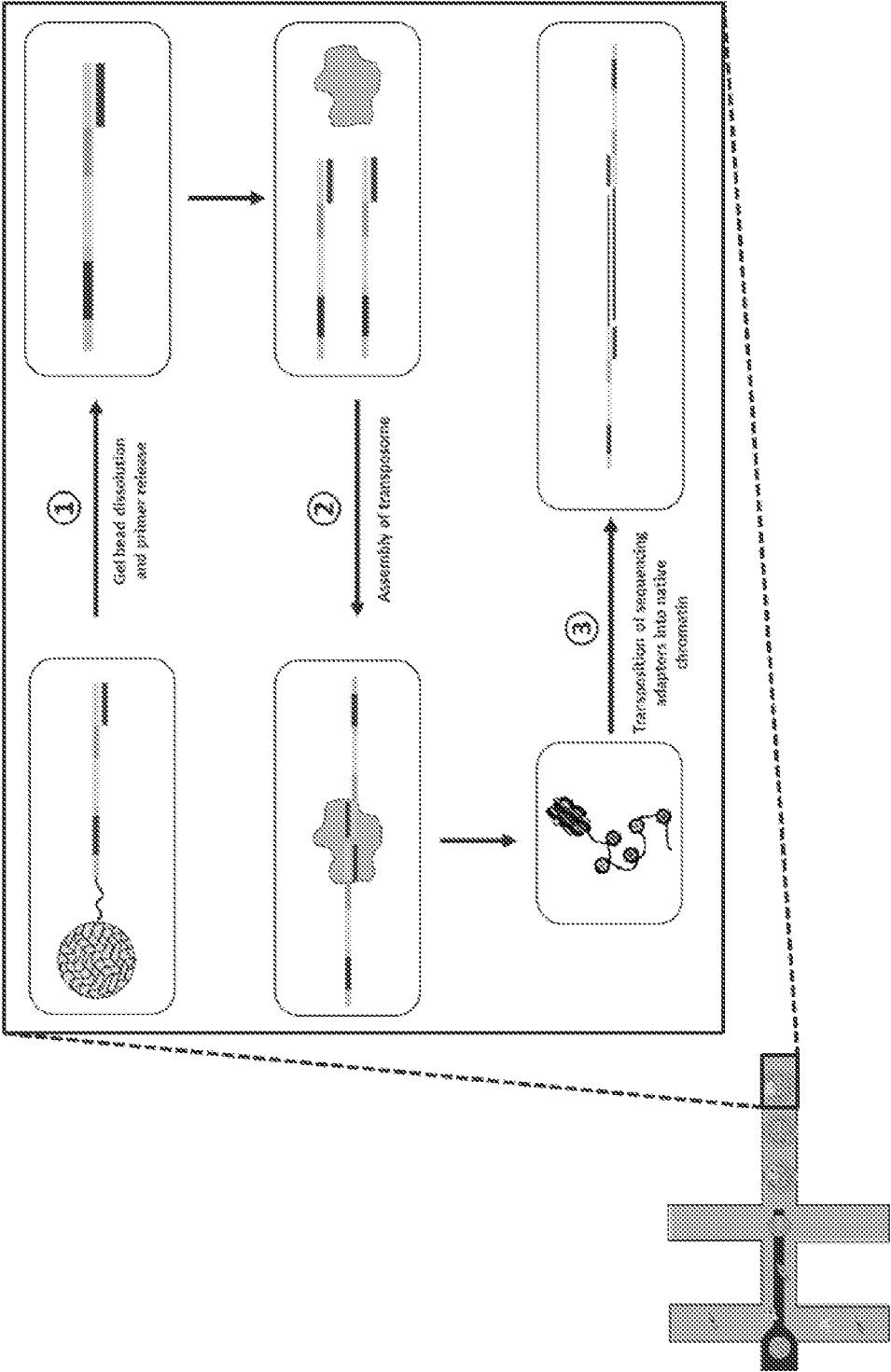


FIG. 17

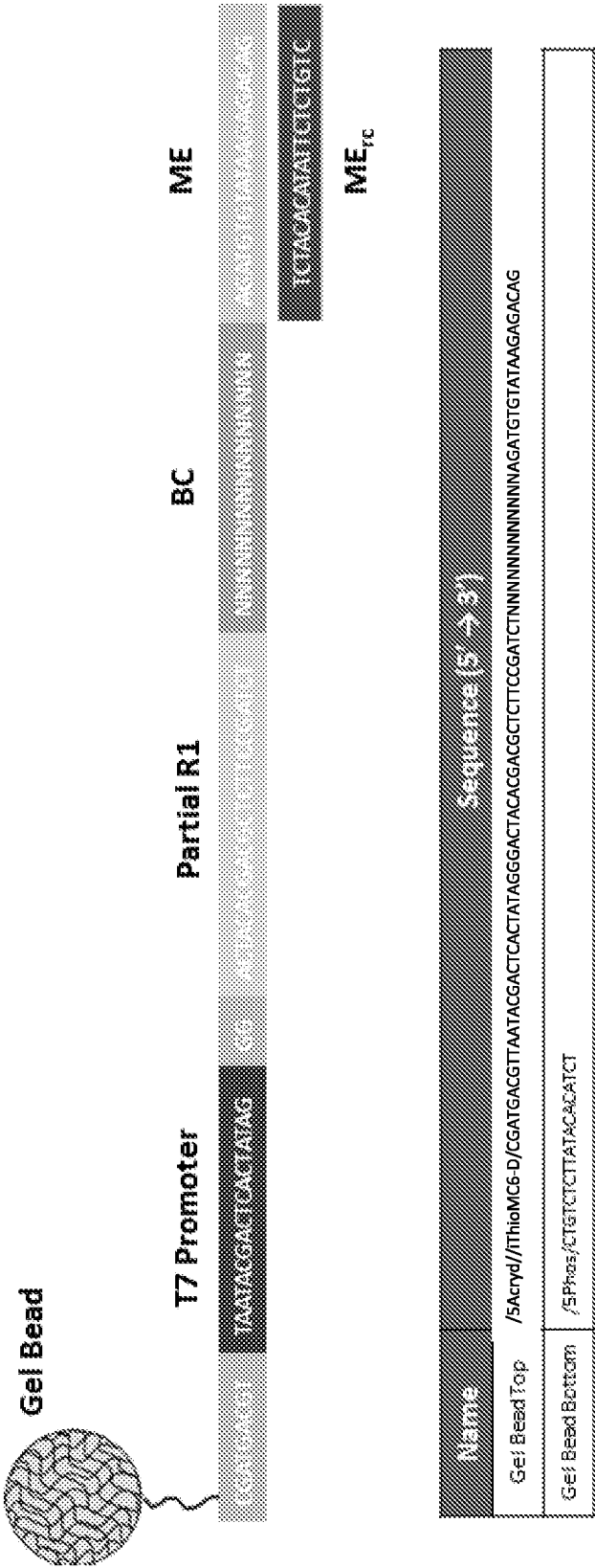


FIG. 18

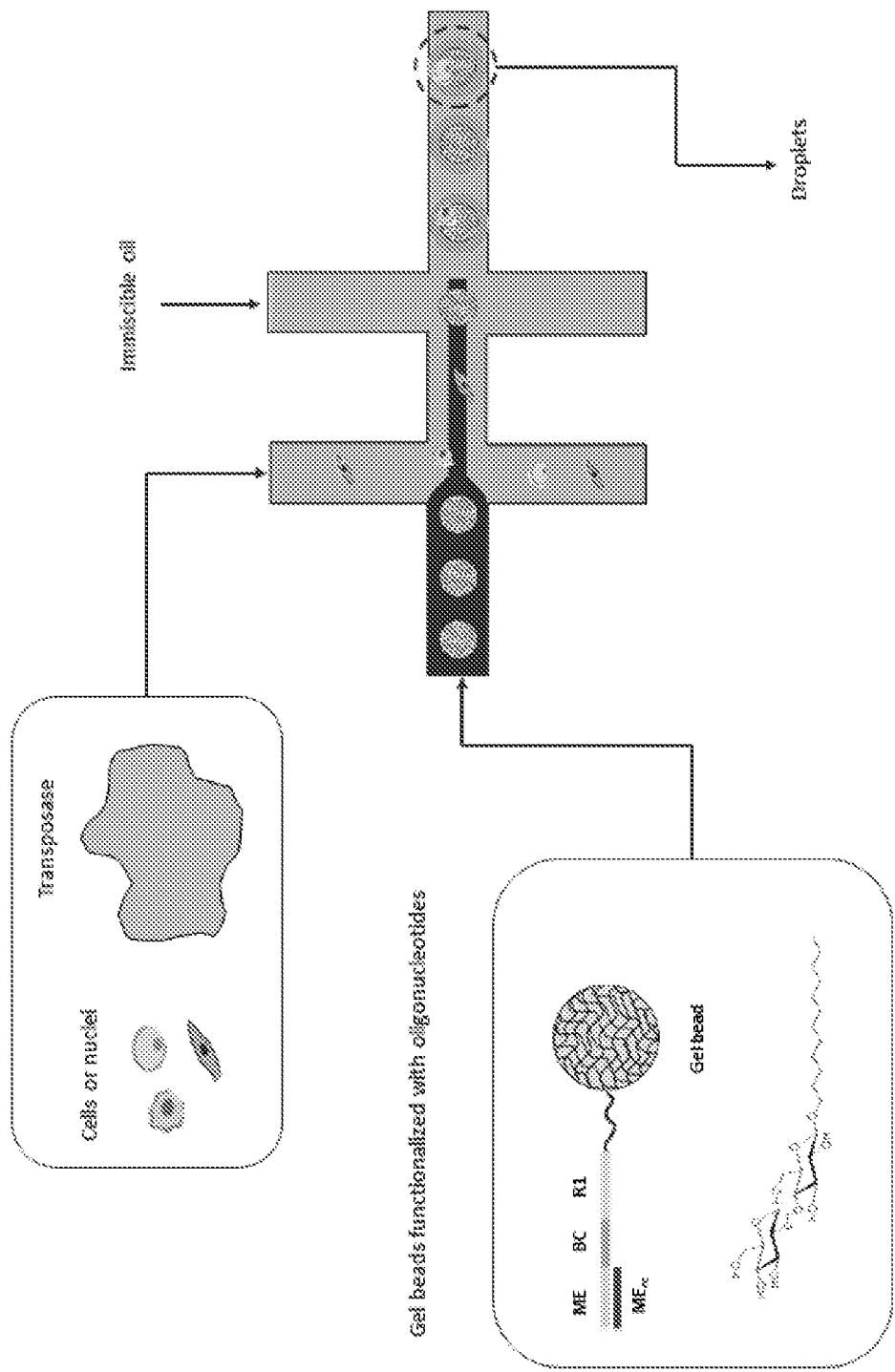
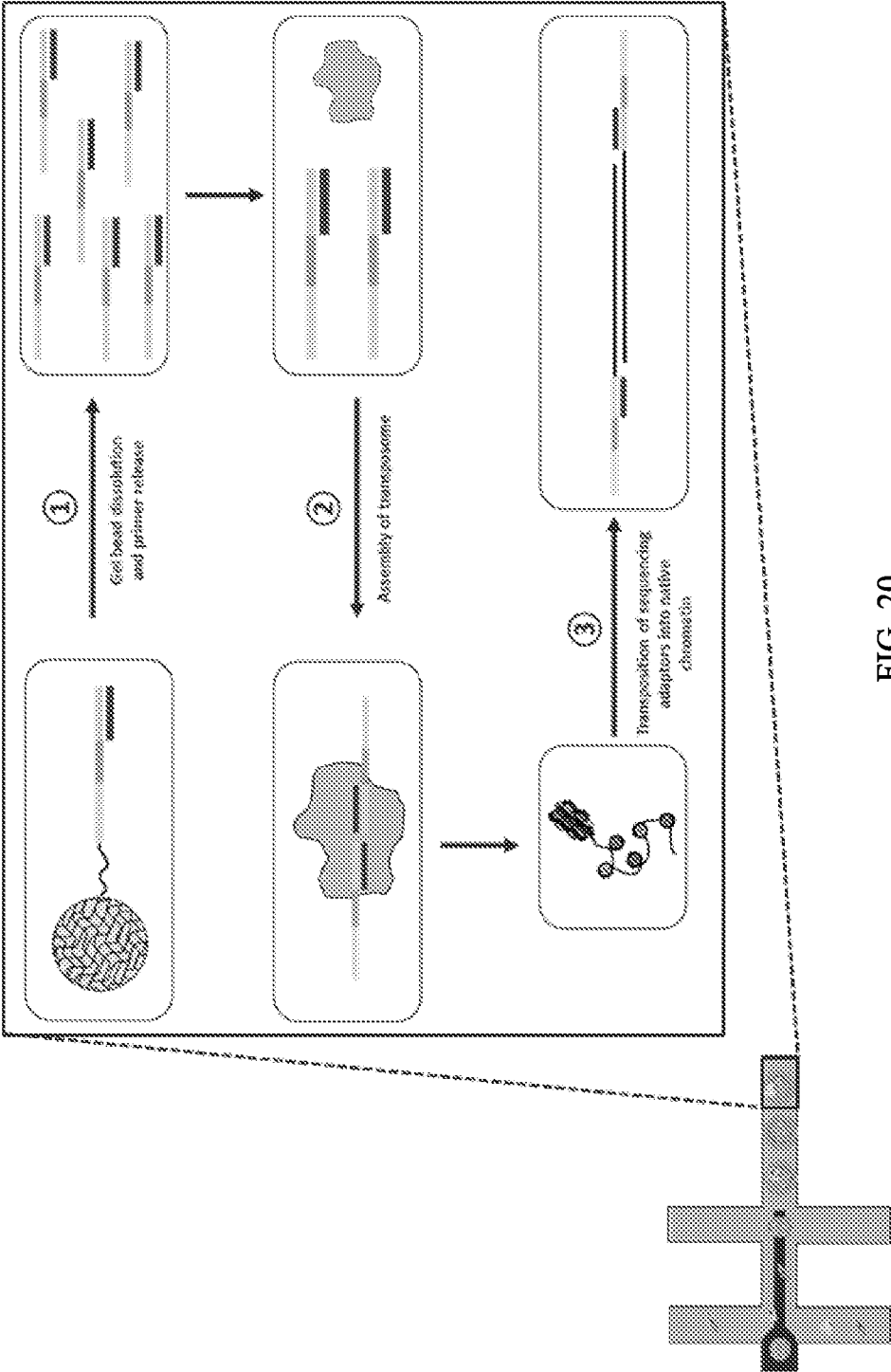
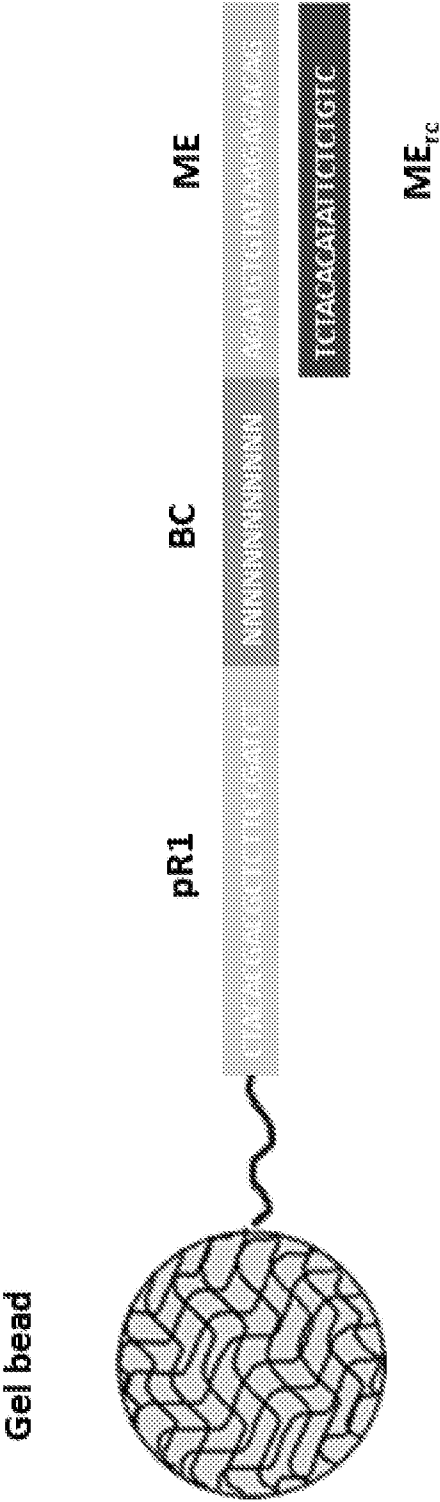


FIG. 19





Sequence (5' → 3')	
5'	/5Acryd//iThioMC6-D/ CTACAGACGCTCTTCGATCTNNNNNNNNNAGATGTGTATAAGAGACAG
3'	/5Phos/CTGTCTCTTATACATCT

FIG. 21

FIG. 22

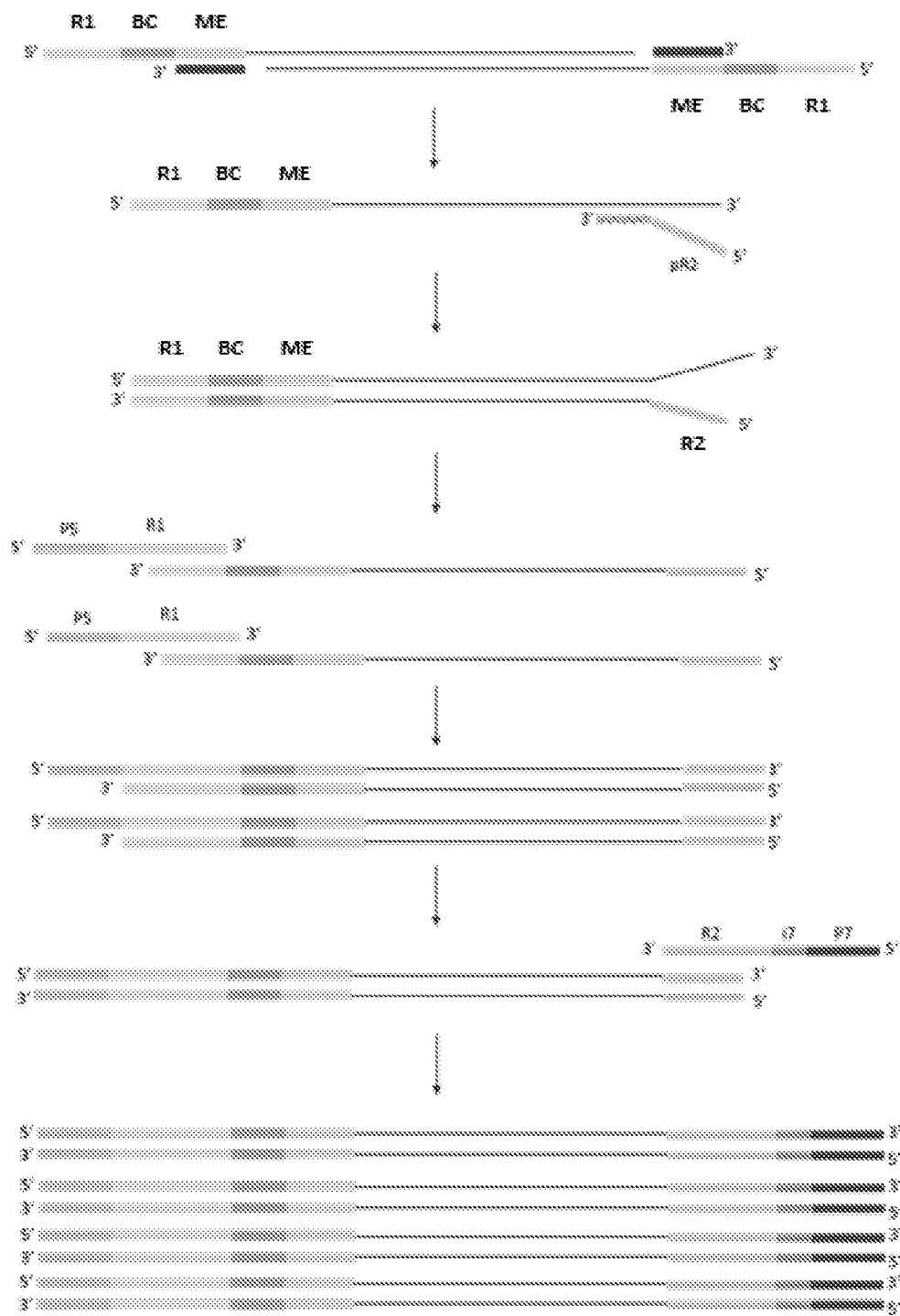


FIG. 23

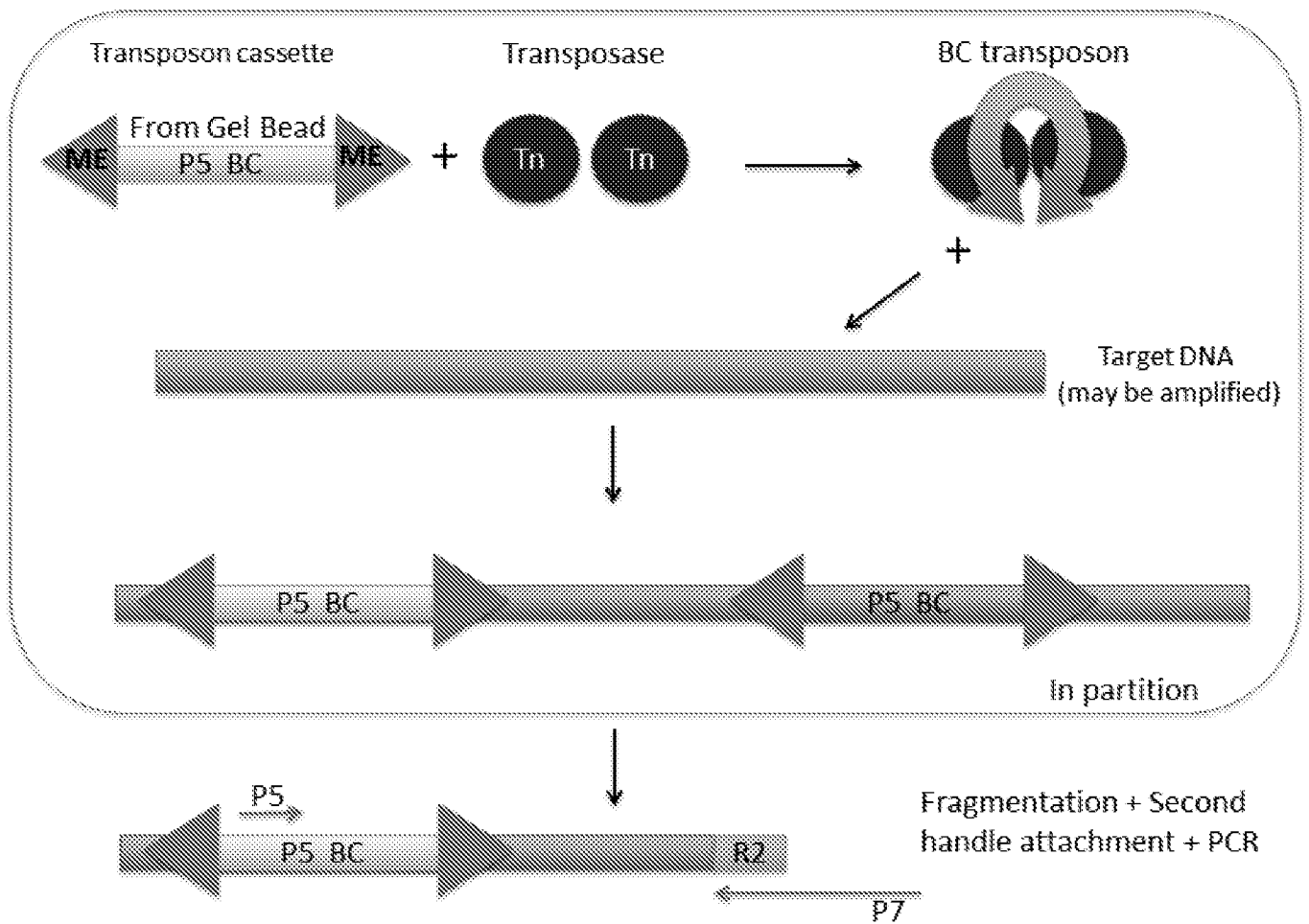


FIG. 24A

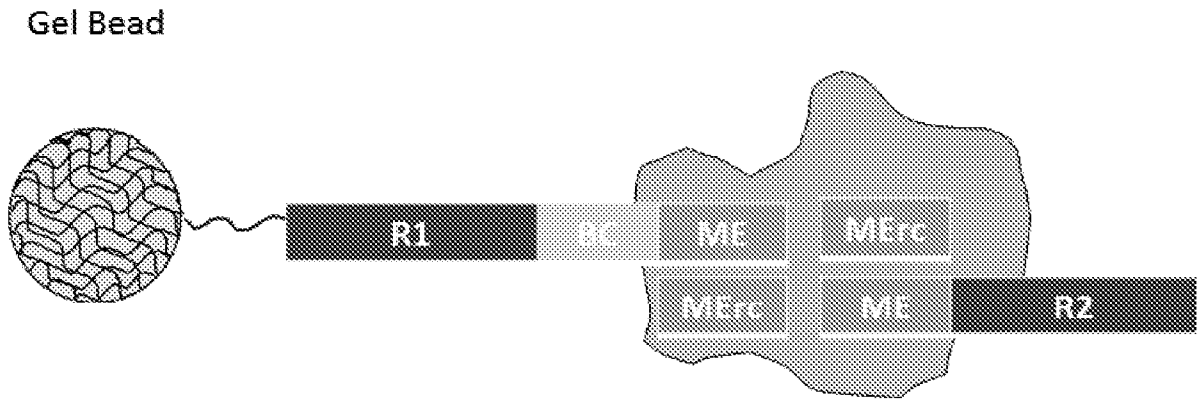


FIG. 24B

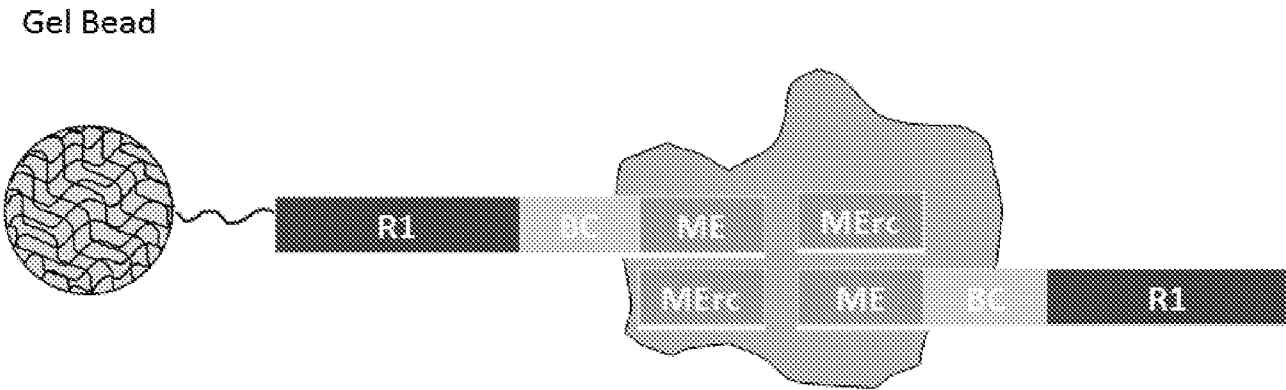


FIG. 25A

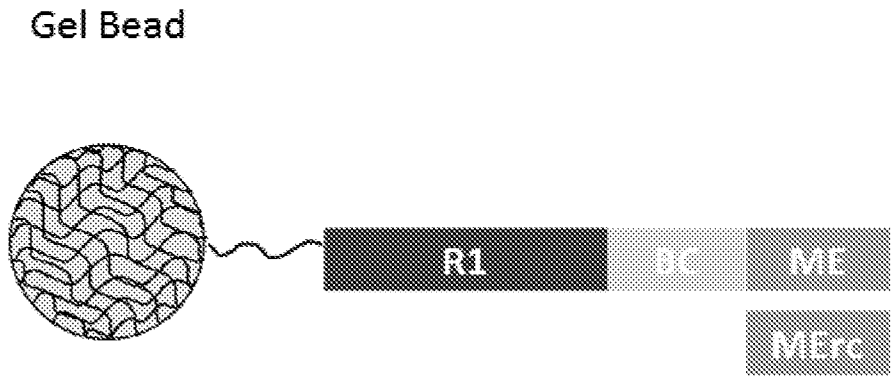


FIG. 25B

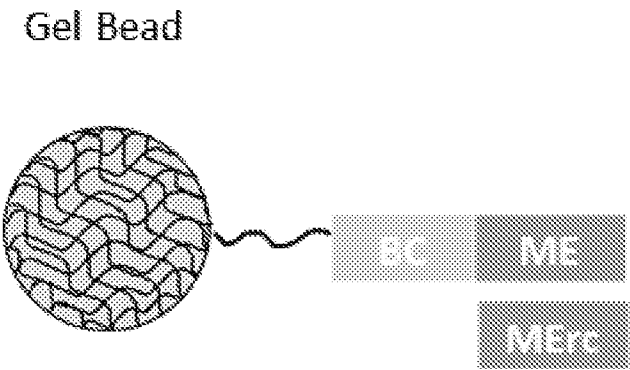


FIG. 26

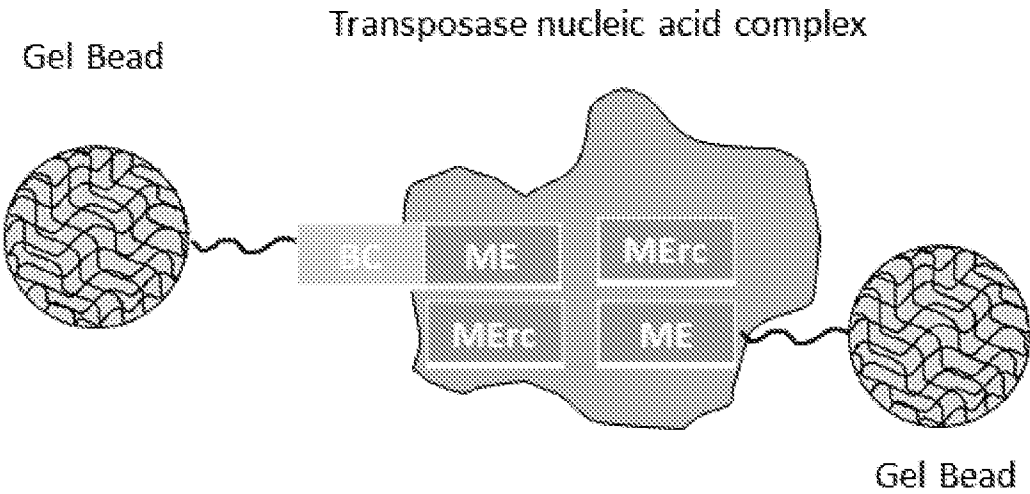


FIG. 27

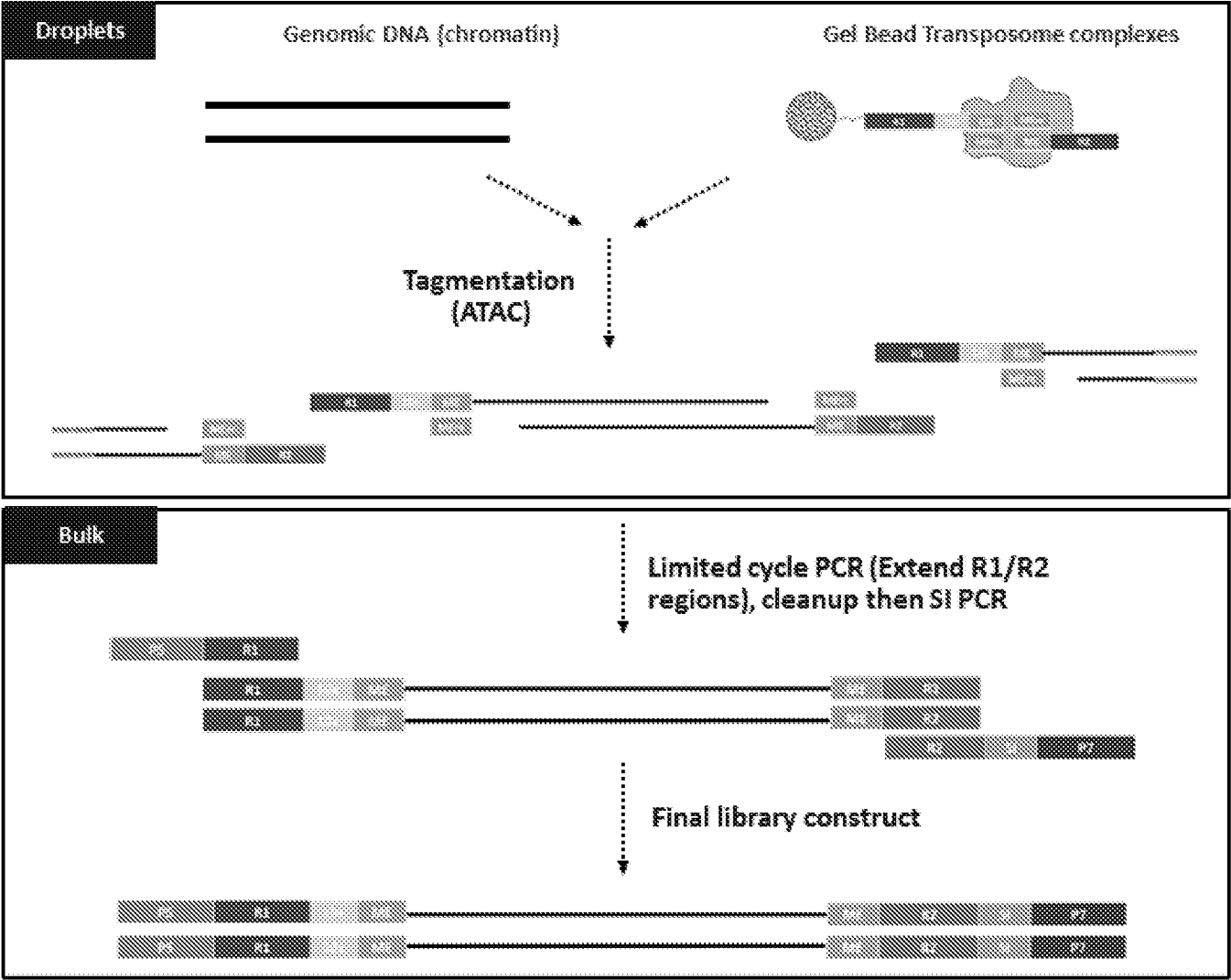


FIG. 28A

Transposase Nucleic Acid Complex

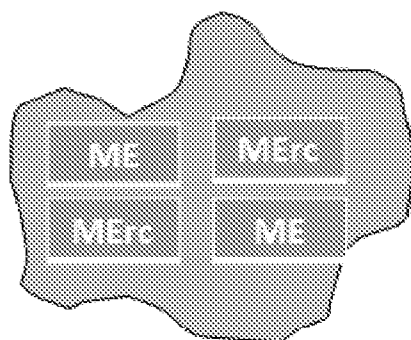


FIG. 28B

Gel Bead



FIG. 29A

Transposase-Nucleic Acid Complex

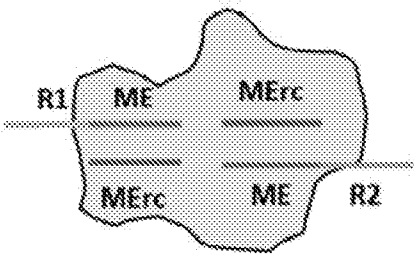


FIG. 29B

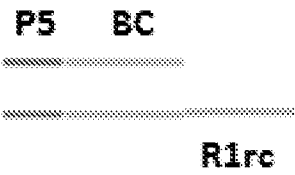


FIG. 29C

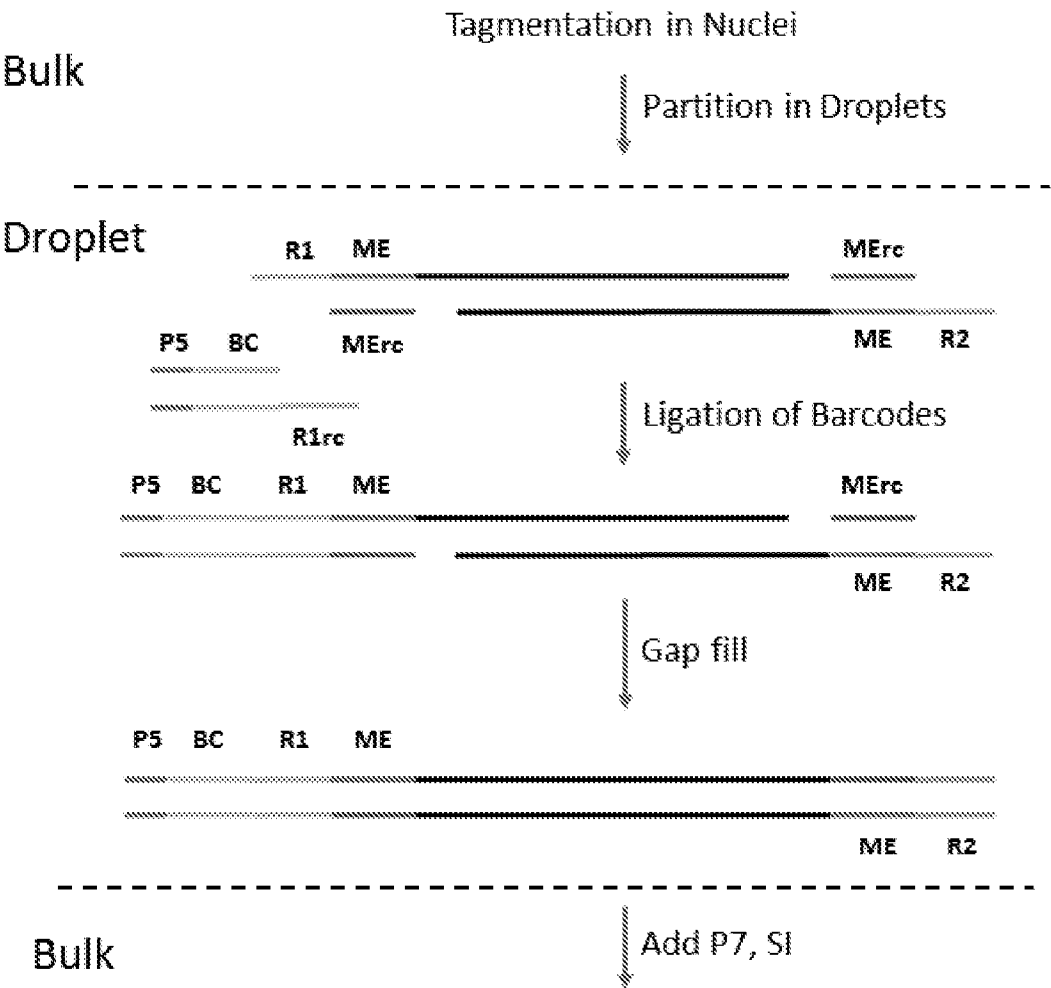


FIG. 29D

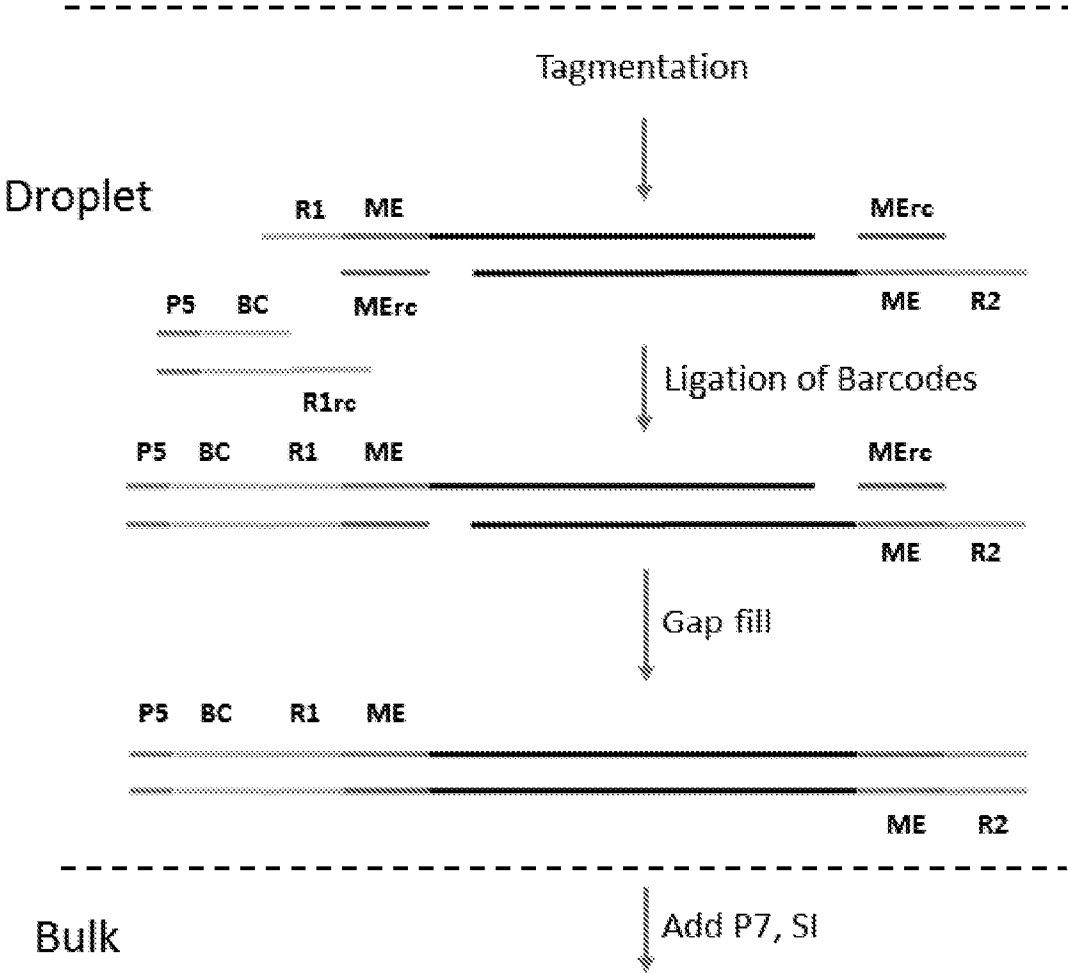


FIG. 30A

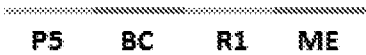


FIG. 30B

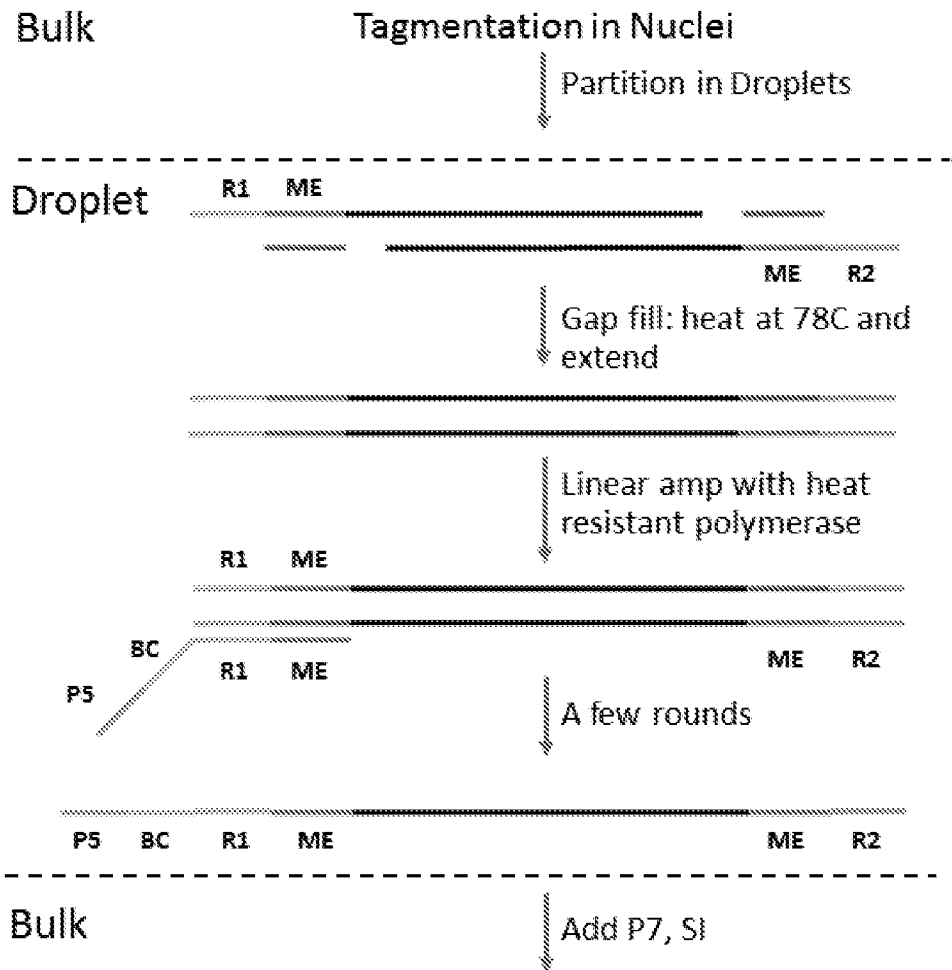


FIG. 31

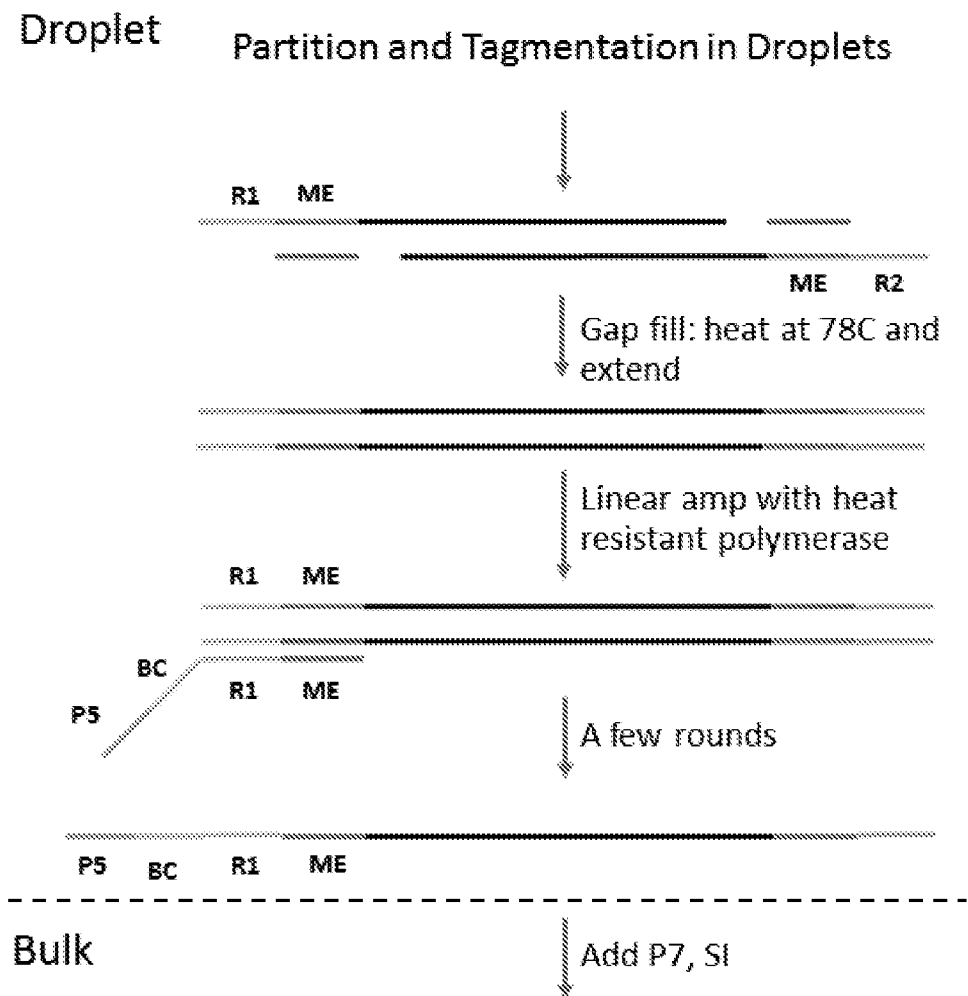


FIG. 32A

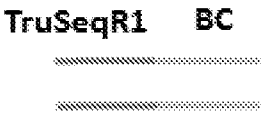


FIG. 32B

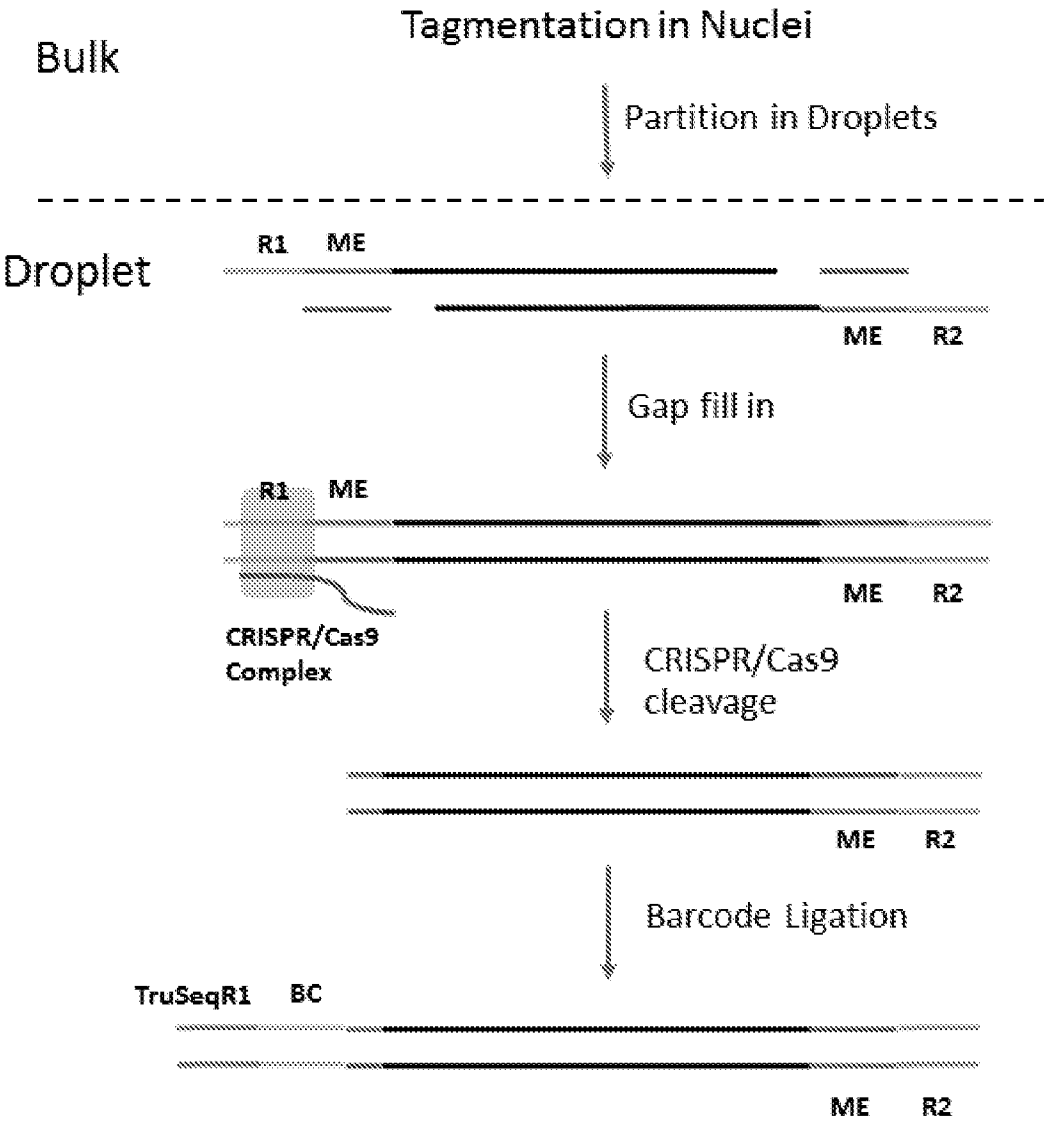


FIG. 32C

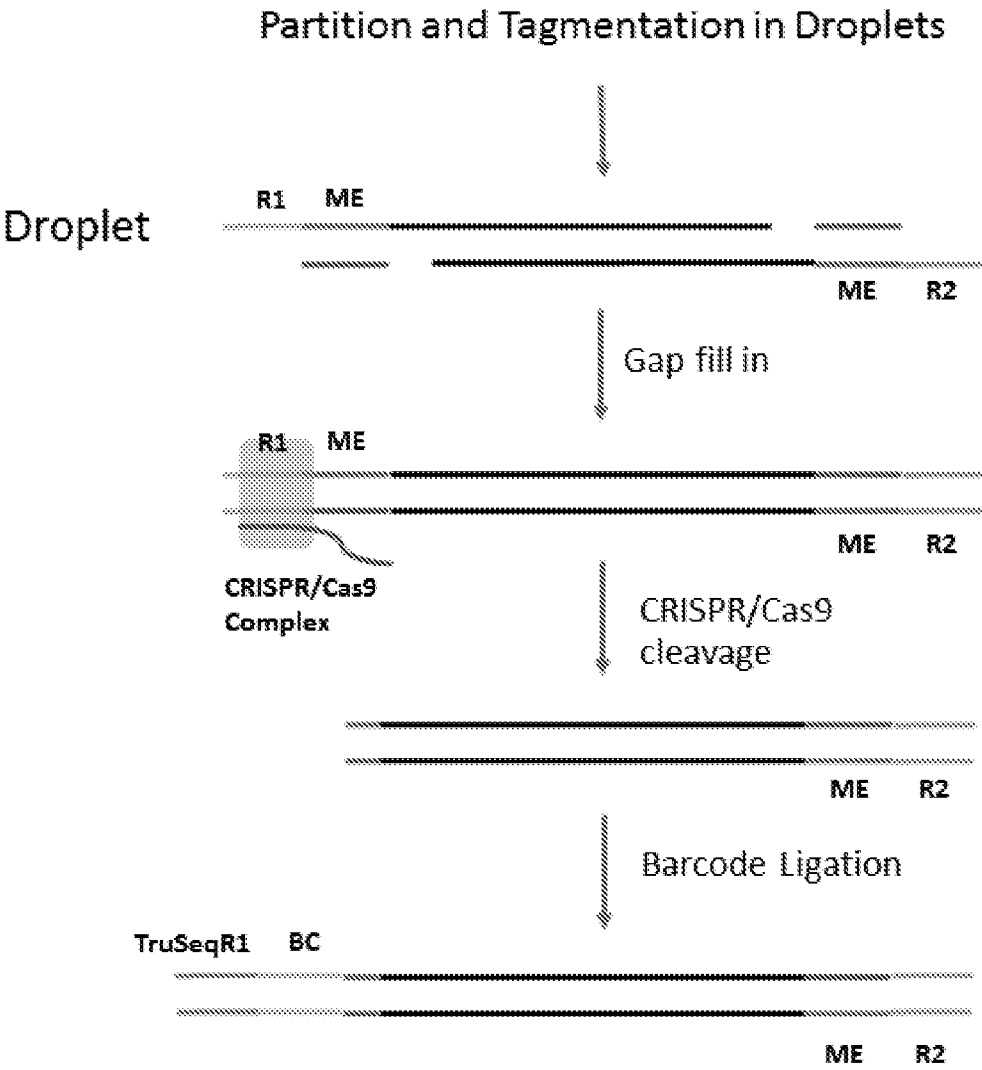


FIG. 33A

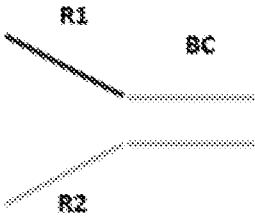


FIG. 33B

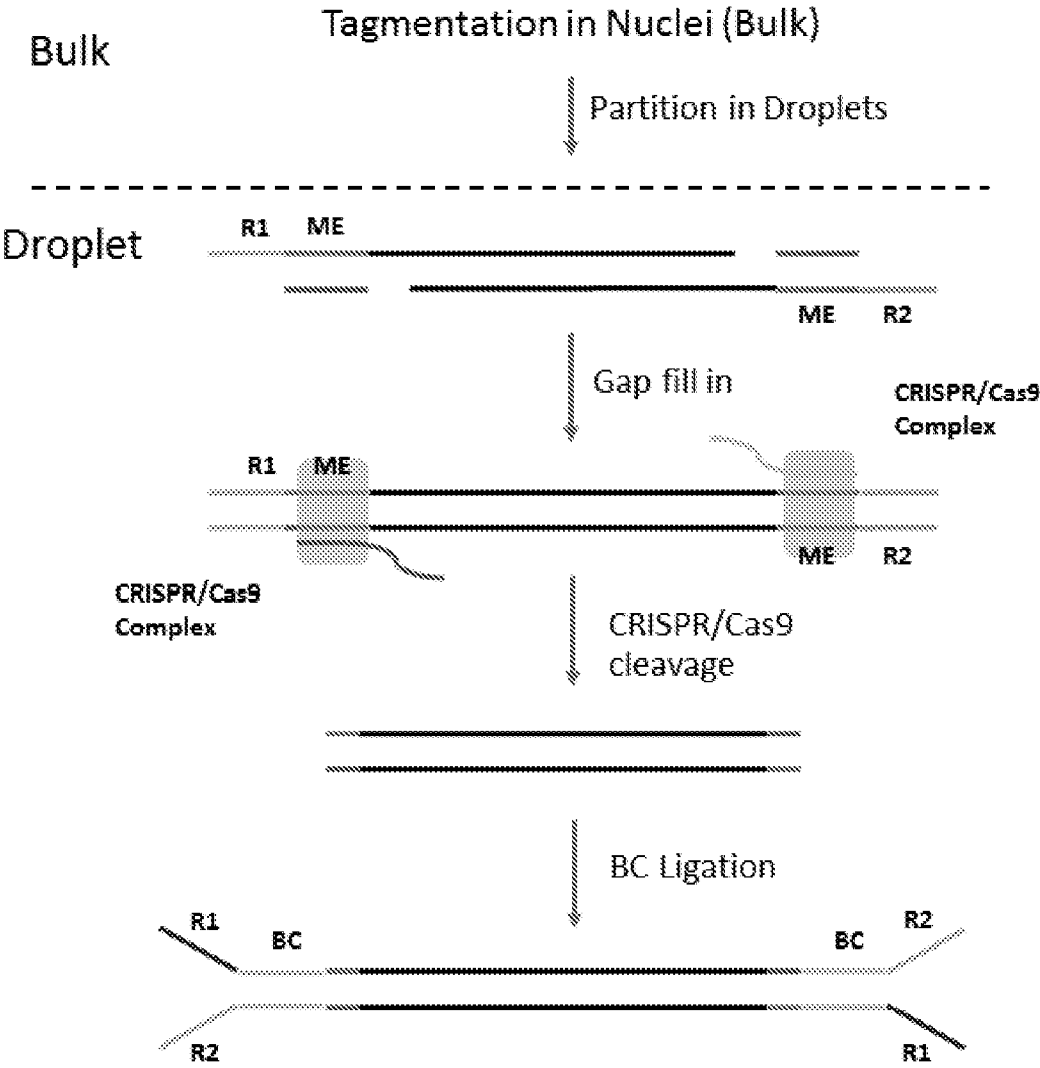


FIG. 33C

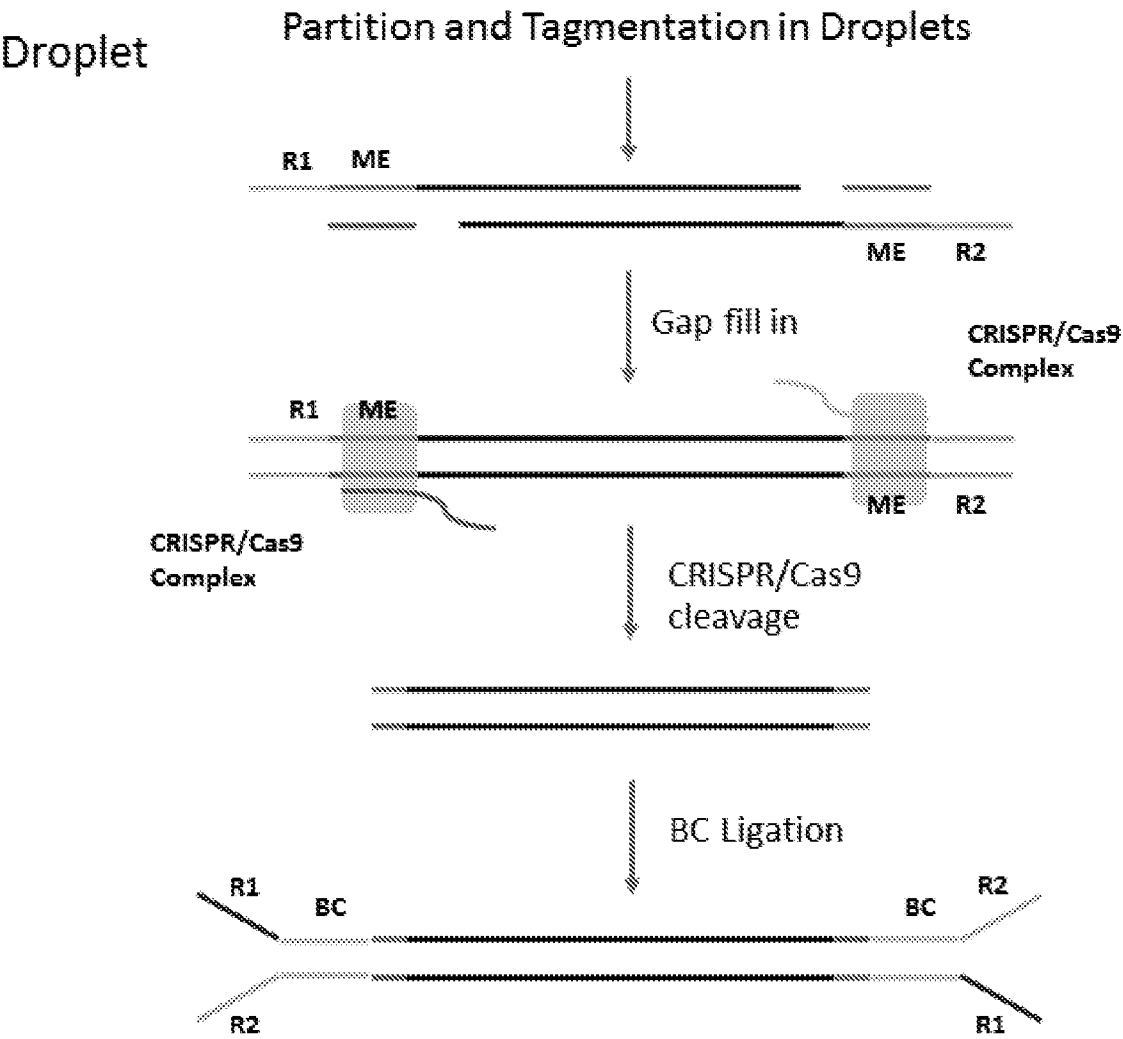


FIG. 34

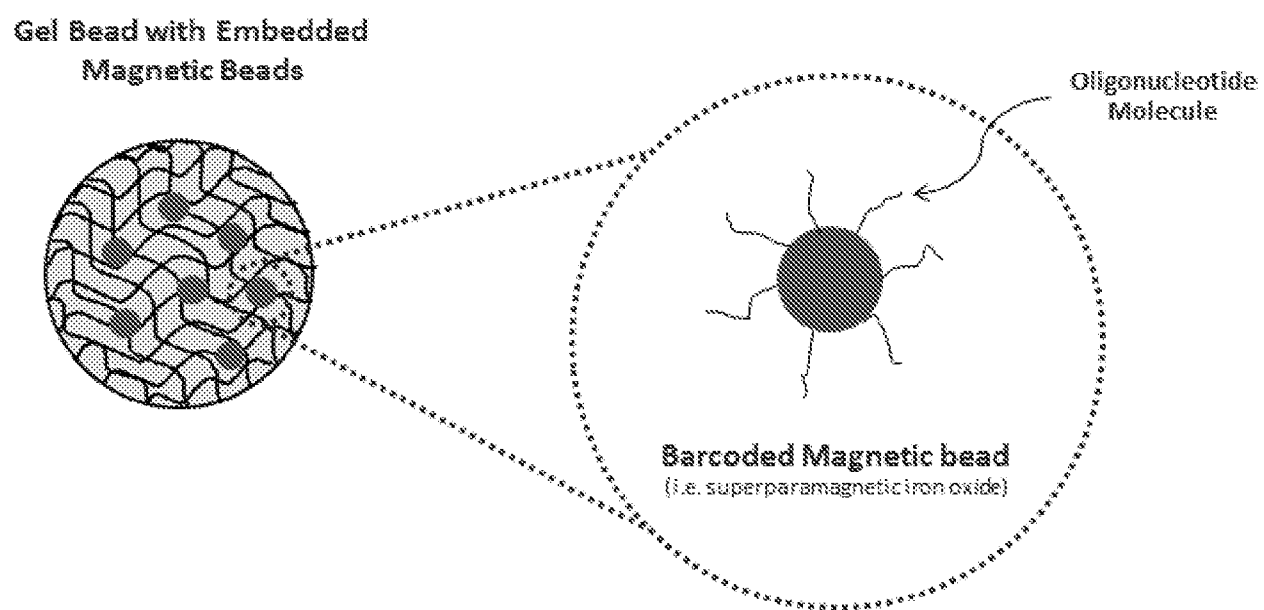


FIG. 35

A. scATAC-seq gel beads (ligation, partially double-stranded)



B. scRNA-seq gel beads (3')



C. scATAC-seq gel beads (linear amp, single-stranded)



D. scRNA-seq gel beads (5')



FIG. 36A

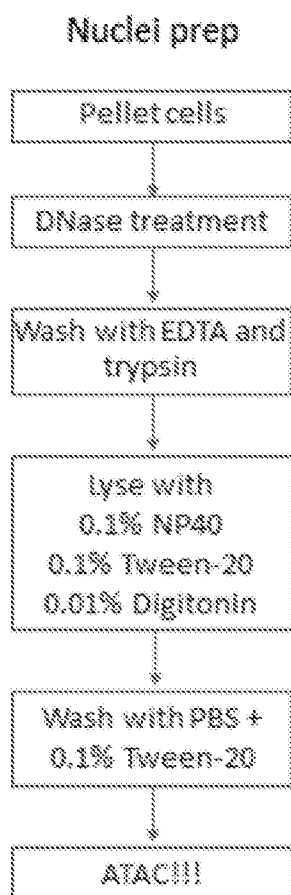


FIG. 36B

Step	Time (hours)
Nuclei prep	1.5
Bulk tagmentation	1
Nuclei partitioning	0.5
Barcoding in droplet	1
Droplet clean-up (Dynal)	0.5
SI PCR	1
Double sided SPRI	0.5
BioA, quant and pool	1
Total	7

FIG. 37**Original gel beads**

AATGATACGGCGACCACCGAGATCTACACXXXXXXXXGTXXXXXXXX
-SP-TTACTATGCCGCTGGTGGCTCTAGATGTGXXXXXXXXCAXXXXXXAGCAGCCGTCGCAG

Shorter R1 (7b)

AATGATACGGCGACCACCGAGATCTACACXXXXXXXXGTXXXXXXXX
-SP-TTACTATGCCGCTGGTGGCTCTAGATGTGXXXXXXXXCAXXXXXXAGCAGCC

U in R1

AATGATACGGCGACCACCGAGATCTACACXXXXXXXXGTXXXXXXXX
-SP-TTACTATGCCGCTGGTGGCTCTAGATGTGXXXXXXXXCAXXXXXXAGCAUCCGTCGCAG

FIG. 38A

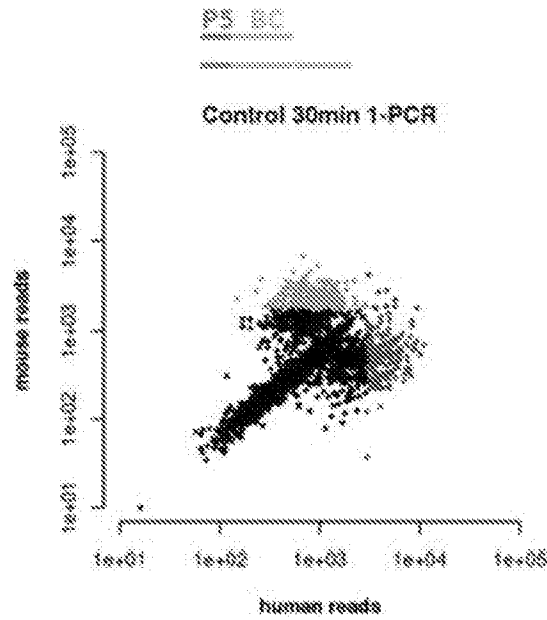


FIG. 38B

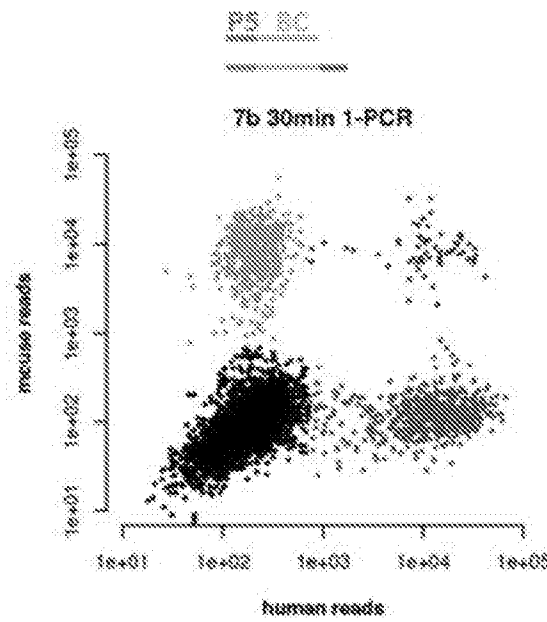


FIG. 38C

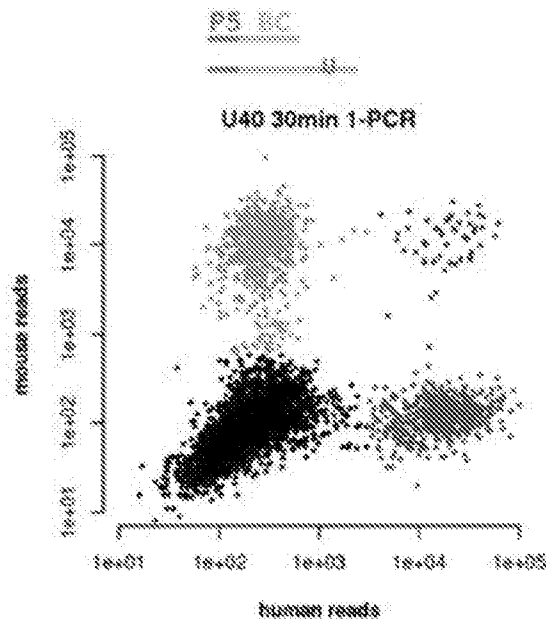


FIG. 39

Original gel bead AATGATACGGCGACCAACGAGATCTACACXXXXXXXXGTXXXXXXXXTCGTCCGCAGCCGTC

				Linear amp 150nM A	Linear amp 150nM B	Ligation U40 A	Ligation U40 B
		Acceptable	Targeted	Observed	Observed	Observed	Observed
Metric				61520	61508	61518	61511
Annotated_cells_hg19				663	410	442	345
Annotated_cells_mm10				660	506	425	407
Inferred doublet rate				0.097	0.076	0.053	0.040
Peaks detected				63,446	49,026	62,856	56,208
Fraction of usable reads in peaks	> 15.0%	> 35.0%		27.60%	27.40%	25.00%	26.70%
Median fragments per noncell barcode	< 250	< 50		25	108	126	129
Median fragments per cell barcode (hg19)	> 6,250	> 18,750		6,022	7,145	10,368	10,609
Median fragments per cell barcode (mm10)	> 6,250	> 18,750		4,359	3,780	9,088	6,657
Fraction insert sizes <294 bp	> 60.0%	> 80.0%		94.40%	89.70%	77.20%	68.30%
Fraction human reads in targeted regions	> 40.0%	> 65.0%		72.40%	72.10%	69.60%	68.30%
Fraction human reads in TSS				25.40%	24.10%	24.50%	22.10%
Fraction human reads in DNase HS regions				50.50%	50.40%	46.80%	46.50%
Fraction human reads in enhancer regions				30.90%	32.10%	29.50%	30.90%
Fraction human reads in promoter regions				28.60%	27.40%	27.30%	24.90%
Ratio of duplicate reads to usable reads in cell barcodes	< 30.0%	< 10.0%		10.50%	17.30%	10.90%	19.30%
Overall fraction non-duplicate wasted reads				47.80%	61.50%	31.90%	44.90%
Fraction mitochondrial reads				0.281	0.403	0.118	0.224

FIG. 40

FIG. 41A

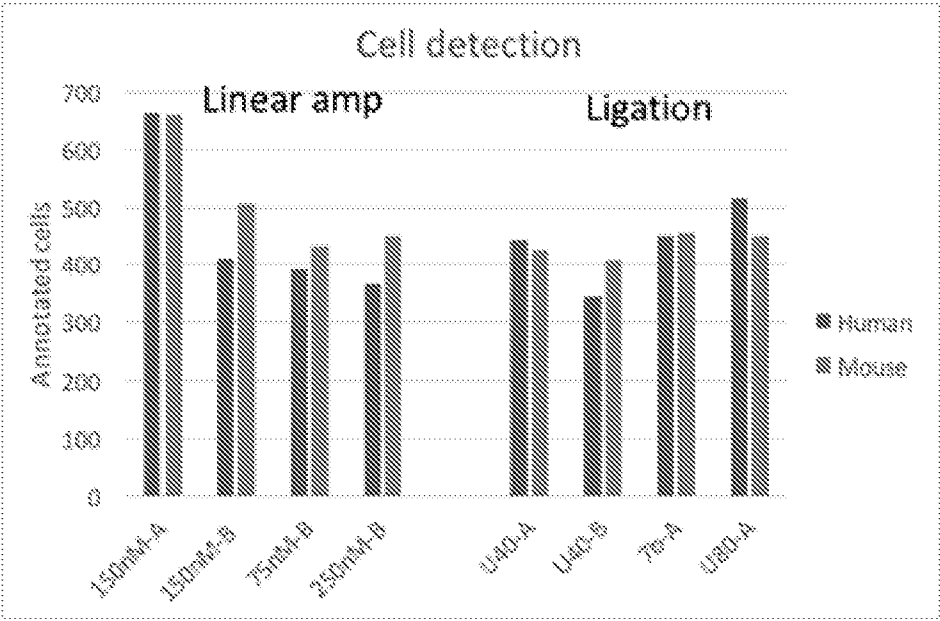


FIG. 41B

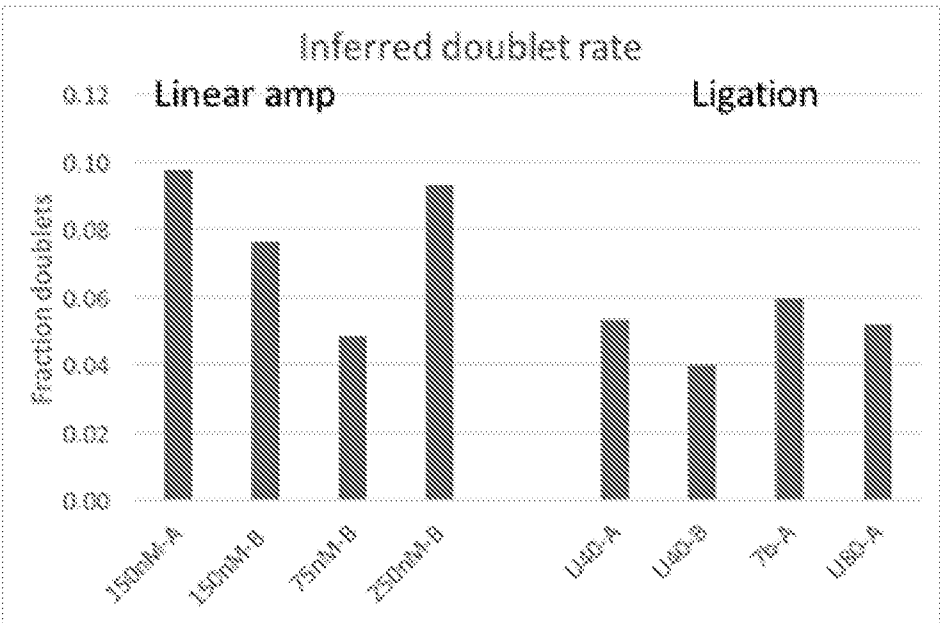


FIG. 42

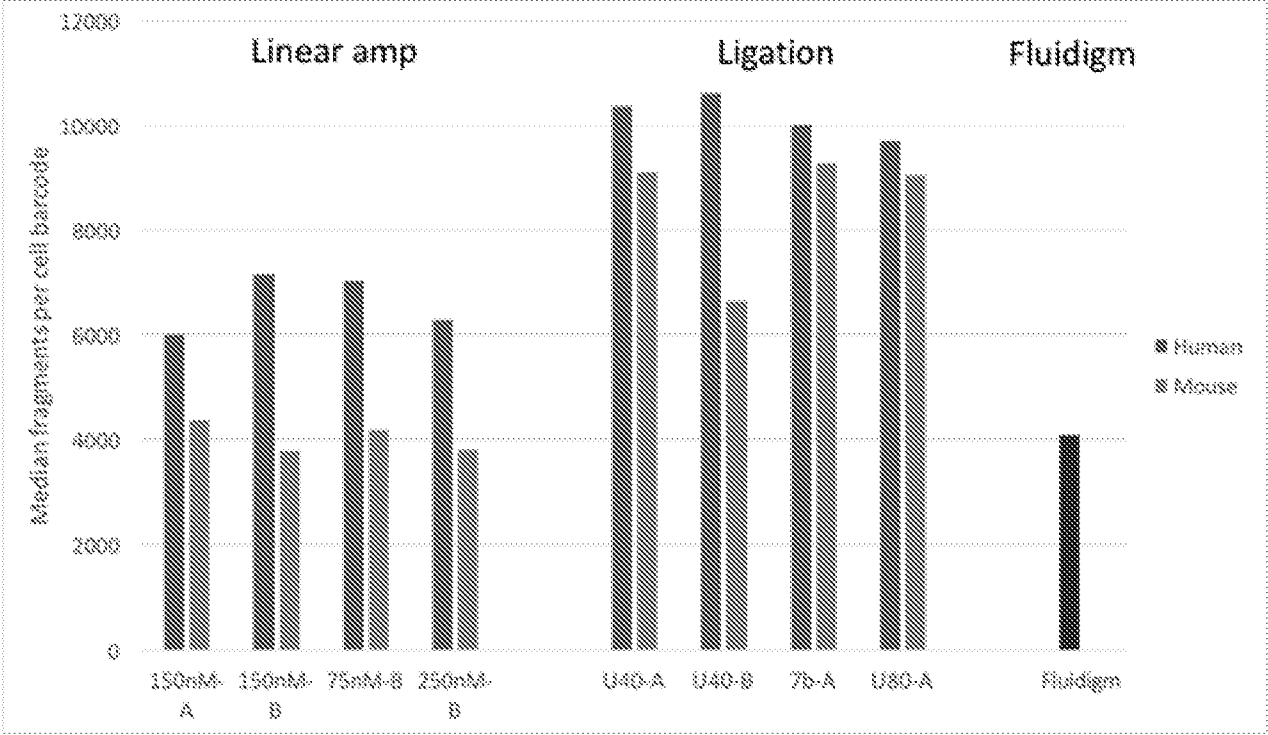


FIG. 43

Metric	Acceptable	Targeted	Ligation U40 30M reads	Ligation U40 800M reads
Annotated_cells_hg19			442	440
Annotated_cells_mm10			425	426
Inferred doublet rate			0.053	0.053
Peaks detected			62,856	310,766
Fraction of usable reads in peaks	> 15.0%	> 35.0%	25.00%	48.40%
Median fragments per noncell barcode	< 250	< 50	126	1,358
Median fragments per cell barcode (hg19)	> 6,250	> 18,750	10,368	94,916
Median fragments per cell barcode (mm10)	> 6,250	> 18,750	9,088	84,259
Fraction insert sizes <294 bp	> 60.0%	> 80.0%	77.20%	65.30%
Fraction human reads in targeted regions	> 40.0%	> 65.0%	69.60%	66.10%
Fraction human reads in TSS			24.50%	21.40%
Fraction human reads in DNase HS regions			46.80%	43.80%
Fraction human reads in enhancer regions			29.50%	29.70%
Fraction human reads in promoter regions			27.30%	23.40%
Ratio of duplicate reads to usable reads in cell barcodes			10.90%	266.40%
Overall fraction non-duplicate wasted reads	< 30.0%	< 10.0%	31.90%	30.40%
Fraction mitochondrial reads			0.118	0.102

FIG. 44

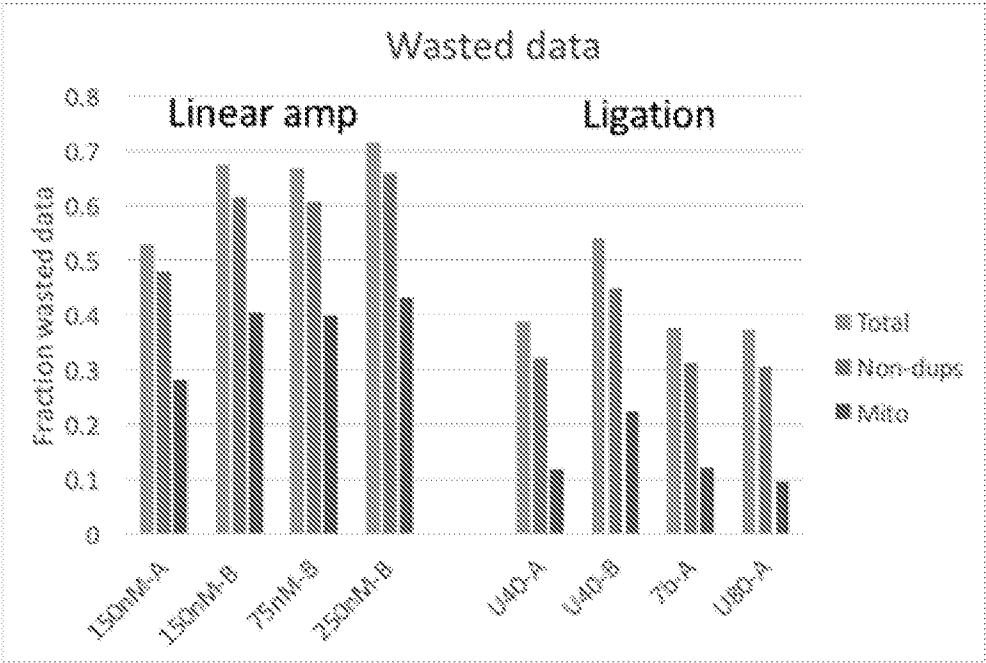


FIG. 45A

Linear amp

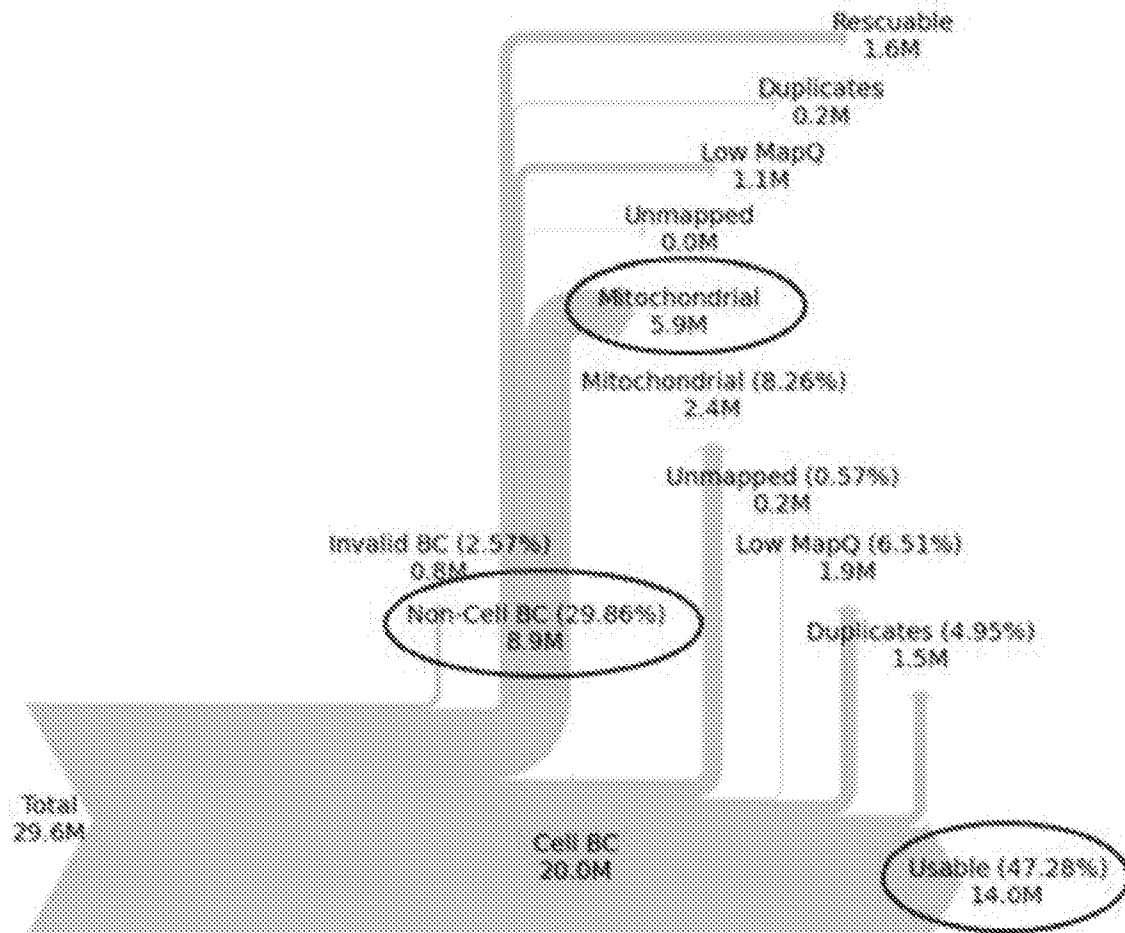


FIG. 45B

Ligation

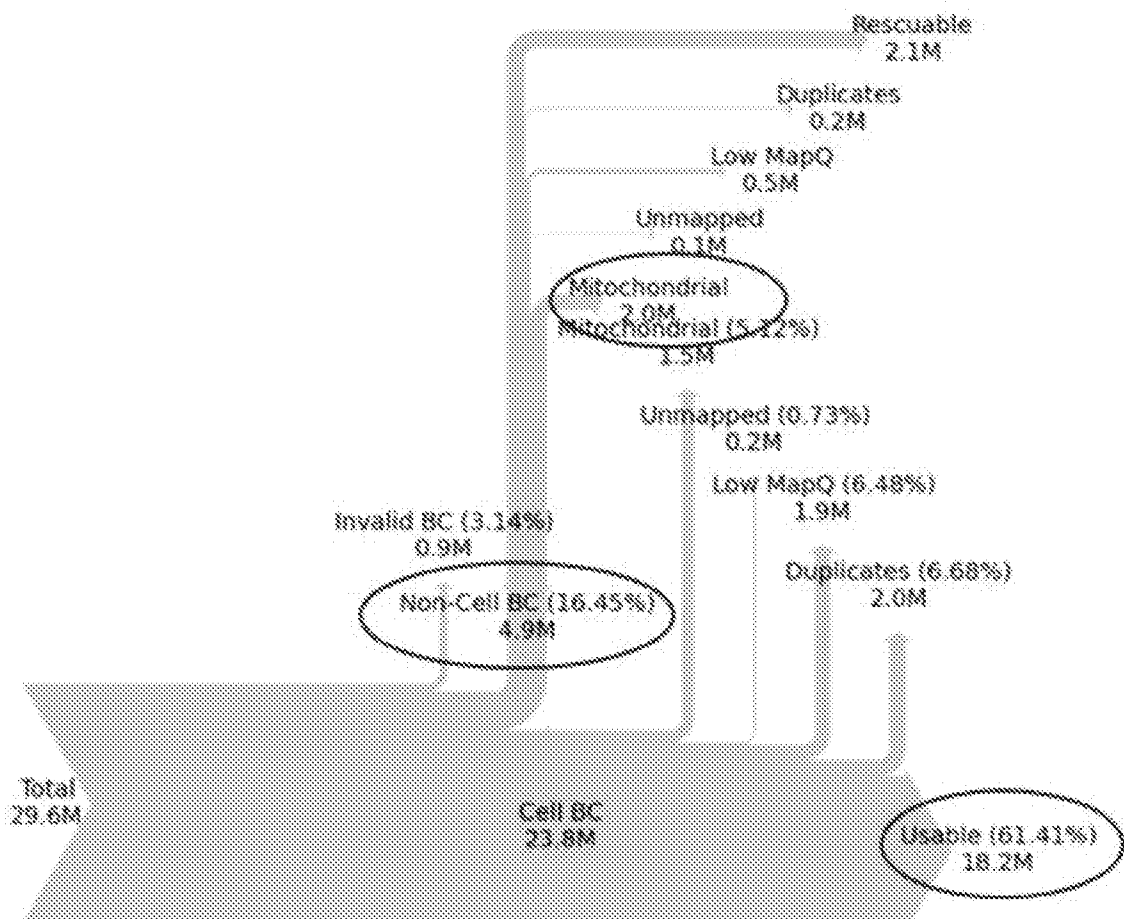


FIG. 46A

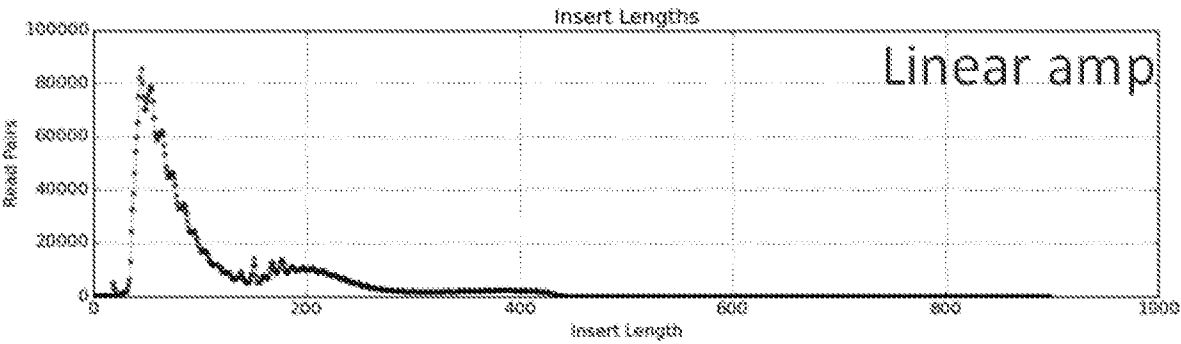


FIG. 46B

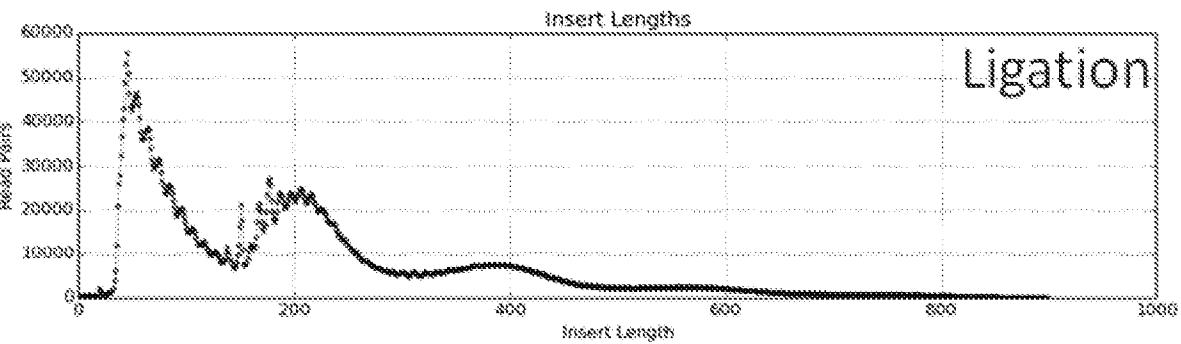


FIG. 47A

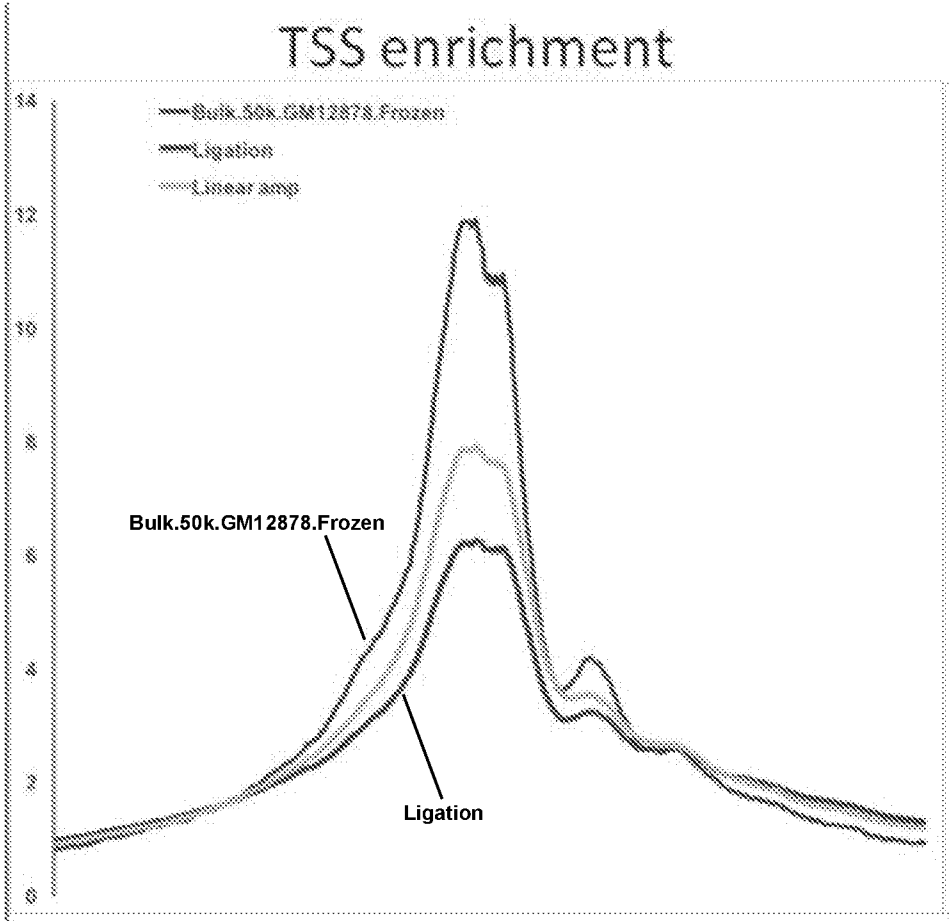
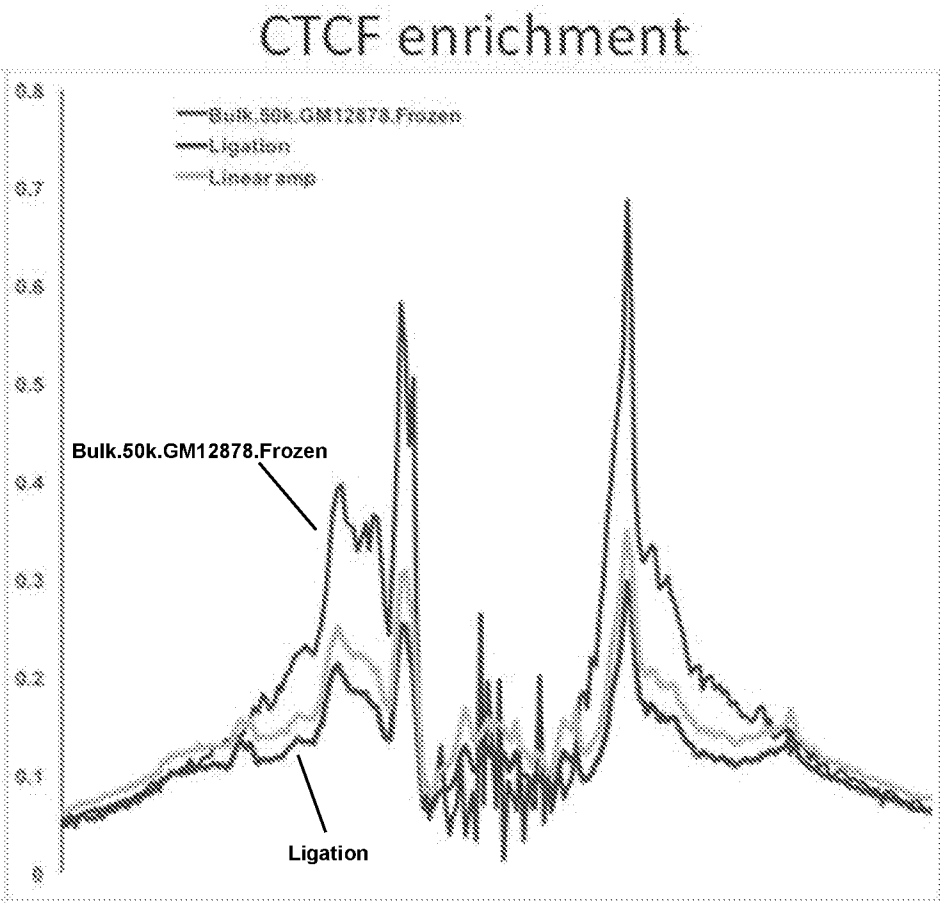


FIG. 47B



Metric	Acceptable	Targeted	Phusion 61520 Observed	Kapa HiFi + betaine 61515 Observed	Deepvent 61521 Observed	Ligation 61518 Observed
Annotated_cells_hg19			563	444	502	442
Annotated_cells_mm10			560	432	497	425
Inferred doublet rate			0.097	0.130	0.128	0.053
Peaks detected			63,446	68,193	66,201	62,856
Fraction of usable reads in peaks	> 15.0%	> 35.0%	27.60%	25.10%	23.60%	25.00%
Median fragments per noncell barcode	< 250	< 50	25	56	60	126
Median fragments per cell barcode (hg19)	> 6,250	> 18,750	6,022	12,192	10,366	10,368
Median fragments per cell barcode (mm10)	> 6,250	> 18,750	4,359	8,806	7,912	9,088
Fraction insert sizes <294 bp	> 60.0%	> 80.0%	94.40%	75.70%	81.10%	77.20%
Fraction human reads in targeted regions	> 40.0%	> 65.0%	72.40%	69.70%	68.40%	69.60%
Fraction human reads in TSS			25.40%	23.90%	22.10%	24.50%
Fraction human reads in DNase HS regions			50.50%	47.30%	46.30%	46.80%
Fraction human reads in enhancer regions			30.90%	30.30%	30.90%	29.50%
Fraction human reads in promoter regions			28.60%	26.60%	24.60%	27.30%
Ratio of duplicate reads to usable reads in cell barcodes			10.50%	13.50%	7.50%	10.90%
Overall fraction non-duplicate wasted reads			47.80%	25.40%	27.30%	31.90%
Fraction mitochondrial reads			0.281	0.094	0.115	0.118

FIG. 48

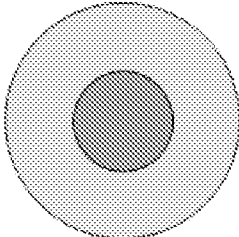
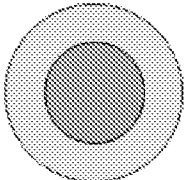
	Current Droplet parameters	Smaller Droplet parameters	
Droplet Volume (pL)	1,047	463	
Droplet Diameter (µm)	126	96	
Gel Bead Volume (pL)	82	82	
Gel Bead Diameter (µm)	54	54	
Cell Multiplet rate @ 1,000 cells	~1%	~0.5%	

FIG. 49

FIG. 50

Metrics	Best Bulk ATAC	Cusanovich (Split-pool)	Buenrostro (Fluidigm)	Ideal Target Metrics	10X Data
Sensitivity: median unique frag/cell	104k	~4k	~50k	30k	>30k
Sensitivity: % reads in promoters	27%	28%	15%	>30%	35%
Sensitivity: % reads in peaks	40%	10%	9.4%	>40%	55%
Wasted data sum (% invalid barcodes, % non-cell barcodes, % mitochondrial reads)	N/A	N/A	N/A	<5%	~2%
	N/A	7%	N/A	<5%	10%
	2%	~30%	65%	<2%	~3%
Library quality: Read1/Read2 Q30, % pass filter	0.96/0.95	0.89/0.85	0.94/0.85	0.9/0.8	0.93/0.90
	N/A	N/A	N/A	80%	78%
Microfluidics: Doublet rate, Cell Throughput	N/A	~10%	N/A	1% for every 1k	~2%
	N/A	10s of 10ks	100s	500 to 10k	1k

FIG. 51A

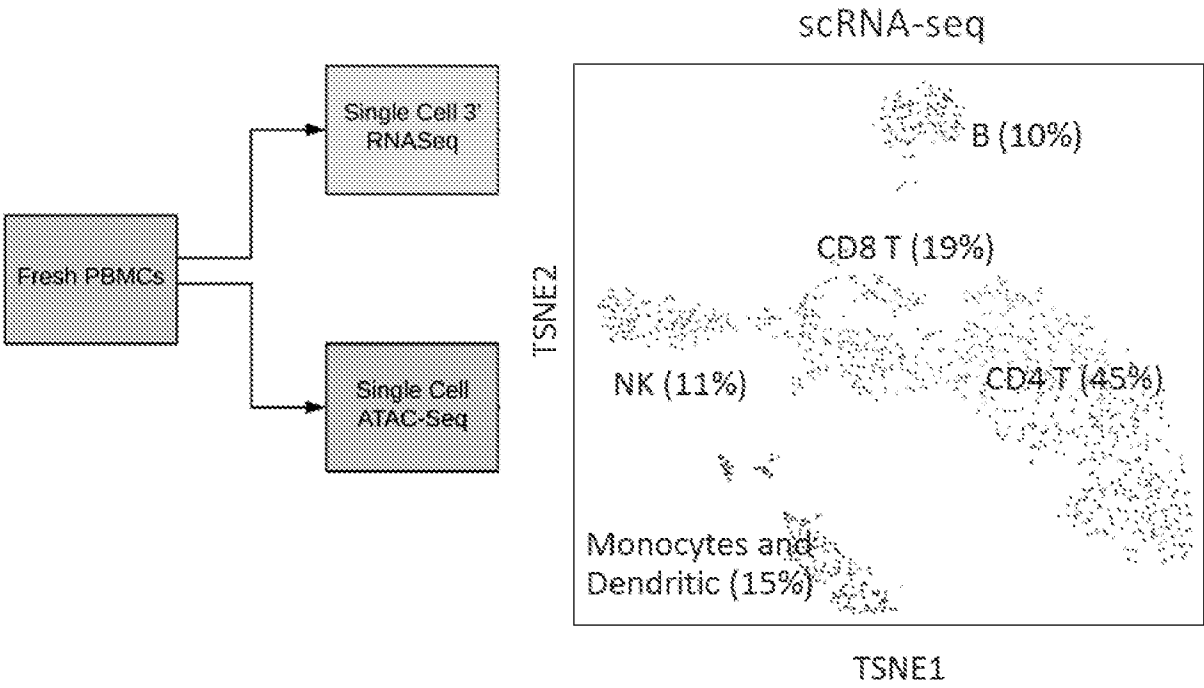


FIG. 51B

