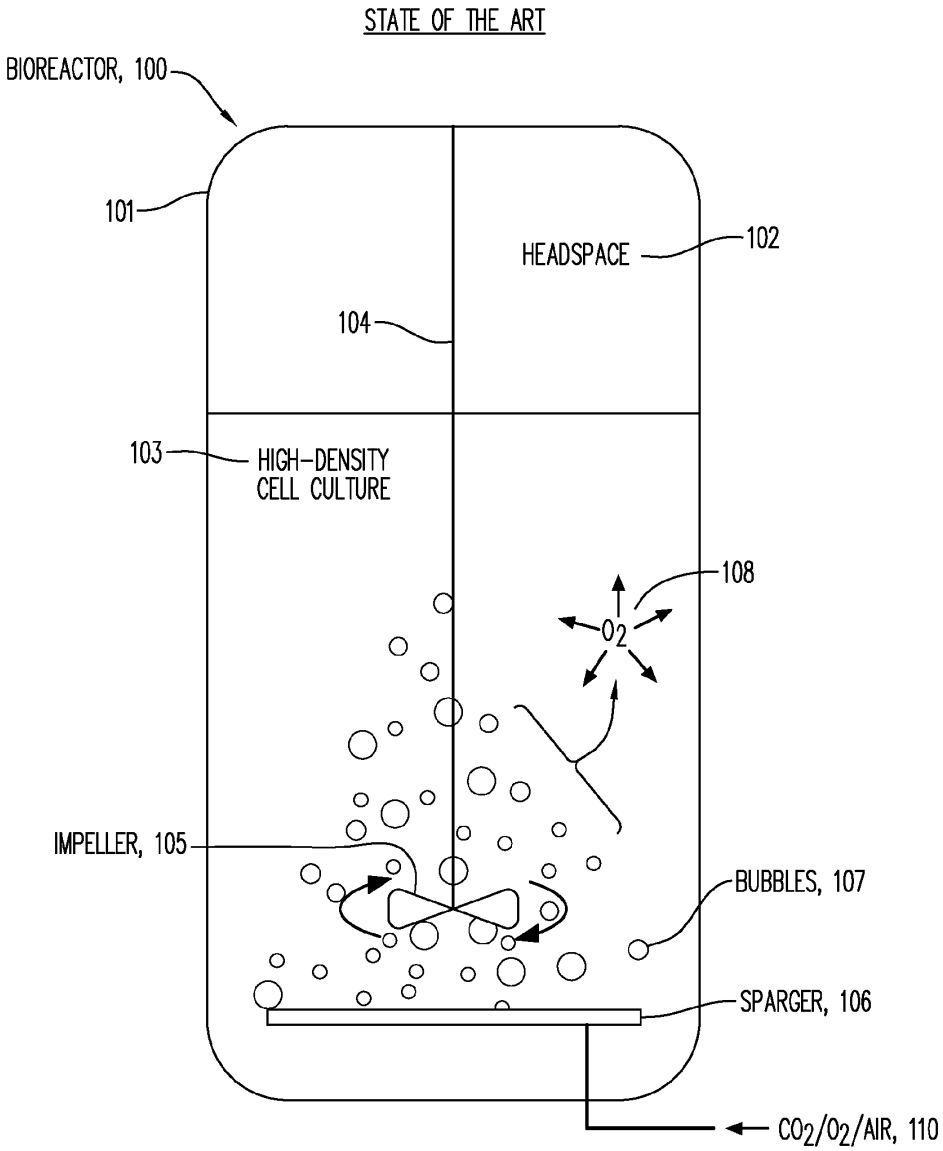

STATE OF THE ART
BIOREACTOR, 100
101
HEADSPACE
102
104
103
HIGH-DENSITY
CELL CULTURE
108
O_2
IMPELLER, 105
BUBBLES, 107
SPARGER, 106
CO_2/O_2/AIR, 110

FIG. 1A

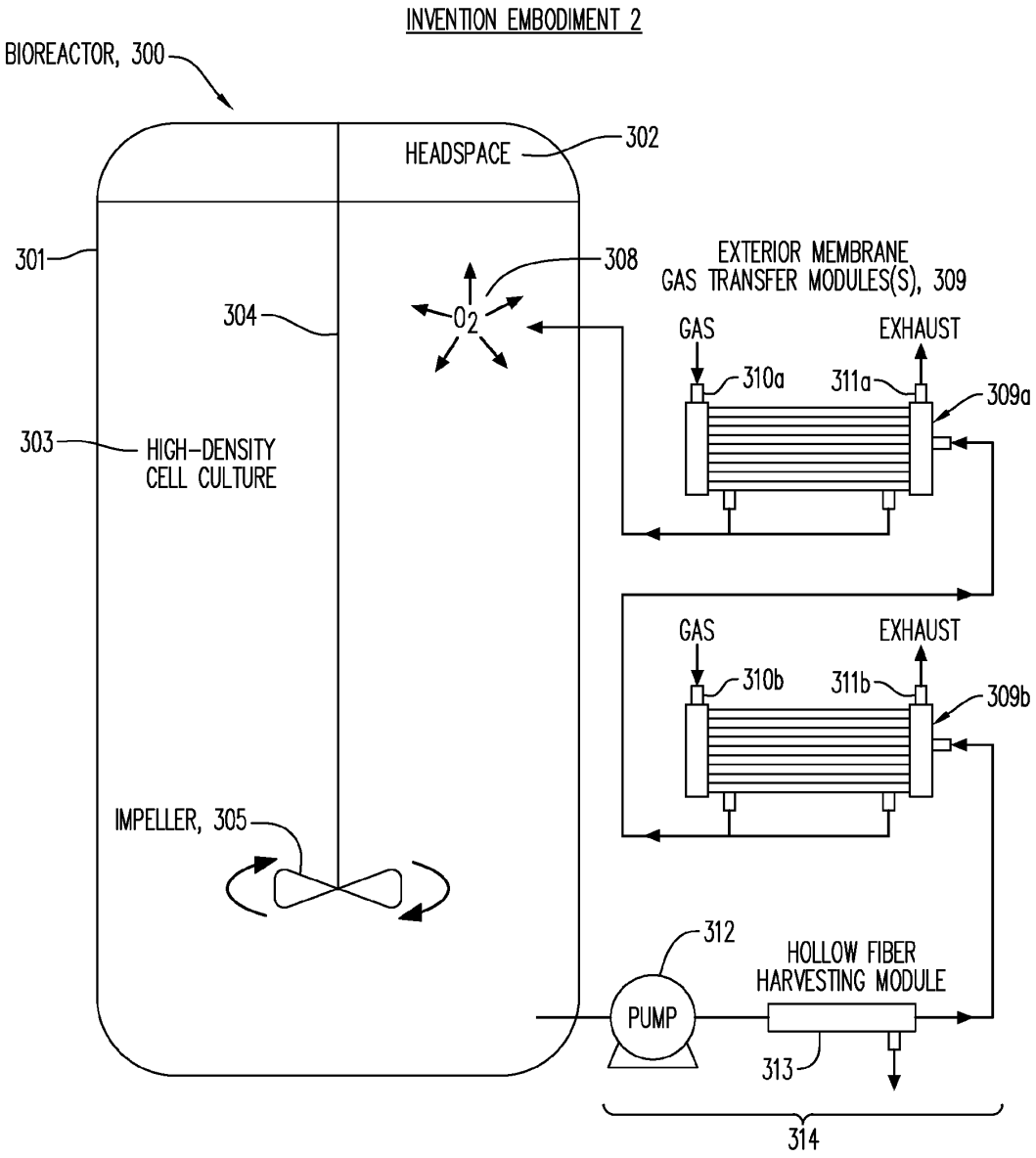

INVENTION EMBODIMENT 2
BIOREACTOR, 300
HEADSPACE
302
301
308
EXTERIOR MEMBRANE
GAS TRANSFER MODULES(S), 309
304
O2
GAS
EXHAUST
310a
311a
309a
303
HIGH-DENSITY
CELL CULTURE
GAS
EXHAUST
310b
311b
309b
IMPELLER, 305
312
HOLLOW FIBER
HARVESTING MODULE
PUMP
313
314

FIG. 1B

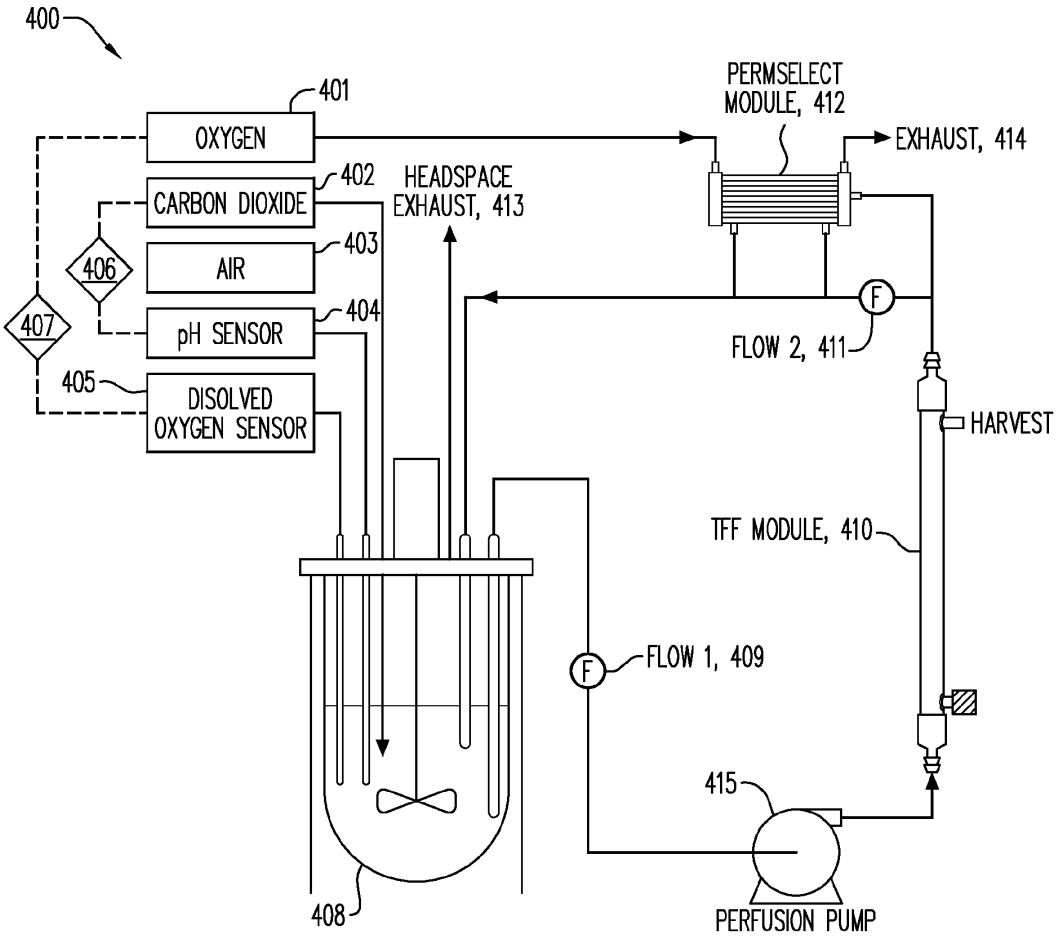

400
401
OXYGEN
402
CARBON DIOXIDE
403
AIR
404
pH SENSOR
405
DISOLVED OXYGEN SENSOR
406
407
HEADSPACE EXHAUST, 413
PERMSELECT MODULE, 412
EXHAUST, 414
F
FLOW 2, 411
HARVEST
TFF MODULE, 410
F
FLOW 1, 409
415
408
PERFUSION PUMP

FIG. 1C

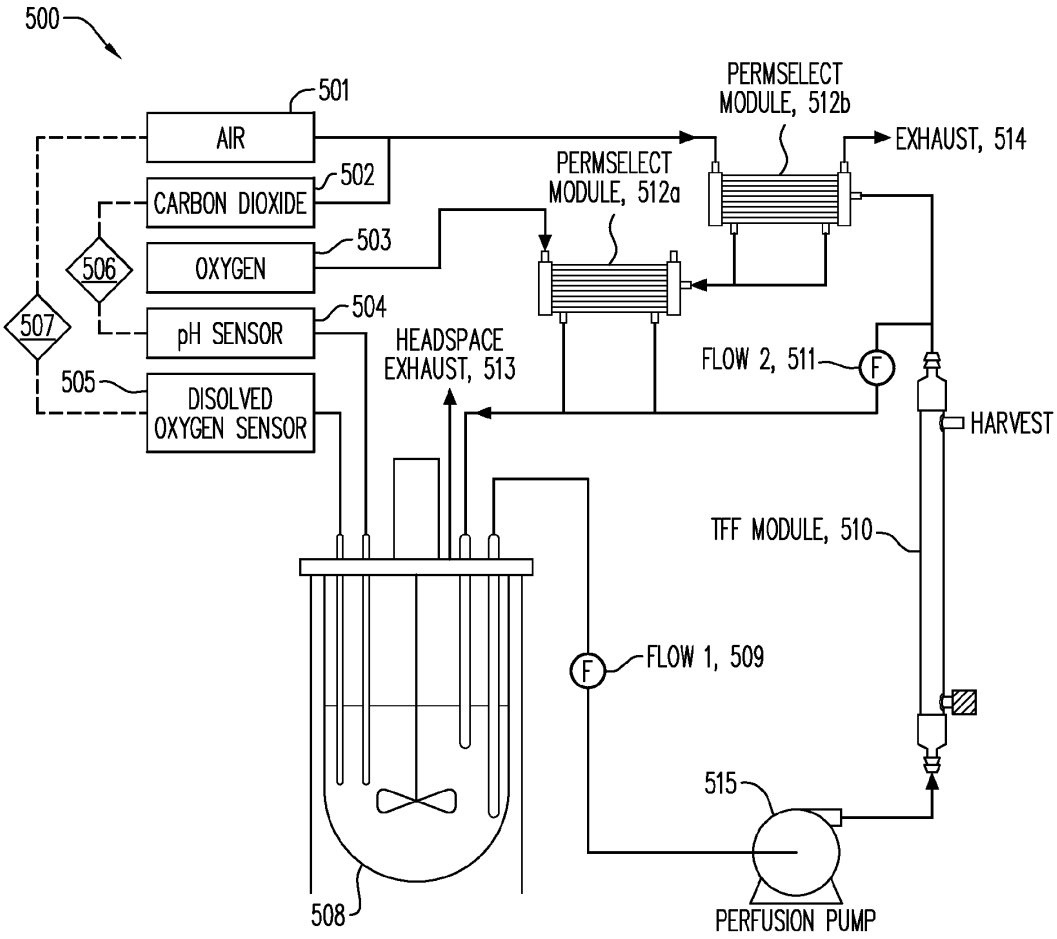

500
501
AIR
502
CARBON DIOXIDE
503
OXYGEN
504
pH SENSOR
505
DISOLVED OXYGEN SENSOR
506
507
PERMSELECT MODULE, 512b
EXHAUST, 514
PERMSELECT MODULE, 512a
HEADSPACE EXHAUST, 513
FLOW 2, 511
F
HARVEST
TFF MODULE, 510
FLOW 1, 509
F
515
508
PERFUSION PUMP

FIG. 1D

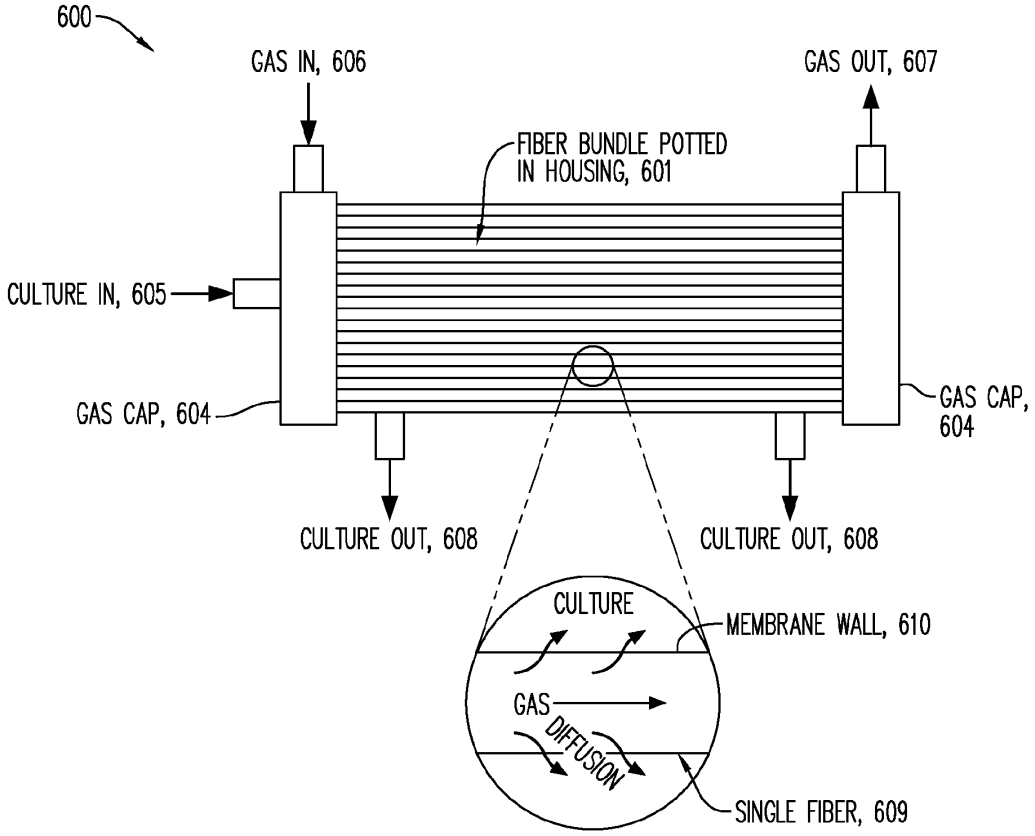

600
GAS IN, 606
GAS OUT, 607
FIBER BUNDLE POTTED IN HOUSING, 601
CULTURE IN, 605
GAS CAP, 604
GAS CAP, 604
CULTURE OUT, 608
CULTURE OUT, 608
CULTURE
MEMBRANE WALL, 610
GAS
DIFFUSION
SINGLE FIBER, 609

FIG. 1E

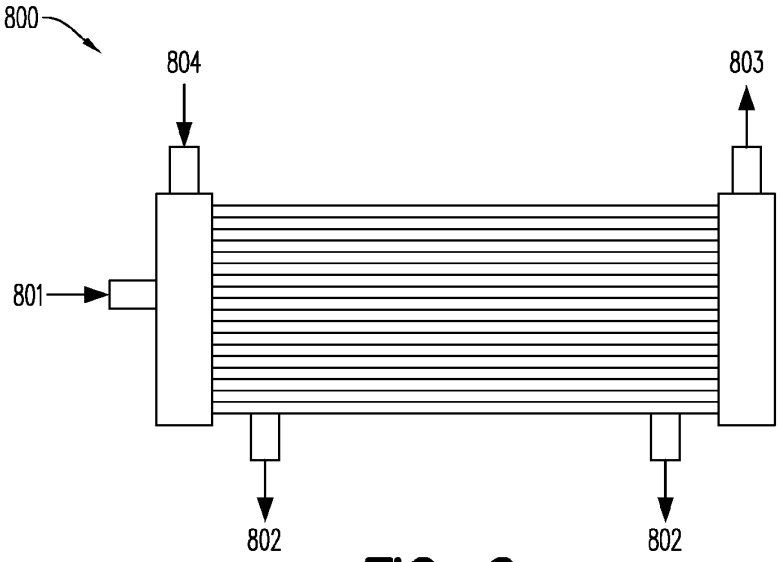
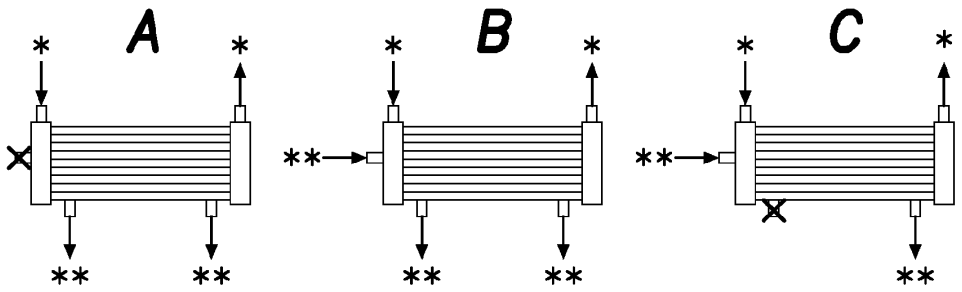

800
804
803
801
802
802

FIG. 2



D

Test Number	Recirculation (LPM)	Flow Path	kLa (hr-1)
1	0.2	A	5.02
2	0.4	A	4.66
3	0.5	A	5.06
4	0.2	B	7.52
5	0.4	B	13.16
6	0.5	B	15.9
7	0.8	B	18.72
8	1	B	20.37
9	1.2	B	24.19
10	1.4	B	25.73
11	1.6	B	27.31
12	1.8	B	28.6
13	0.2	C	12.69
14	0.4	C	18.67
15	0.5	C	19.53

FIG. 3

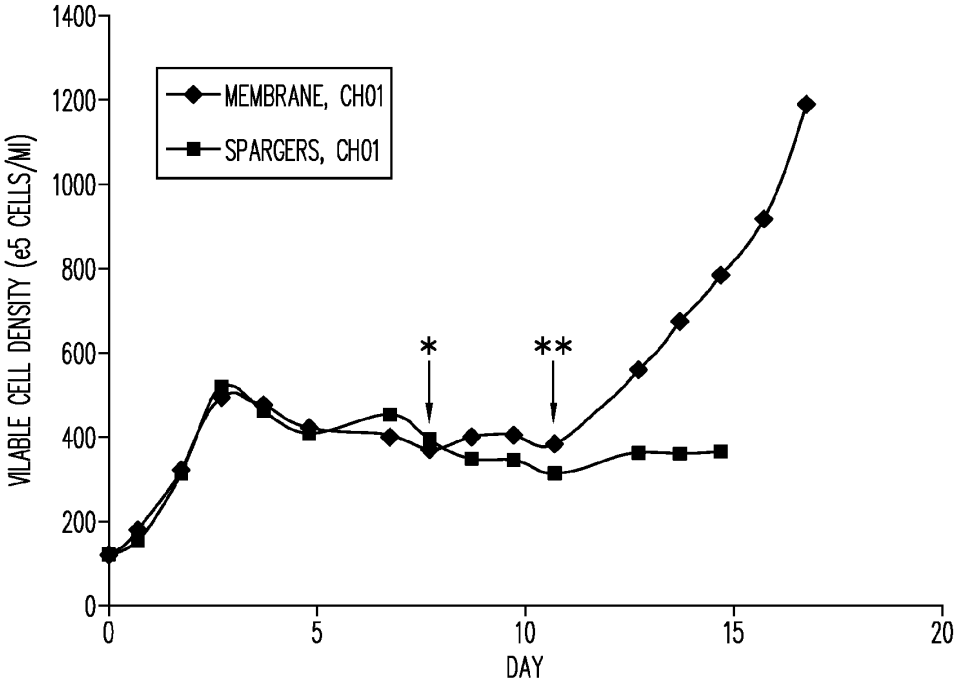

1400
1200
1000
800
600
400
200
0
VIABLE CELL DENSITY (e5 CELLS/ML)
MEMBRANE, CH01
SPARGERS, CH01
*
**
0
5
10
15
20
DAY

FIG. 4A

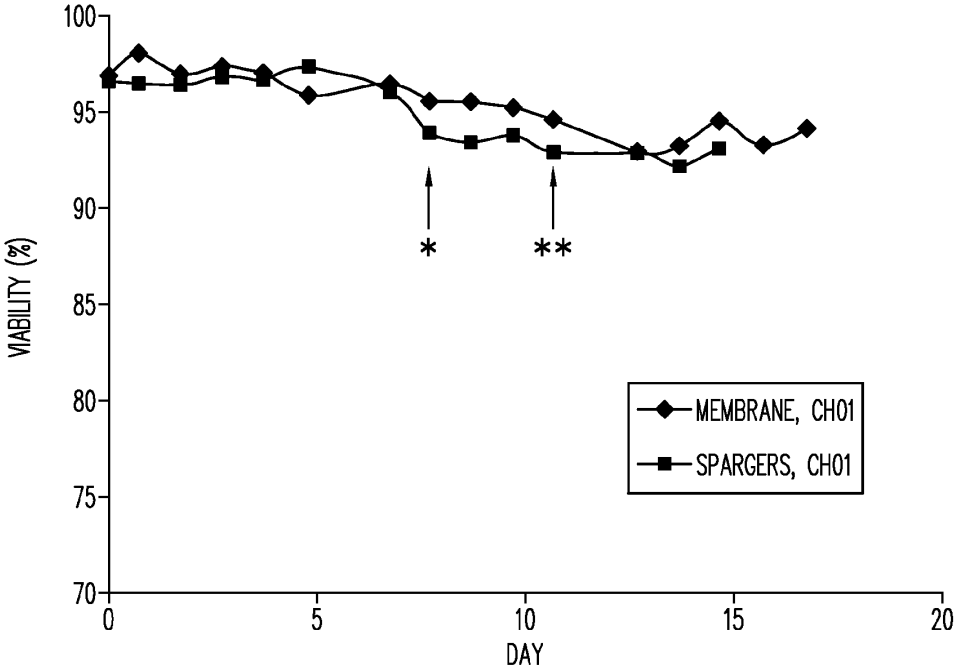

100
95
90
85
80
75
70
VIABILITY (%)
*
**
MEMBRANE, CH01
SPARGERS, CH01
0
5
10
15
20
DAY

FIG. 4B

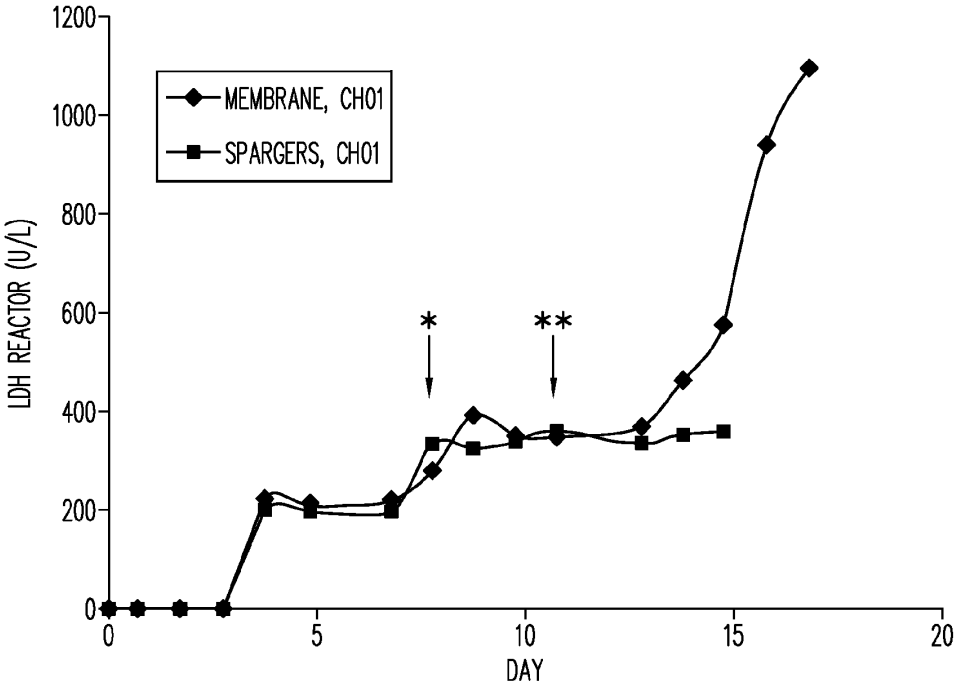

1200
1000
800
600
400
200
0
LDH REACTOR (U/L)
MEMBRANE, CH01
SPARGERS, CH01
*
**
0
5
10
15
20
DAY

FIG. 4C

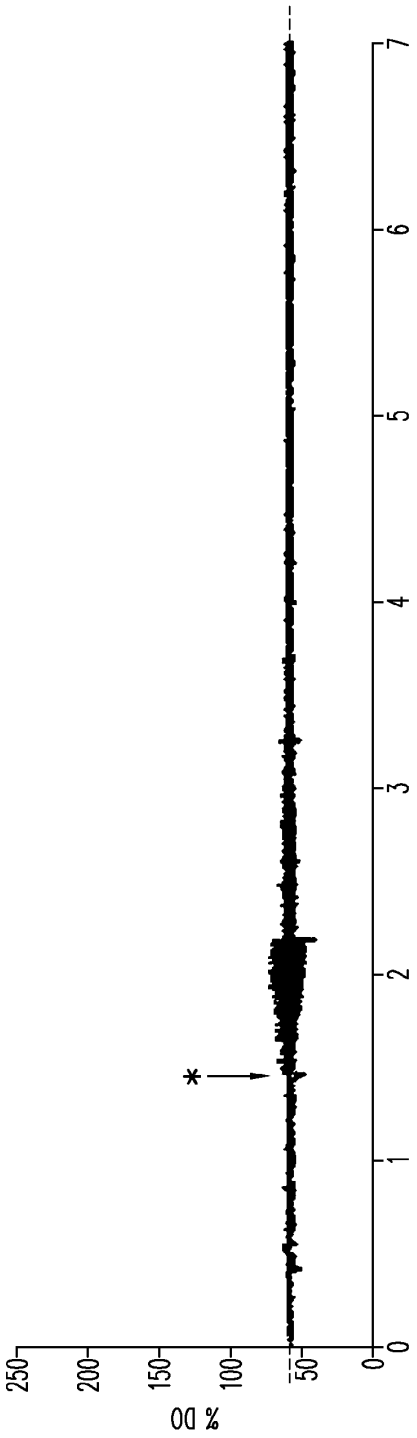


FIG. 5A

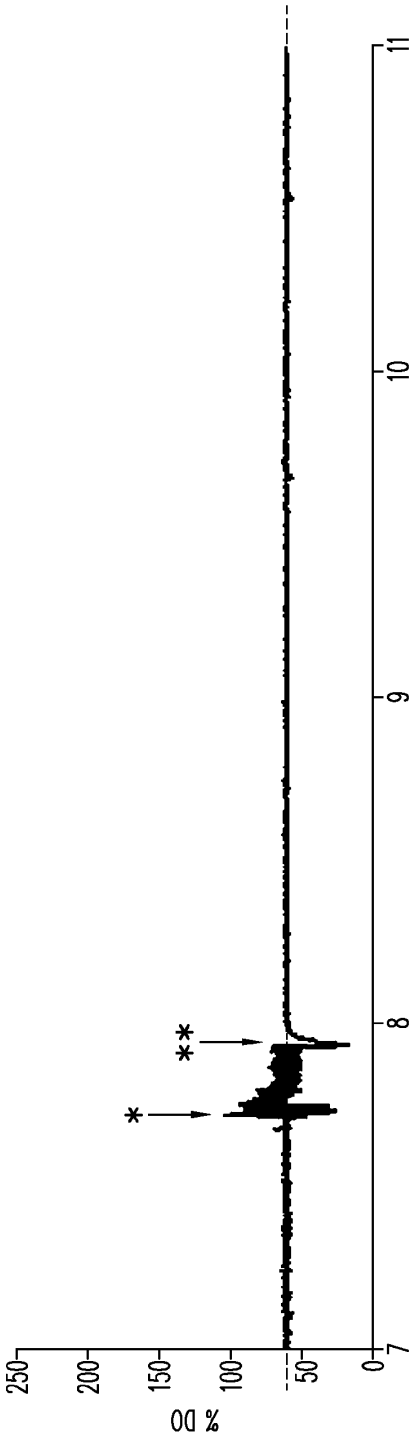


FIG. 5B

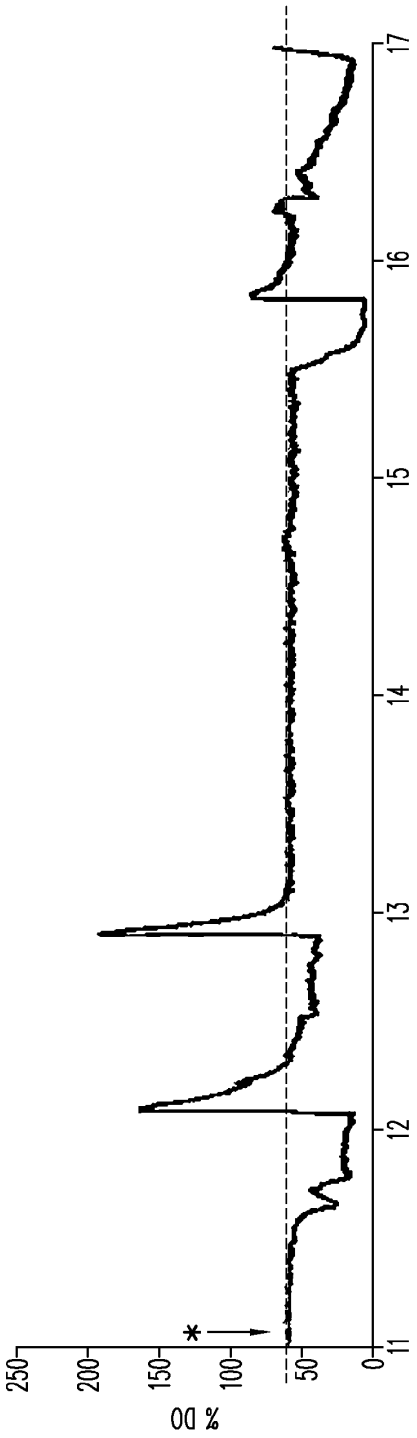


FIG. 5C

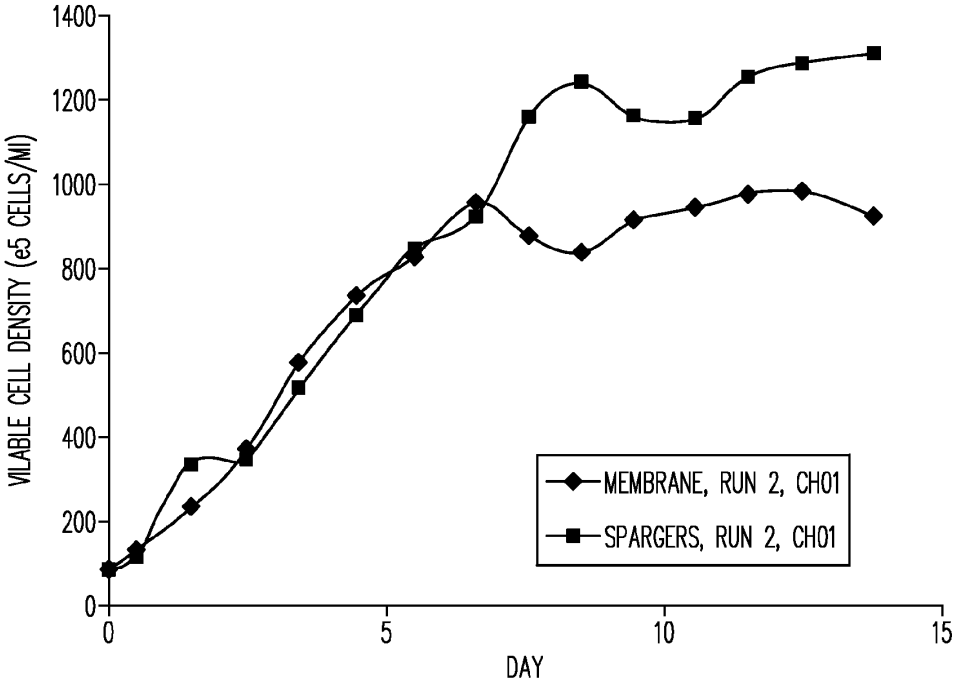

VIABLE CELL DENSITY (e5 CELLS/ML)
1400
1200
1000
800
600
400
200
0
0
5
10
15
DAY
MEMBRANE, RUN 2, CH01
SPARGERS, RUN 2, CH01

FIG. 6A

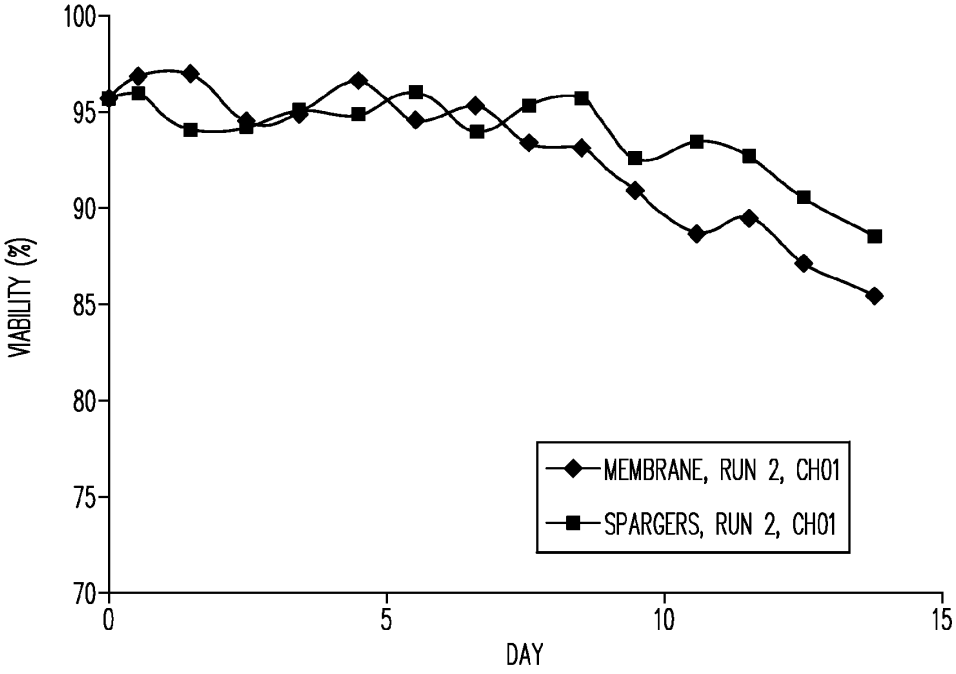

VIABILITY (%)
100
95
90
85
80
75
70
0
5
10
15
DAY
MEMBRANE, RUN 2, CH01
SPARGERS, RUN 2, CH01

FIG. 6B

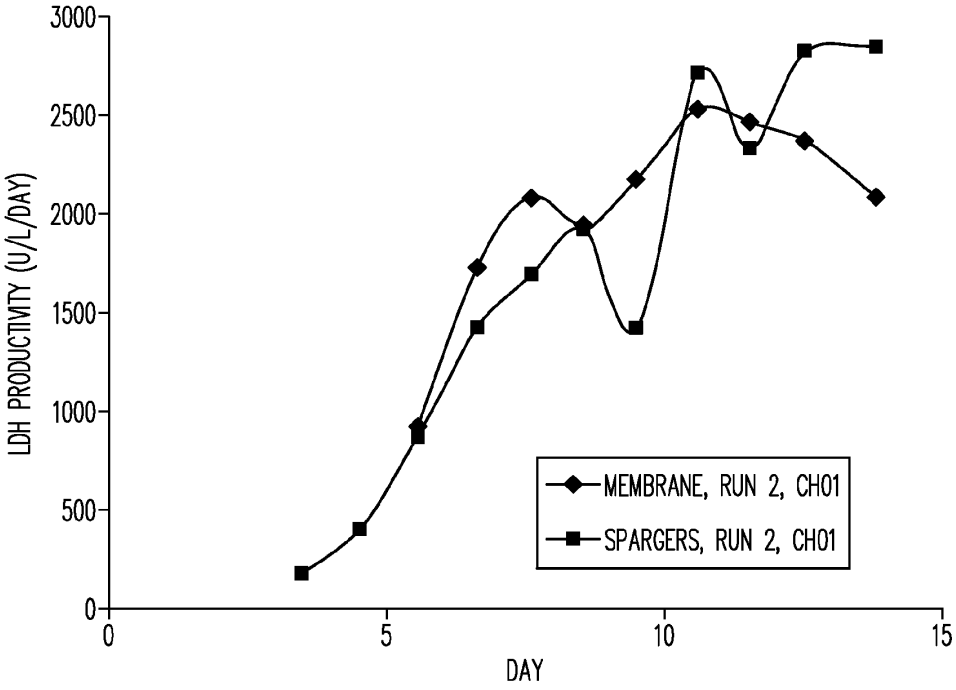

3000
2500
2000
1500
1000
500
0
LDH PRODUCTIVITY (U/L/DAY)
0
5
10
15
DAY
MEMBRANE, RUN 2, CH01
SPARGERS, RUN 2, CH01

FIG. 6C

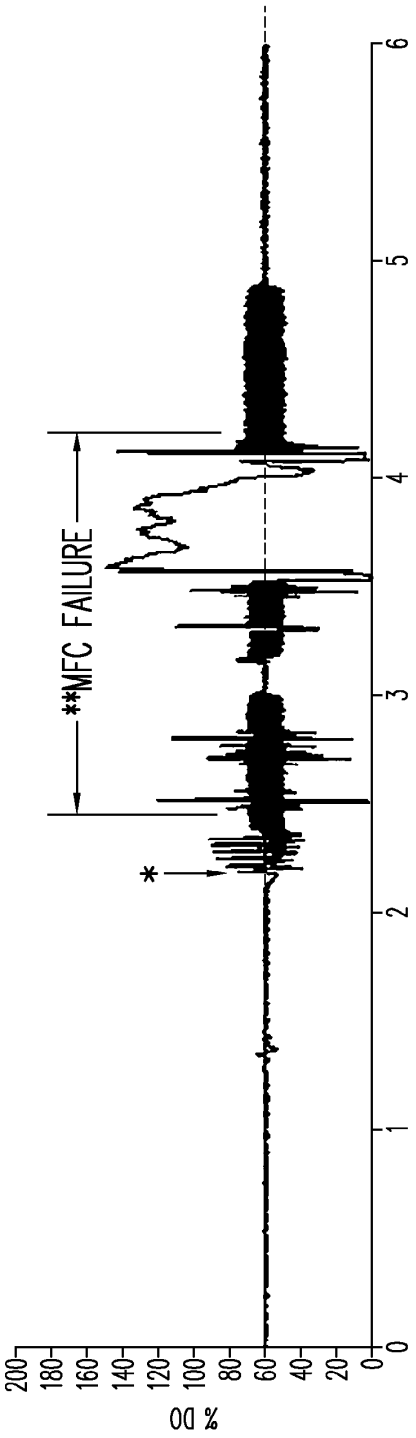


FIG. 7A

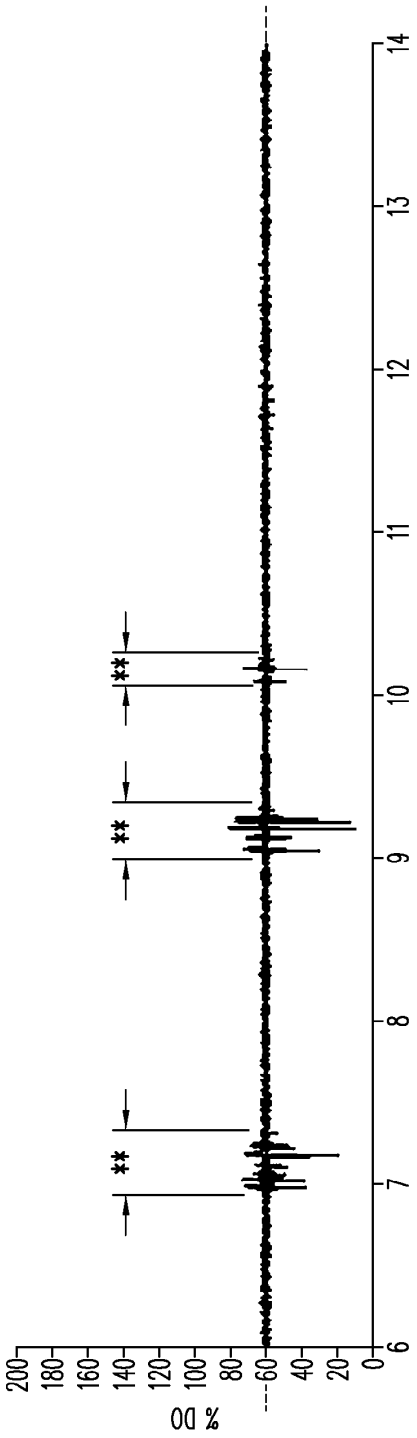


FIG. 7B

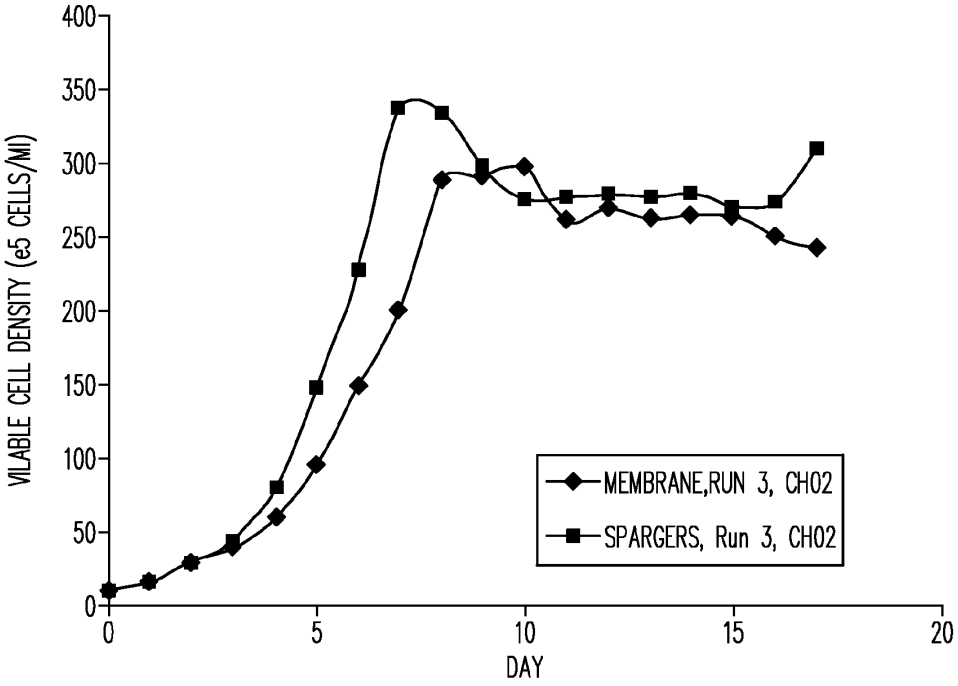

VIABLE CELL DENSITY (e5 CELLS/ML)
400
350
300
250
200
150
100
50
0
0
5
10
15
20
DAY
MEMBRANE,RUN 3, CHO2
SPARGERS, Run 3, CHO2

FIG. 8A

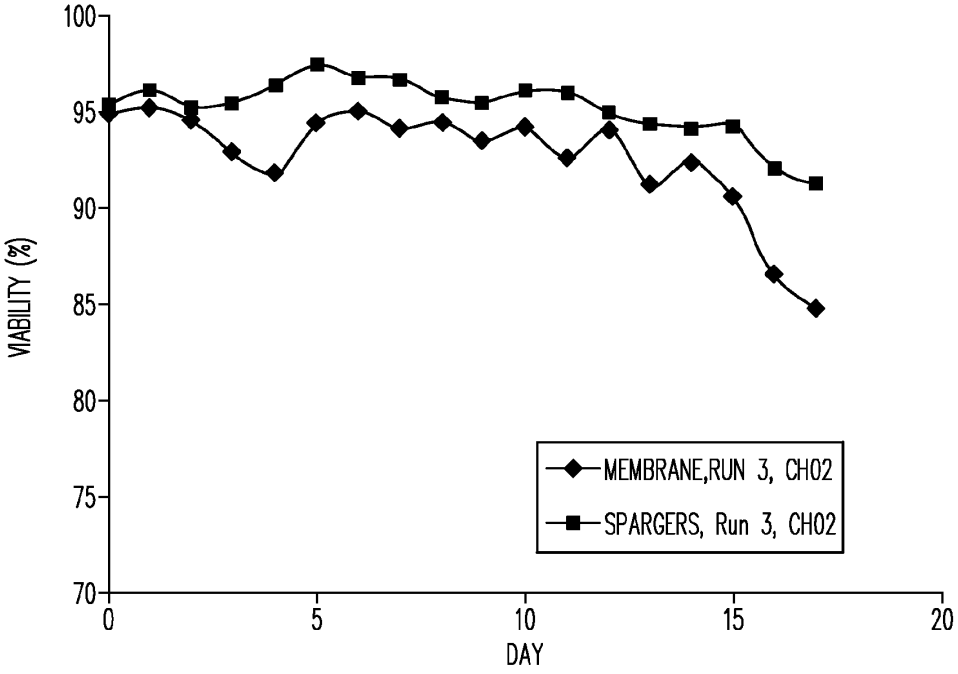

VIABILITY (%)
100
95
90
85
80
75
70
0
5
10
15
20
DAY
MEMBRANE,RUN 3, CHO2
SPARGERS, Run 3, CHO2

FIG. 8B

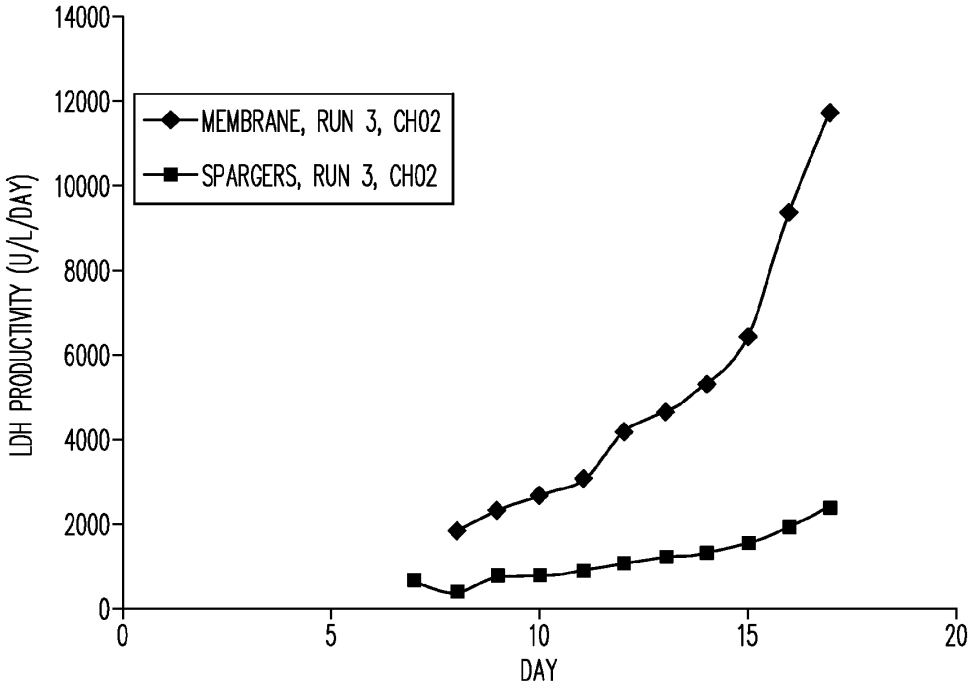

14000
12000
10000
8000
6000
4000
2000
0
LDH PRODUCTIVITY (U/L/DAY)
MEMBRANE, RUN 3, CHO2
SPARGERS, RUN 3, CHO2
0
5
10
15
20
DAY

FIG. 8C

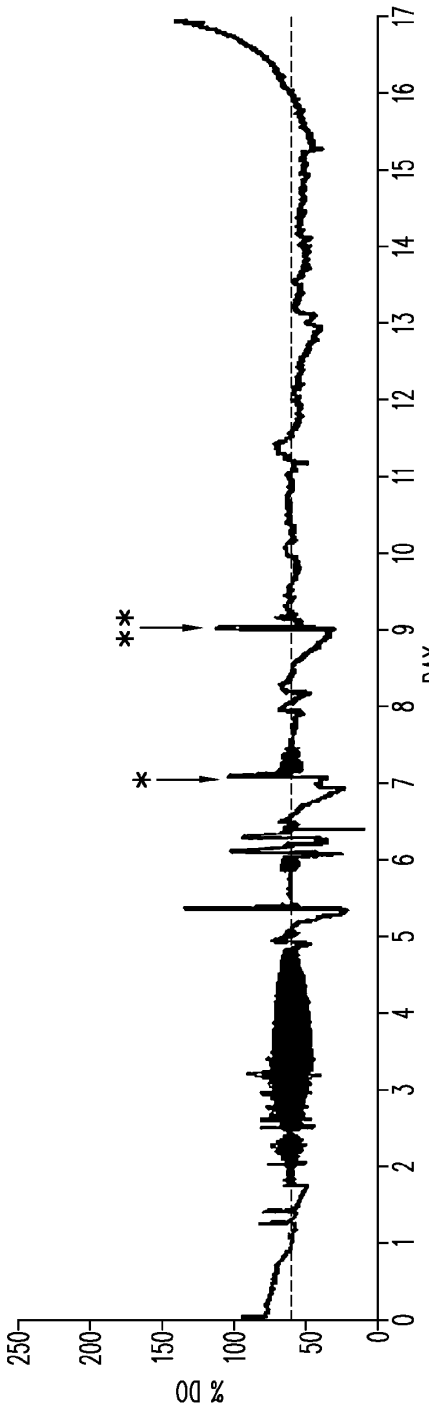


FIG. 9A

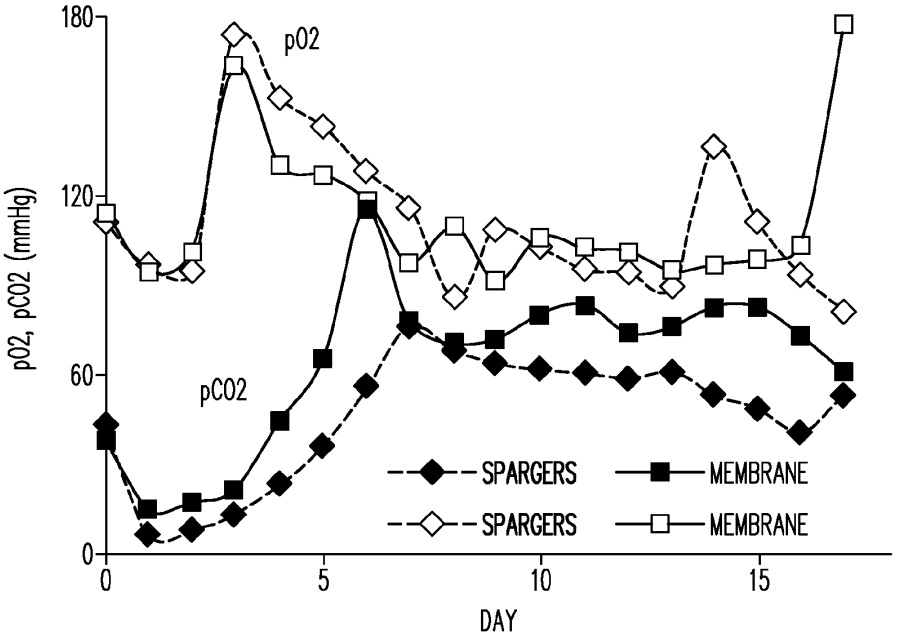

180
120
60
0
pO2
pCO2
pO2, pCO2 (mmHg)
0
5
10
15
DAY
SPARGERS
MEMBRANE
SPARGERS
MEMBRANE

FIG. 9B

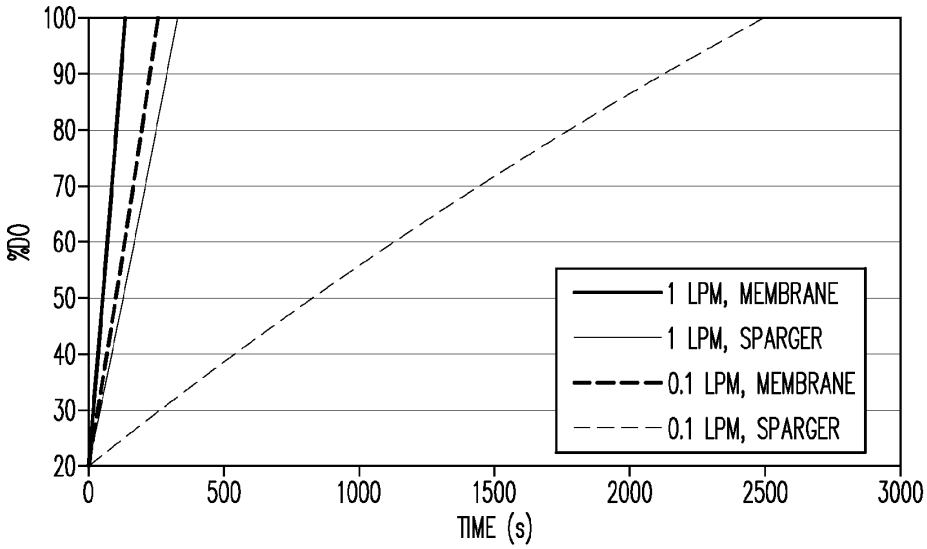
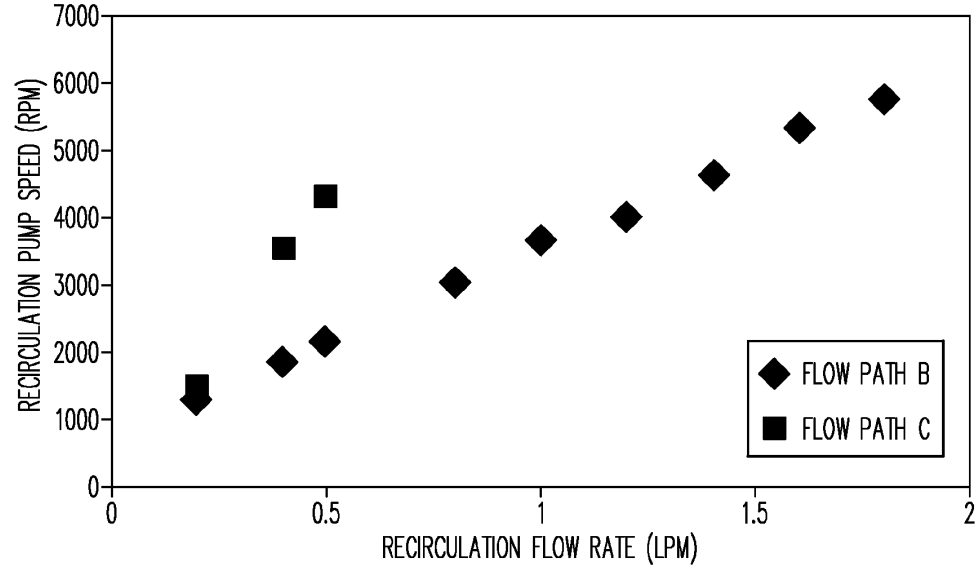

100
90
80
70
60
50
40
30
20
%DO
0
500
1000
1500
2000
2500
3000
TIME (s)
1 LPM, MEMBRANE
1 LPM, SPARGER
0.1 LPM, MEMBRANE
0.1 LPM, SPARGER

FIG. 10


RECIRCULATION PUMP SPEED (RPM)
7000
6000
5000
4000
3000
2000
1000
0
0
0.5
1
1.5
2
RECIRCULATION FLOW RATE (LPM)
FLOW PATH B
FLOW PATH C

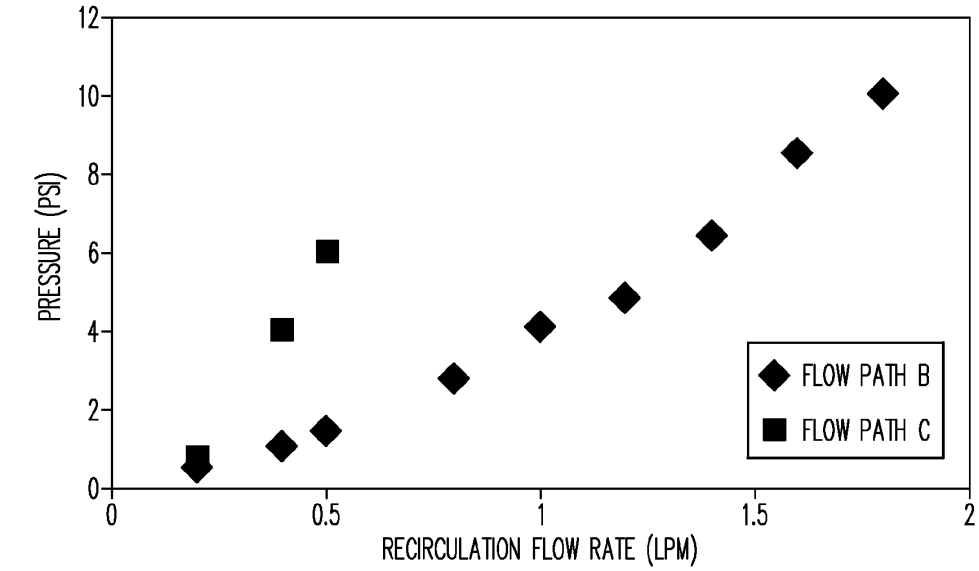

PRESSURE (PSI)
12
10
8
6
4
2
0
0
0.5
1
1.5
2
RECIRCULATION FLOW RATE (LPM)
FLOW PATH B
FLOW PATH C

FIG. 11