FIG. 1A

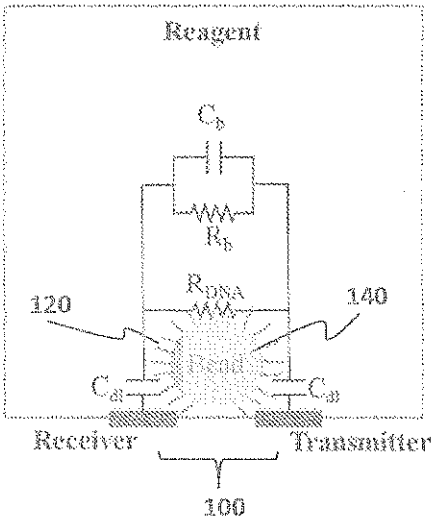


FIG. 1B

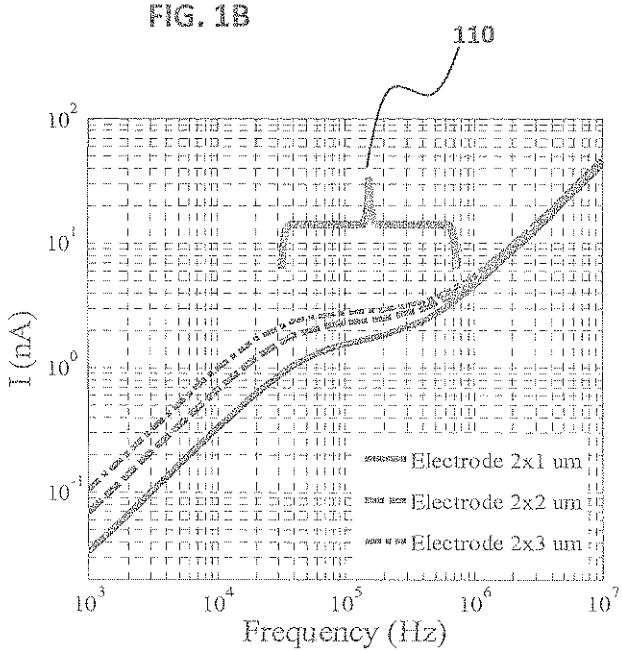


FIG. 1C

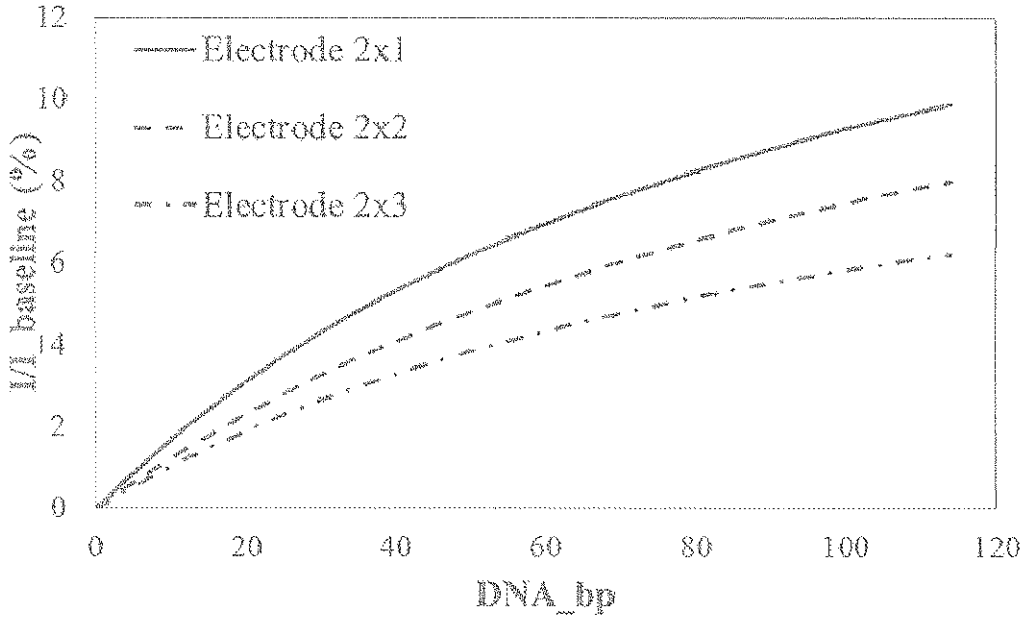


FIG. 1D

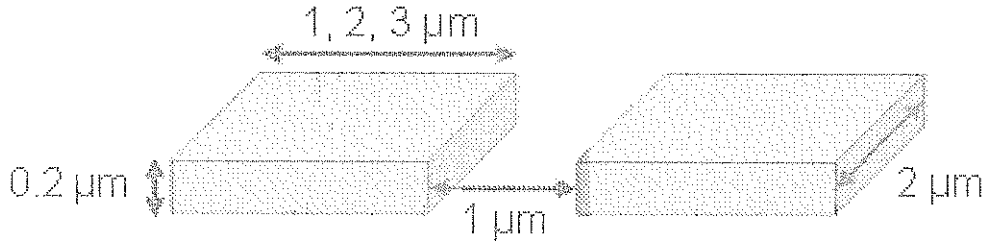


FIG. 1E

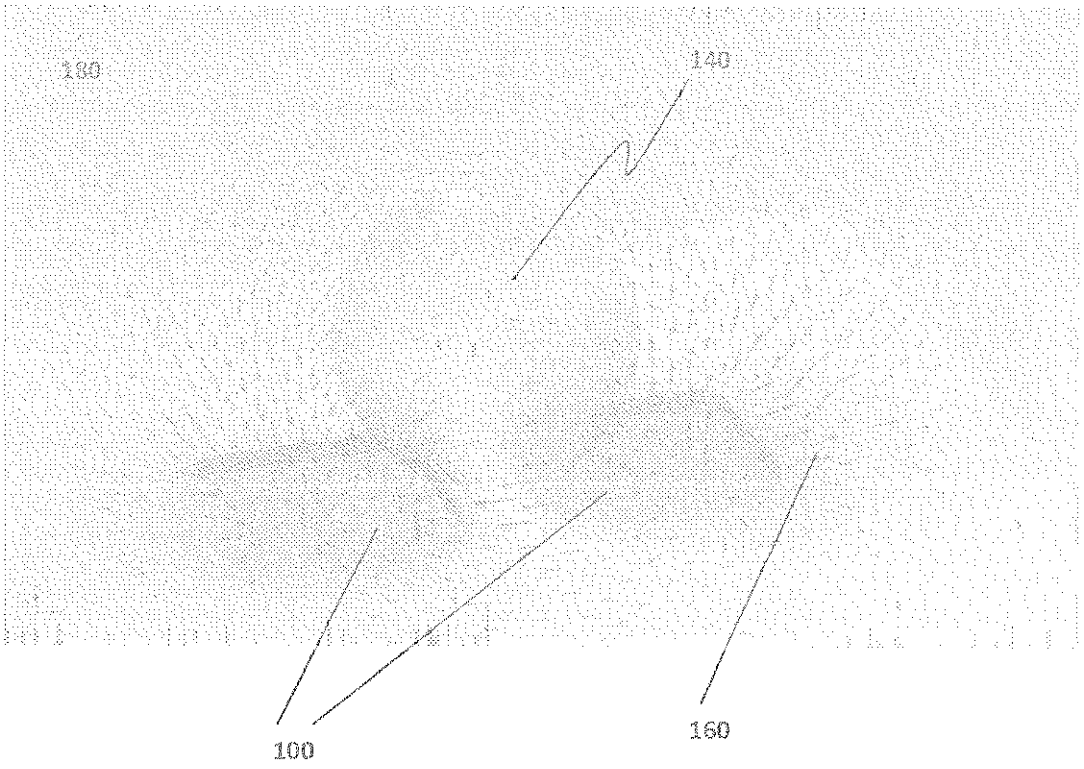


FIG. 2A

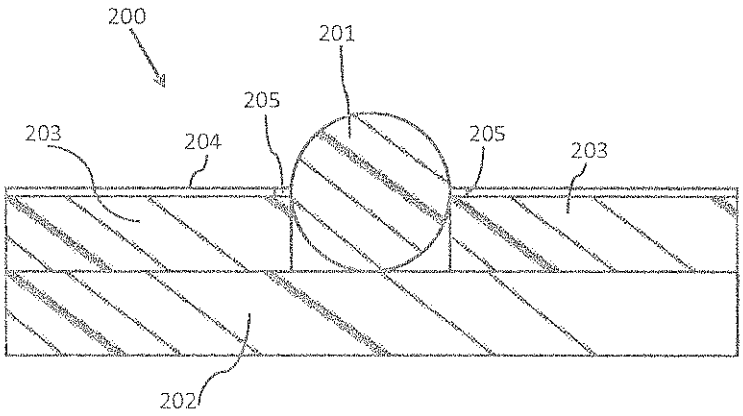


FIG. 2B

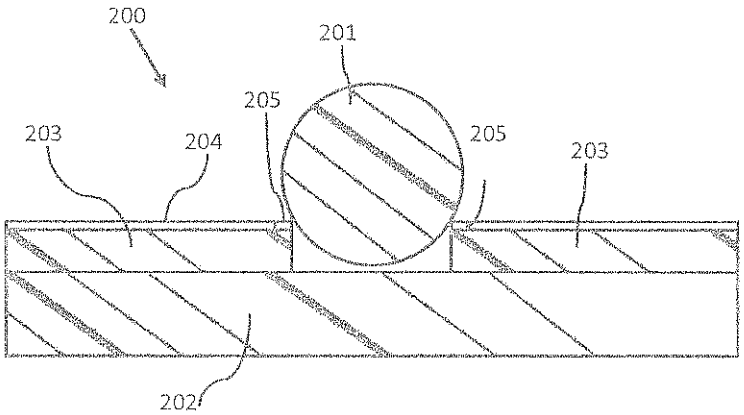


FIG. 2C

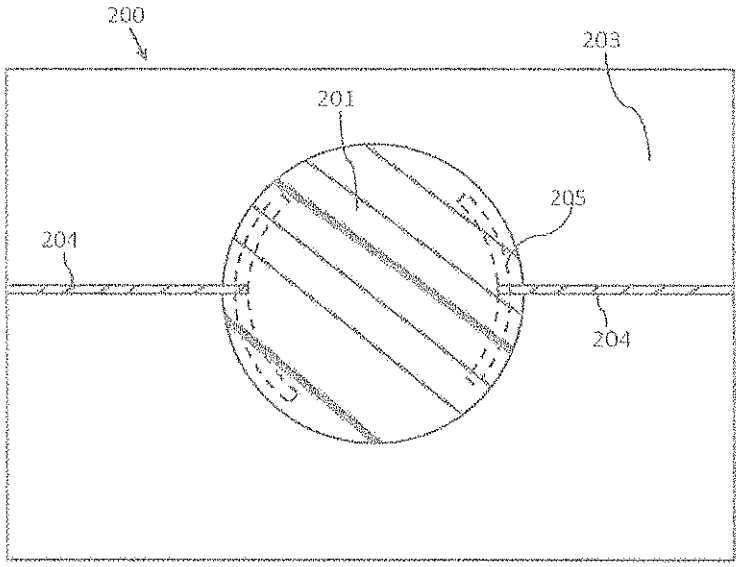


FIG. 3

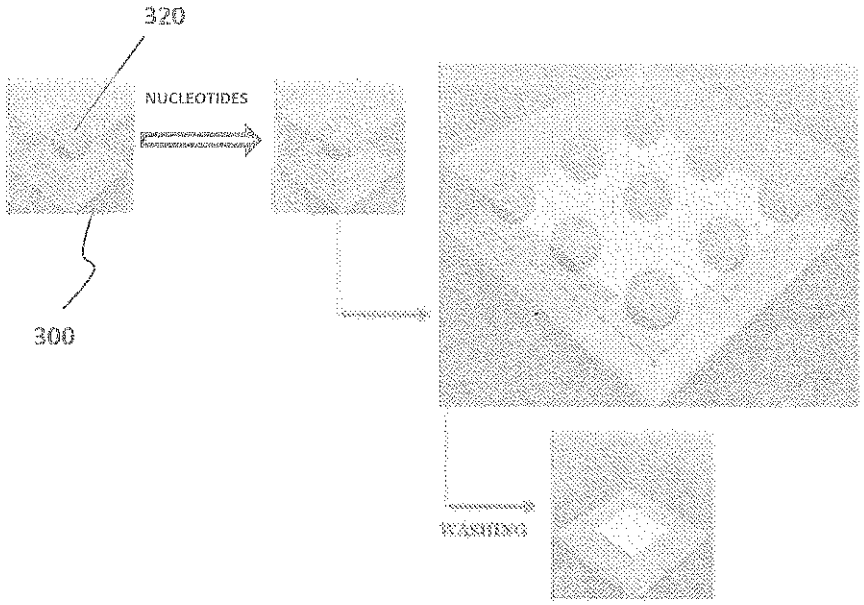


FIG. 4A

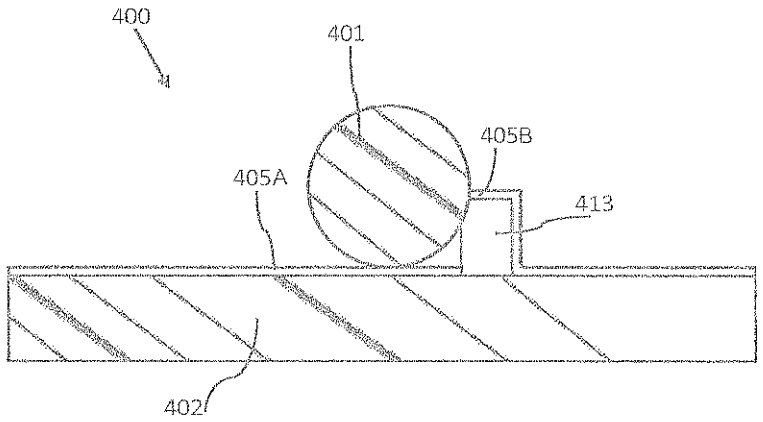


FIG. 4B

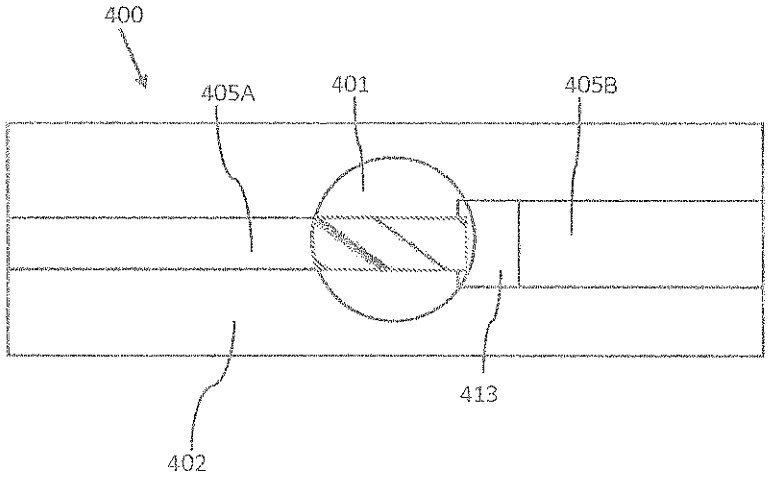


FIG. 4C

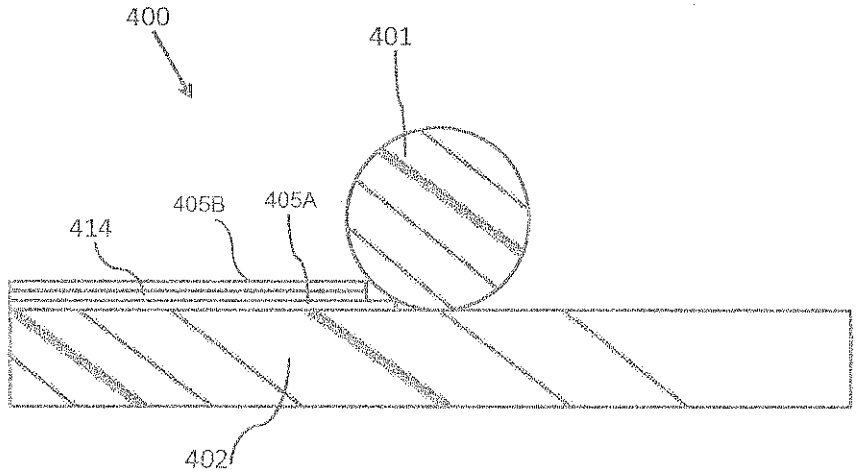

400
401
405B
405A
414
402

FIG. 4D

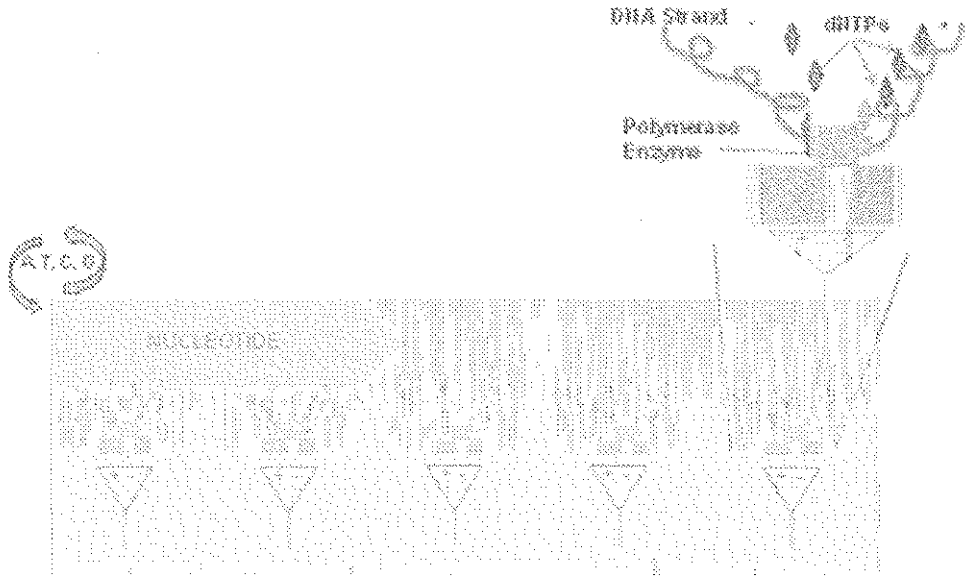

DNA Strand
dNTPs
Polymerase
Enzyme
A T C G
NUCLEOTIDE

FIG. 5A

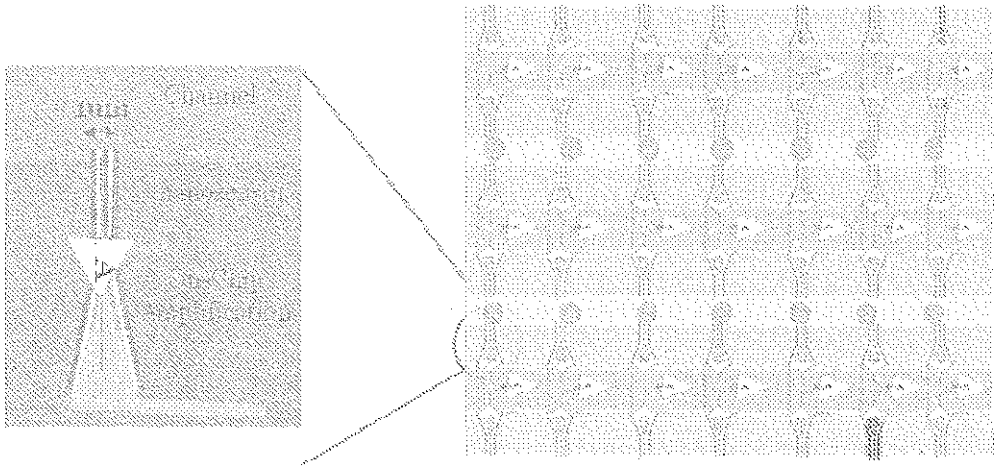


FIG. 5B

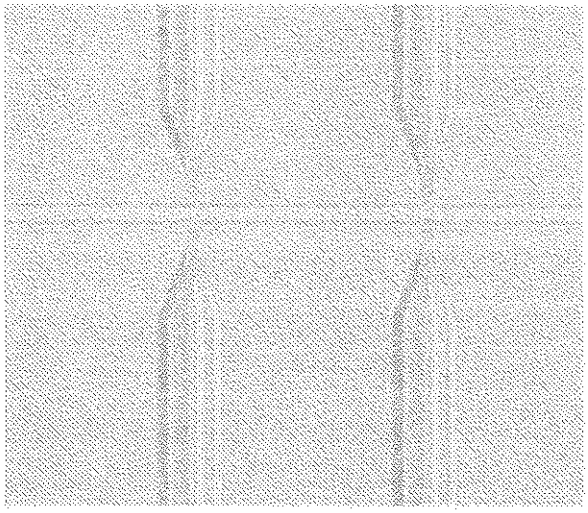


FIG. 6

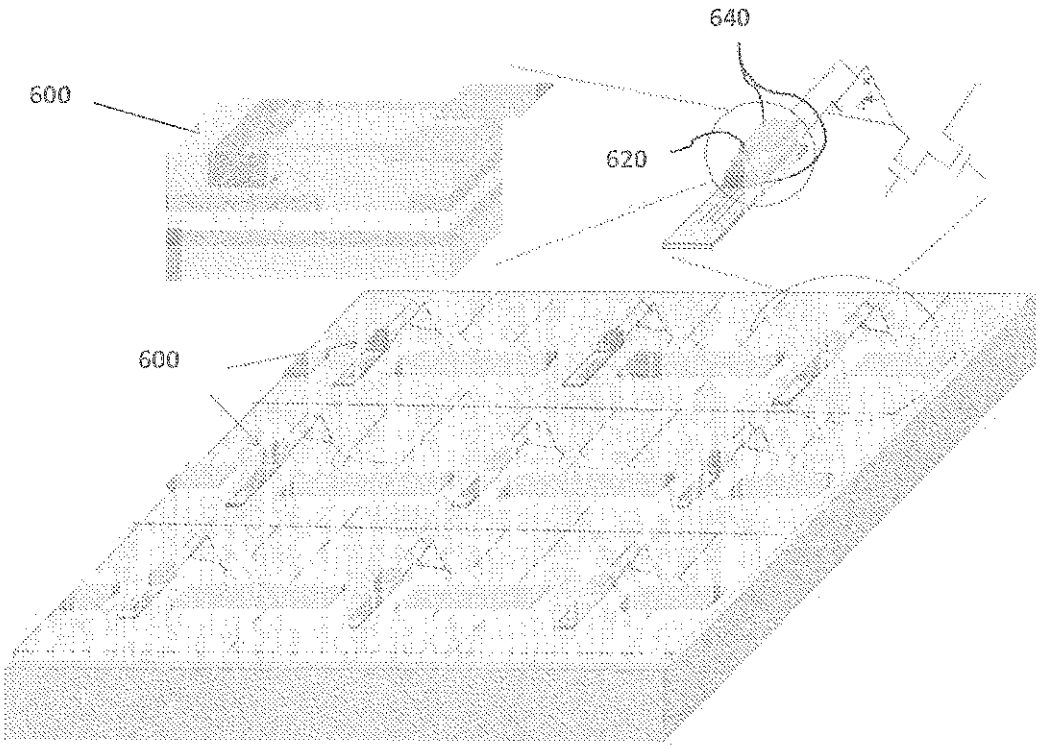


FIG. 7

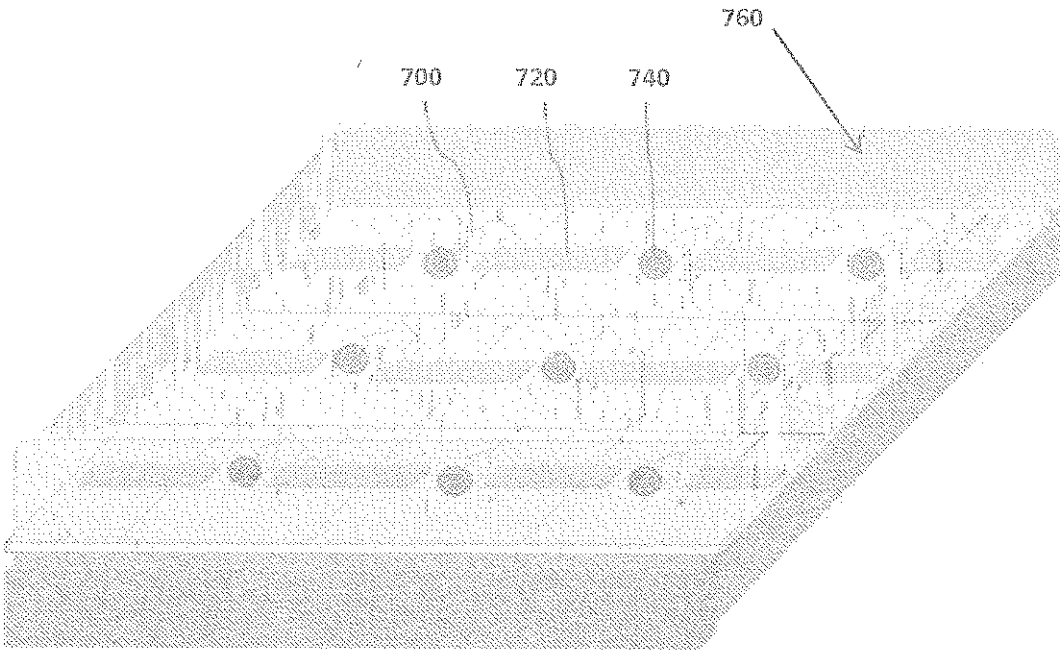


FIG. 8

hydroquinone ⇌ *p*-benzoquinone + $2H^+$ + 2e;
$E^\circ_{red} = 0.699$ V (vs SHE)

$2H_2O(l) \rightleftharpoons O_2(g) + 4H^+ + 4e$; $E^\circ_{red} = 1.229$ V (vs SHE)

anodic reaction $C_6H_4O_2H_2 \rightarrow C_6H_4O_2 + 2H^+(aq) + 2e^-$ cathodic reaction $C_6H_4O_2 + 2H_2O + 2e^- \rightarrow C_6H_4O_2H_2 + 2OH^-$

FIG. 9A

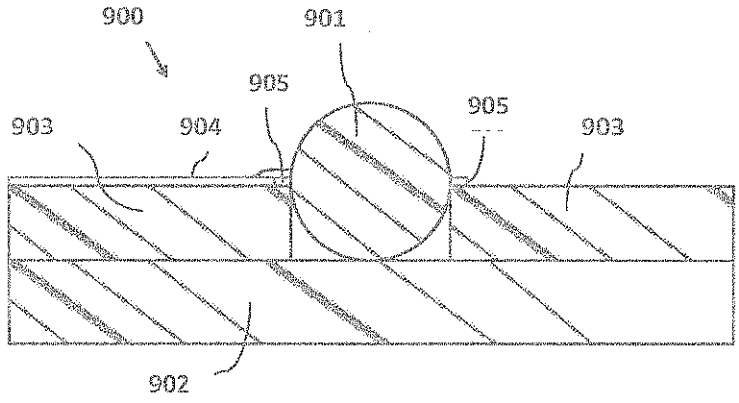


FIG. 9B

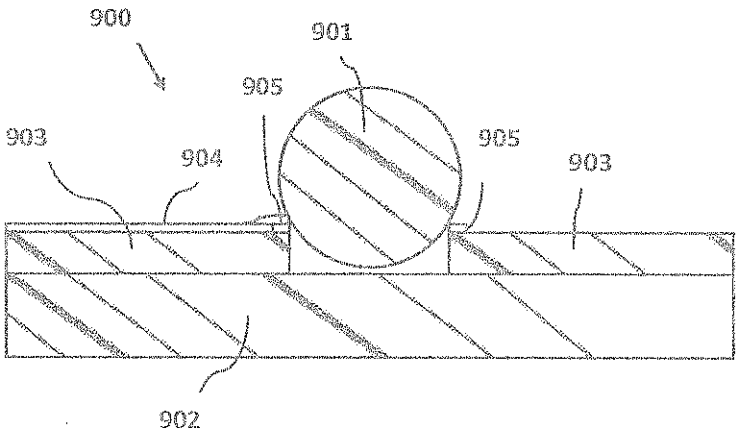


FIG. 9C

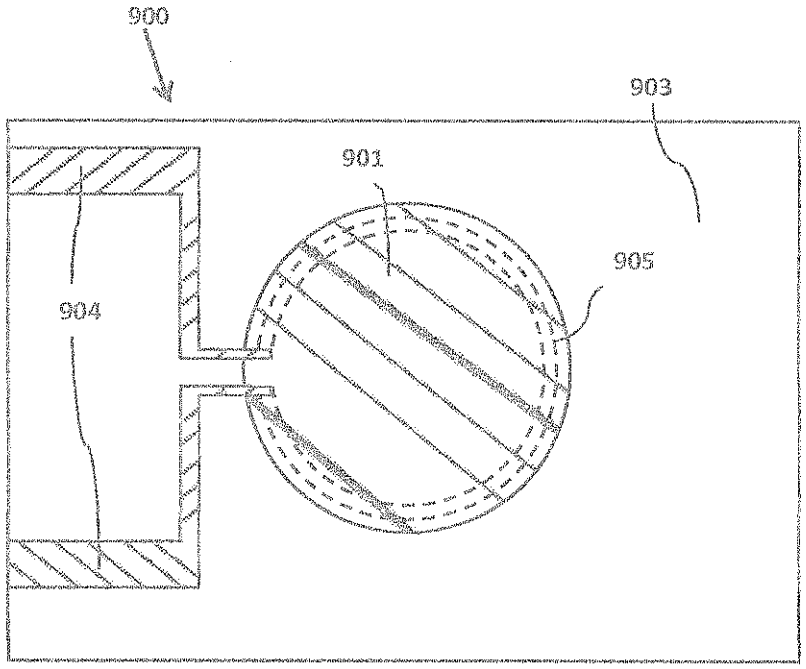


FIG. 10

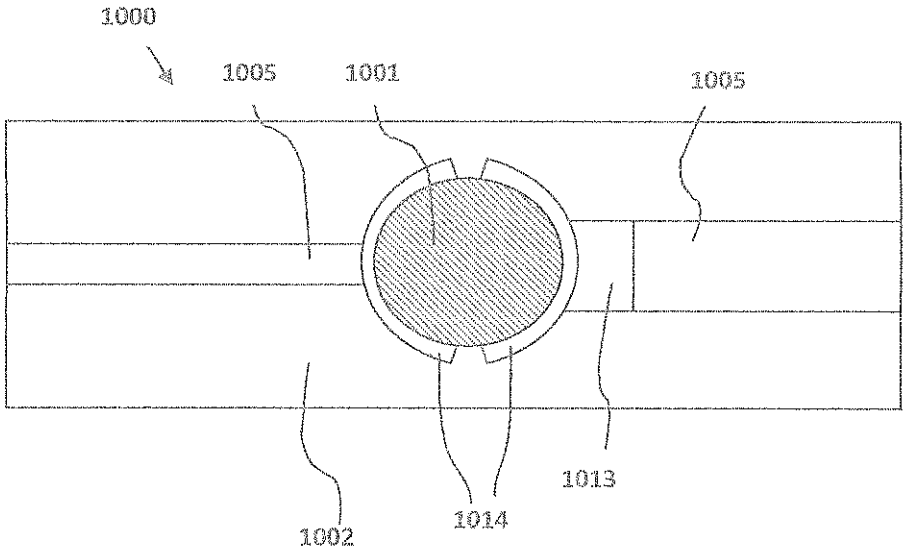


FIG. 11A

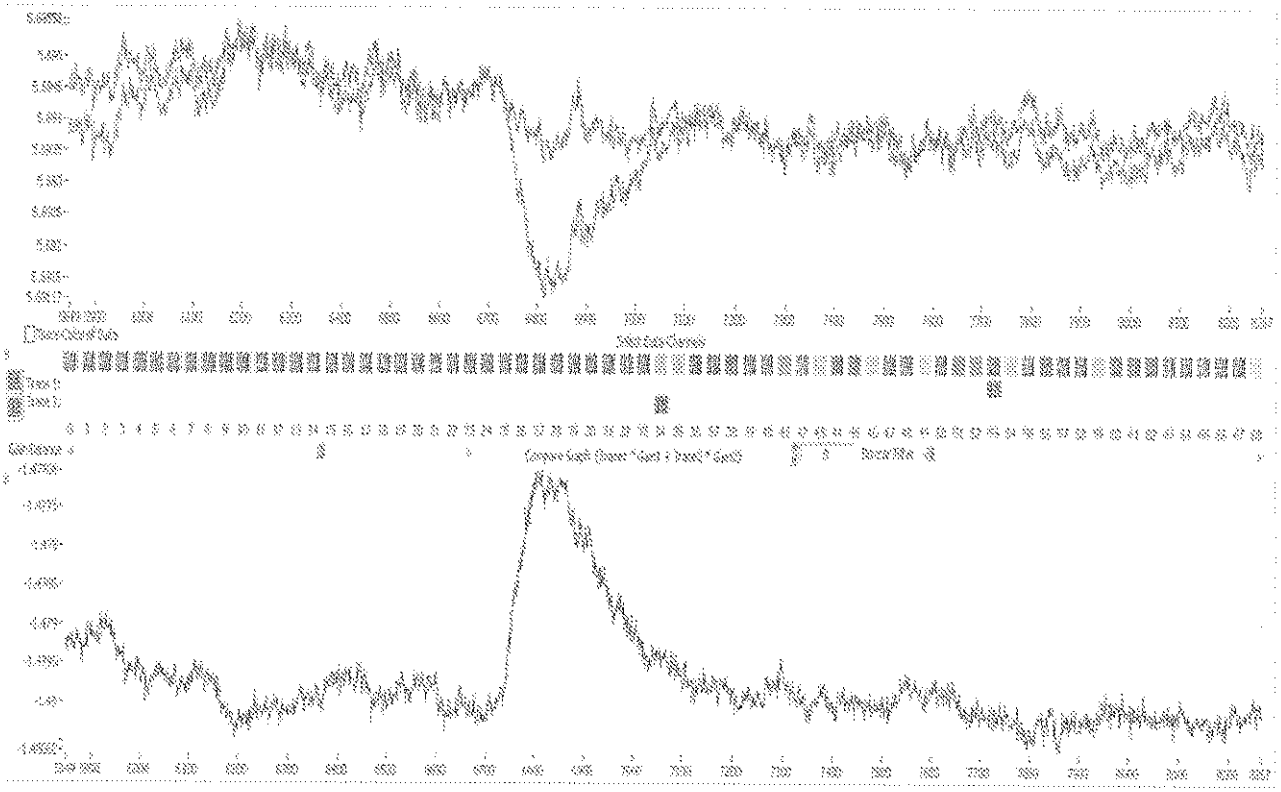


FIG. 11B

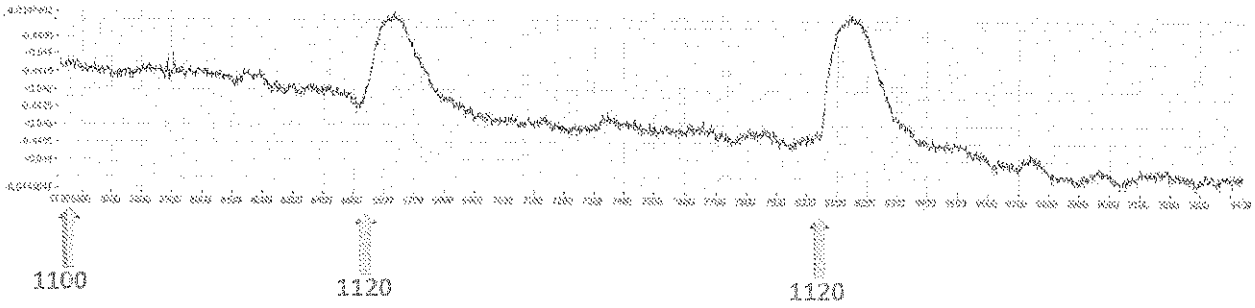


FIG. 11C

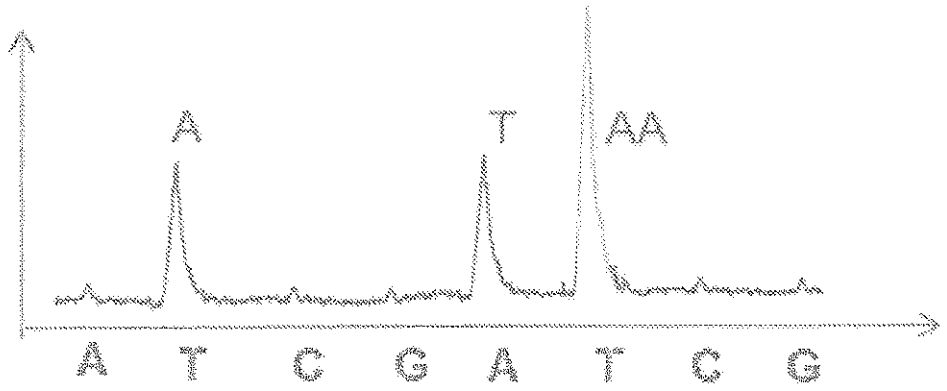


FIG. 12A

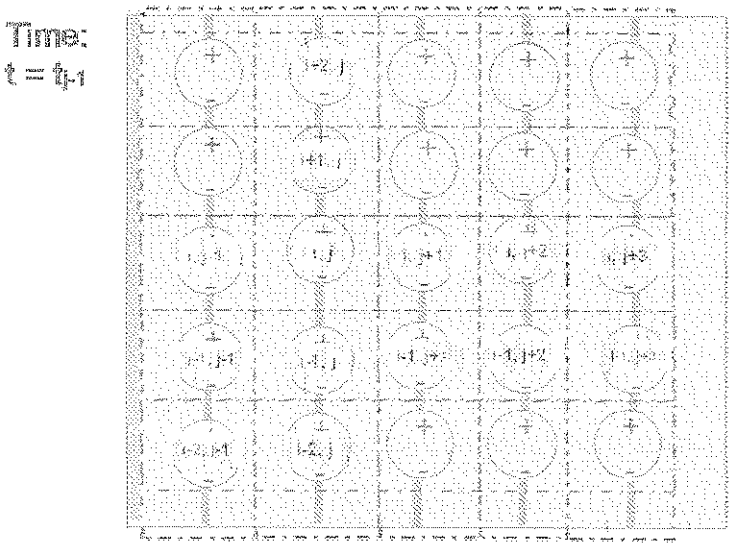
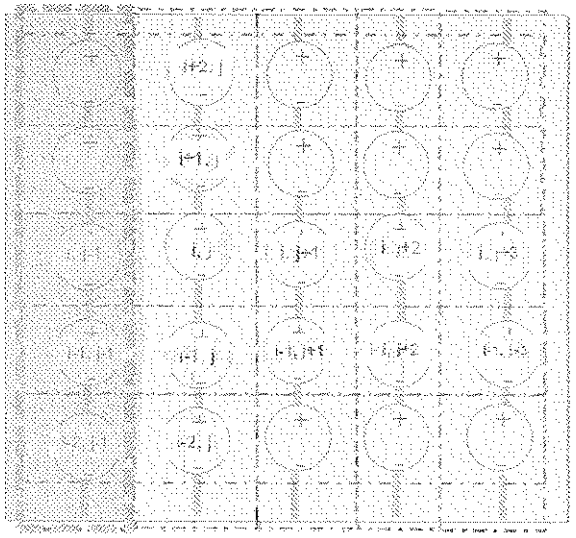


FIG. 12B



In case of constant speed flow:

$t \sim = t_0 + dt$

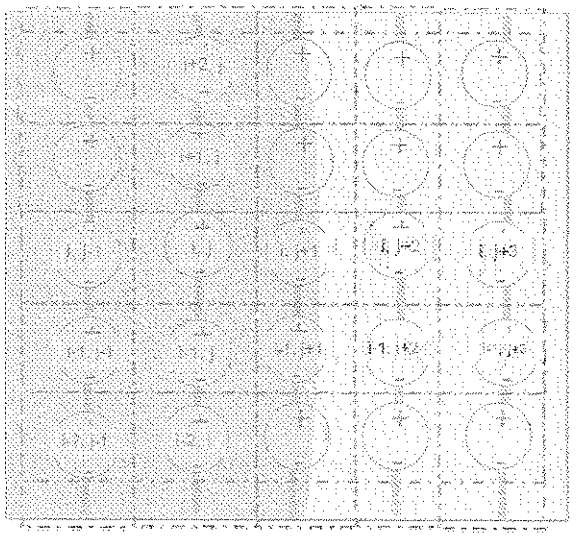
t_{j-1} is the time that the flow hit the "j-1" column (in average).

The time that we like to monitor the reaction of cells in column j-1 is around (record the signal of j-1 column sensors):

$$dt_{j-1} \sim = t_j - t_{j-1} (+ t_{reaction})$$

rather than continues read out of the cells

FIG. 12C



In case of constant speed flow :

$t_{j+1} \sim = t_0 + 3dt$

t_{j+1} is the time that the flow hit the "j+1" column (in average) at first point.

The time that we like to monitor the reaction of cells in column j+1 is around (record the signal of j+1 column sensors):

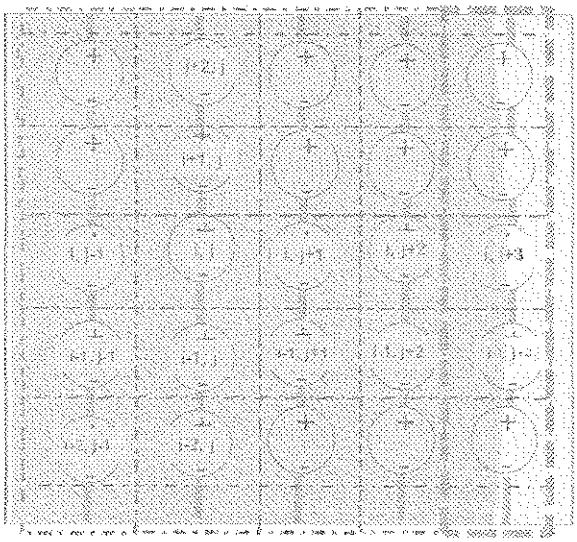
$$dt_{j+3} \sim = t_{j+2} - t_{j+1} (+ t_{reaction})$$

rather than continues read out of the cells

FIG. 12D

In case of constant speed flow :

$t_{j+3} \sim = t_0 + 5dt$



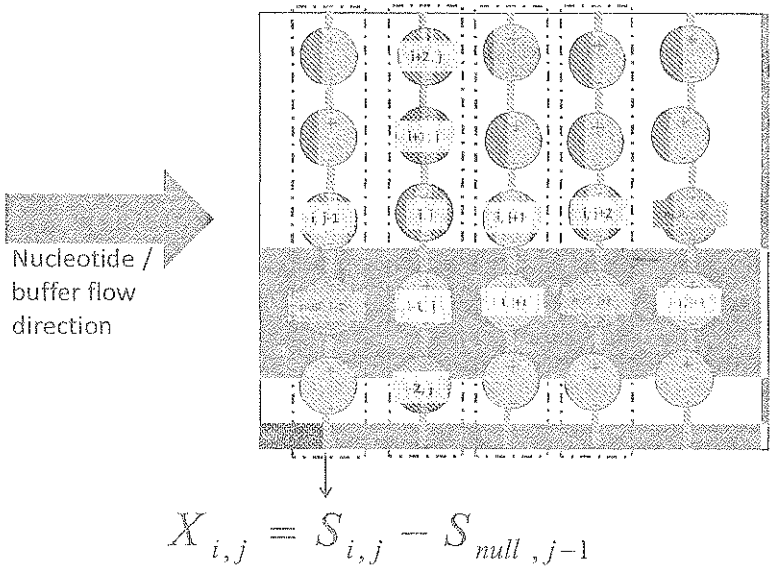
t_{j+3} is the time that the flow hit the "j+3" column (in average) at first point.

The time that we like to monitor the reaction of cells in column j+3 is around (record the signal of j+3 column sensors):

$dt_{j+3} \sim = t_{j+4} - t_{j+3}$ (+ bias)

rather than continues read out of the cells

FIG. 12E



$$X_{i,j} = S_{i,j} - S_{null,j-1}$$

FIG. 12F

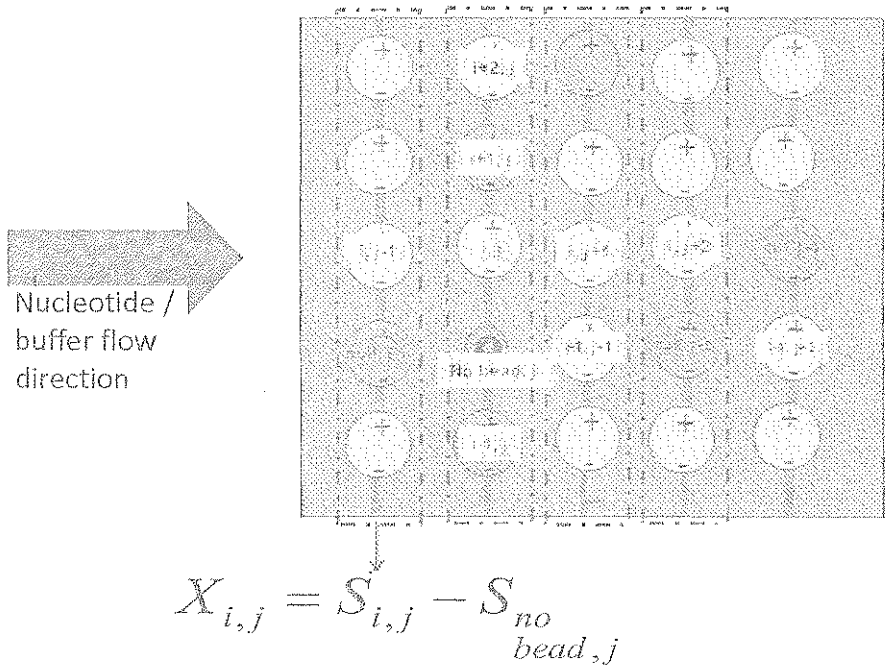


FIG. 12G

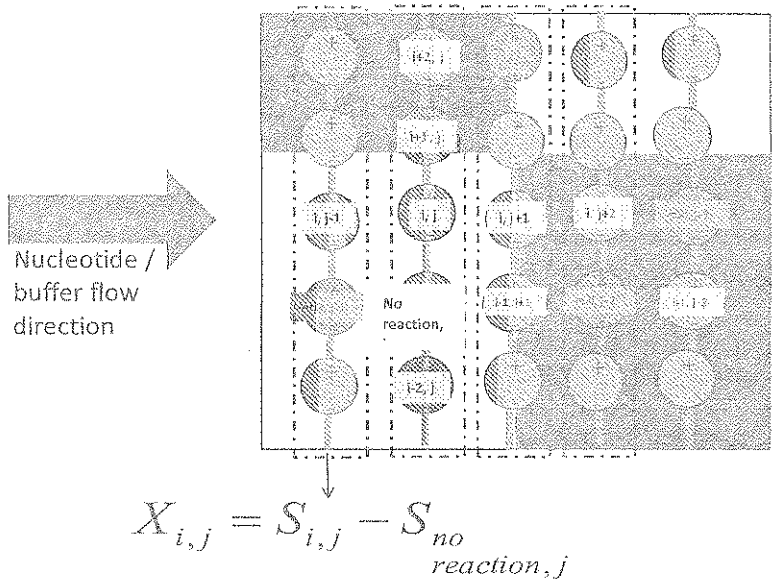
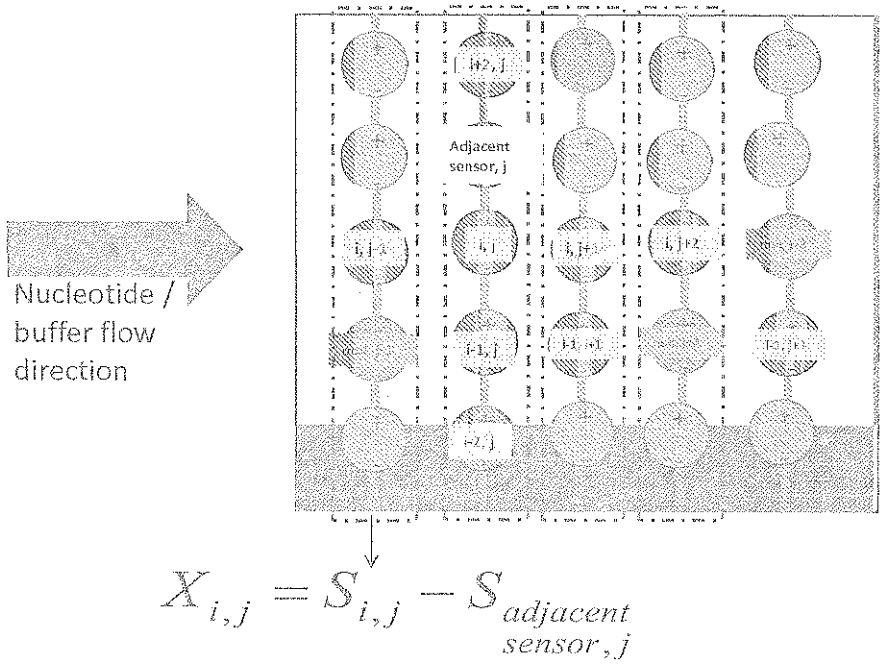
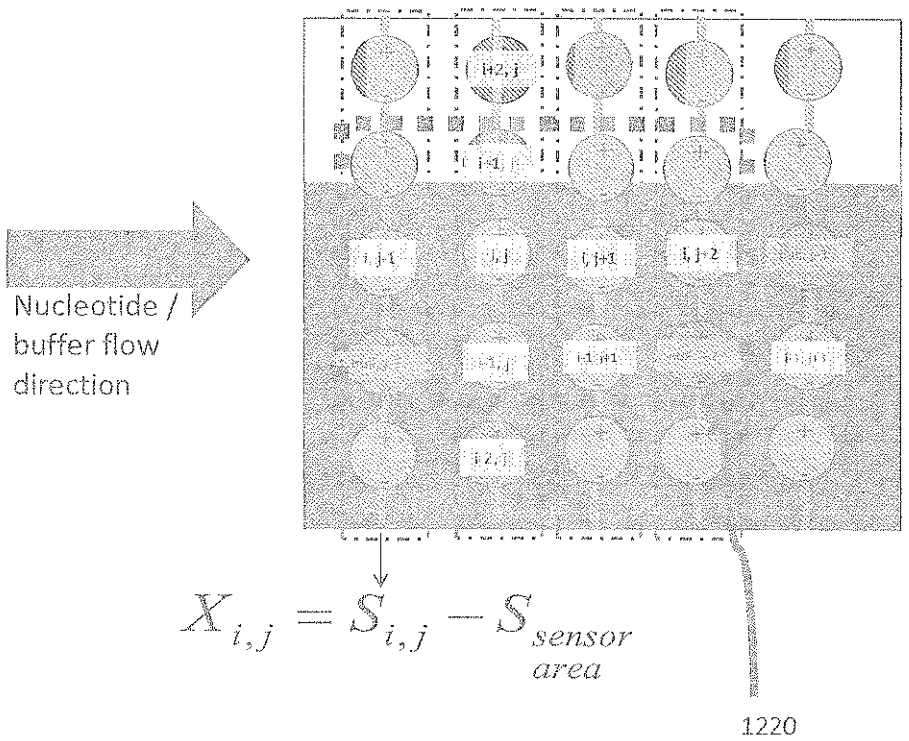


FIG. 12H



$$X_{i,j} = S_{i,j} - S_{\substack{adjacent \\ sensor,j}}$$

FIG. 12I



$$X_{i,j} = S_{i,j} - S_{\substack{sensor \\ area}}$$

FIG. 12J

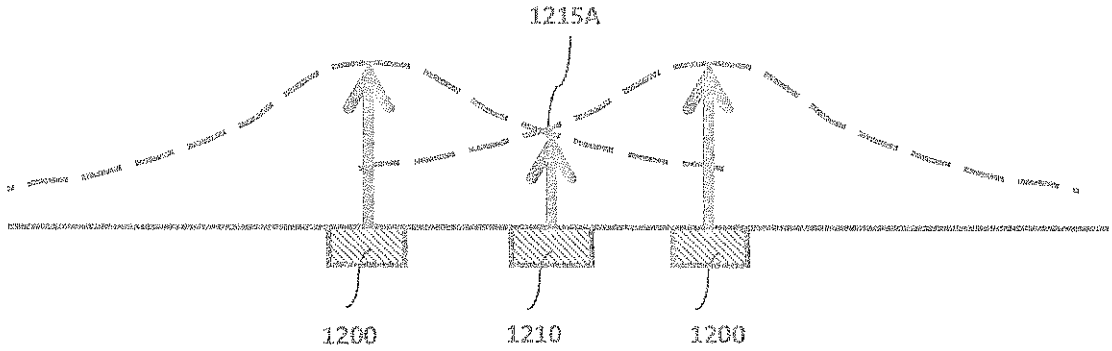


FIG. 12K

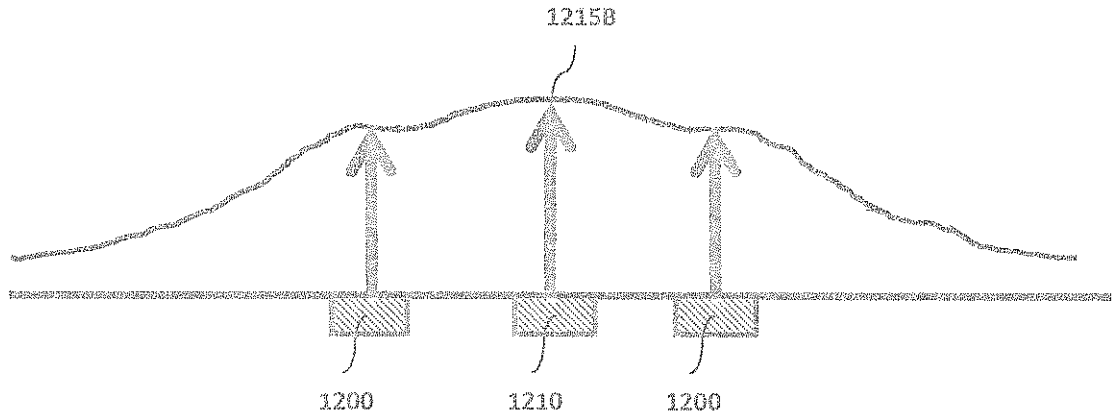
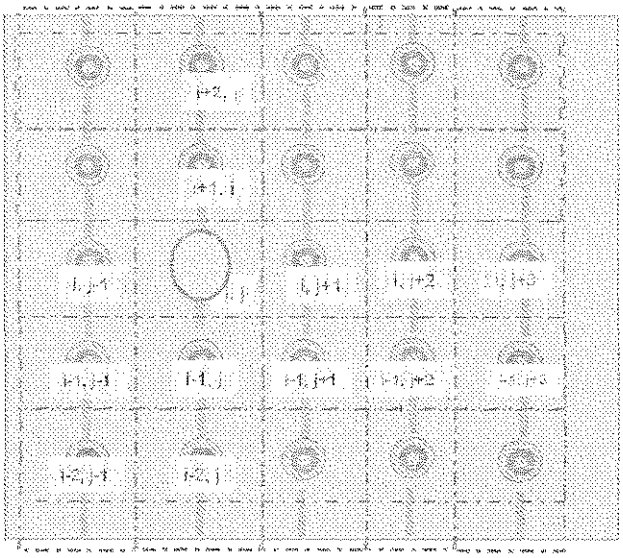


FIG. 12L

Calibration:
- Monitor the effect of a DNA-bead signal (or any signal) from a pixel on the neighbor cells (by reading with the neighbor sensors).
-Extract the nxn matrix of Ai,j for each pixel/cell either in time or frequency domain
- post processing the output signals during the sequencing of beads by inverse post-processing.

$$Ai,j(t) = \begin{bmatrix} \dots & A_{(k,p)} & \dots \\ f(\text{cell } (k,p) \text{ over cell}(i,j)) & & \end{bmatrix}$$



$$Ai,j(k,p) = f(\text{cell } (k,p) \text{ over cell}(i,j))$$

FIG. 12M

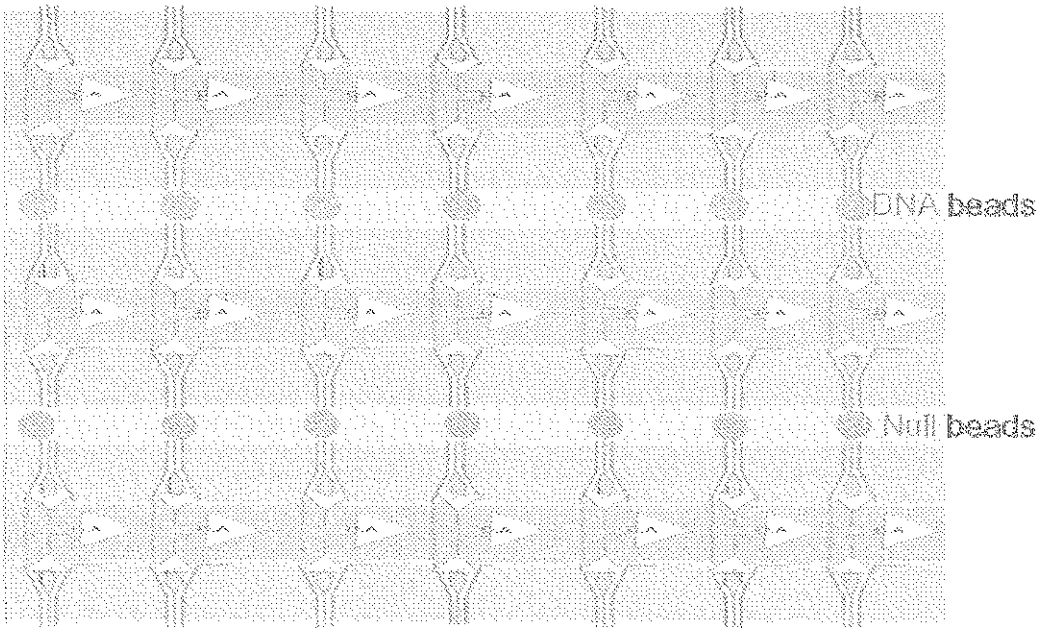


FIG. 12N

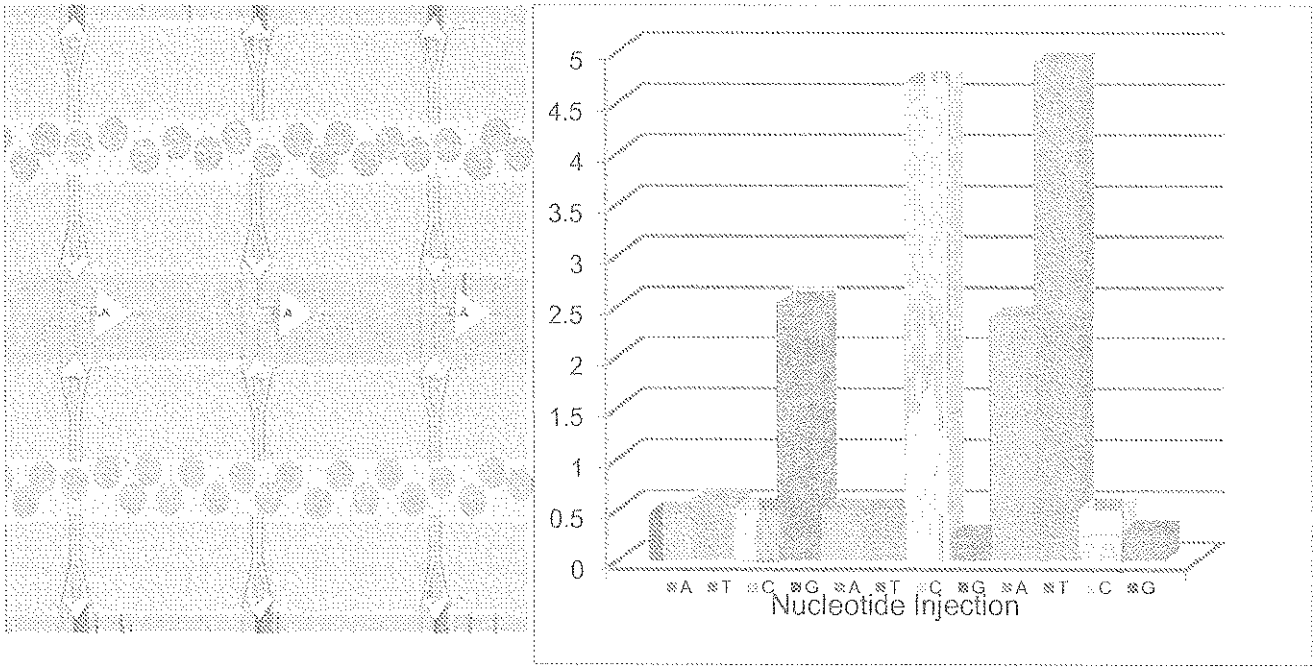


FIG. 13B

$$DNA_n + dNTP \xrightarrow{\text{polymerase}} DNA_{n+1} + PPi + \underset{\sim\sim\sim\sim\sim\sim\sim}{\Delta H} + \Delta pH + \underline{\Delta Q}$$

FIG. 14

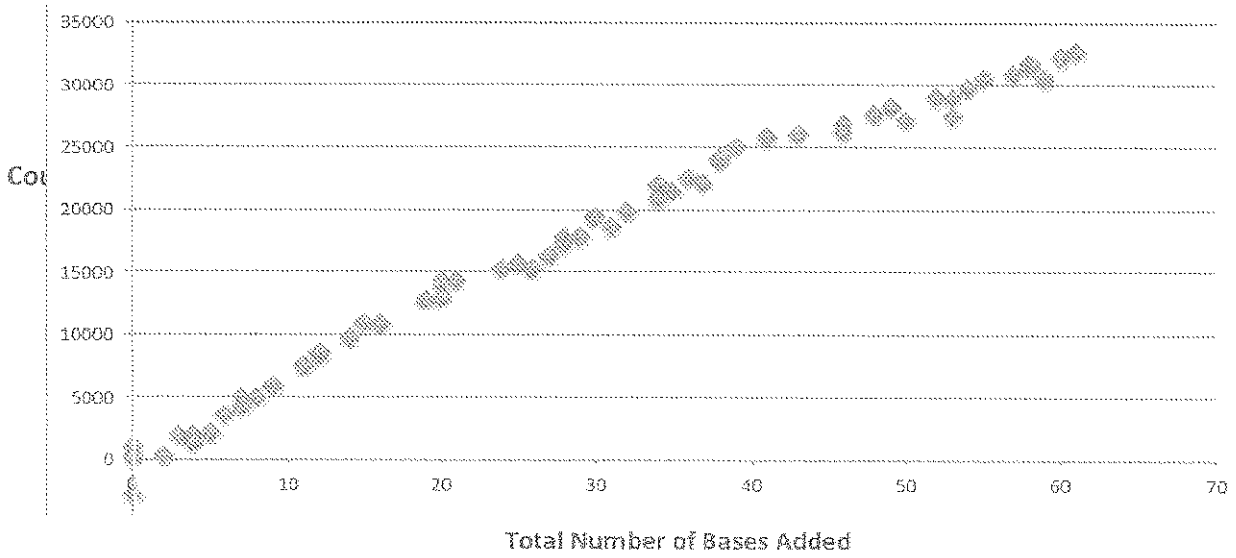


FIG. 15

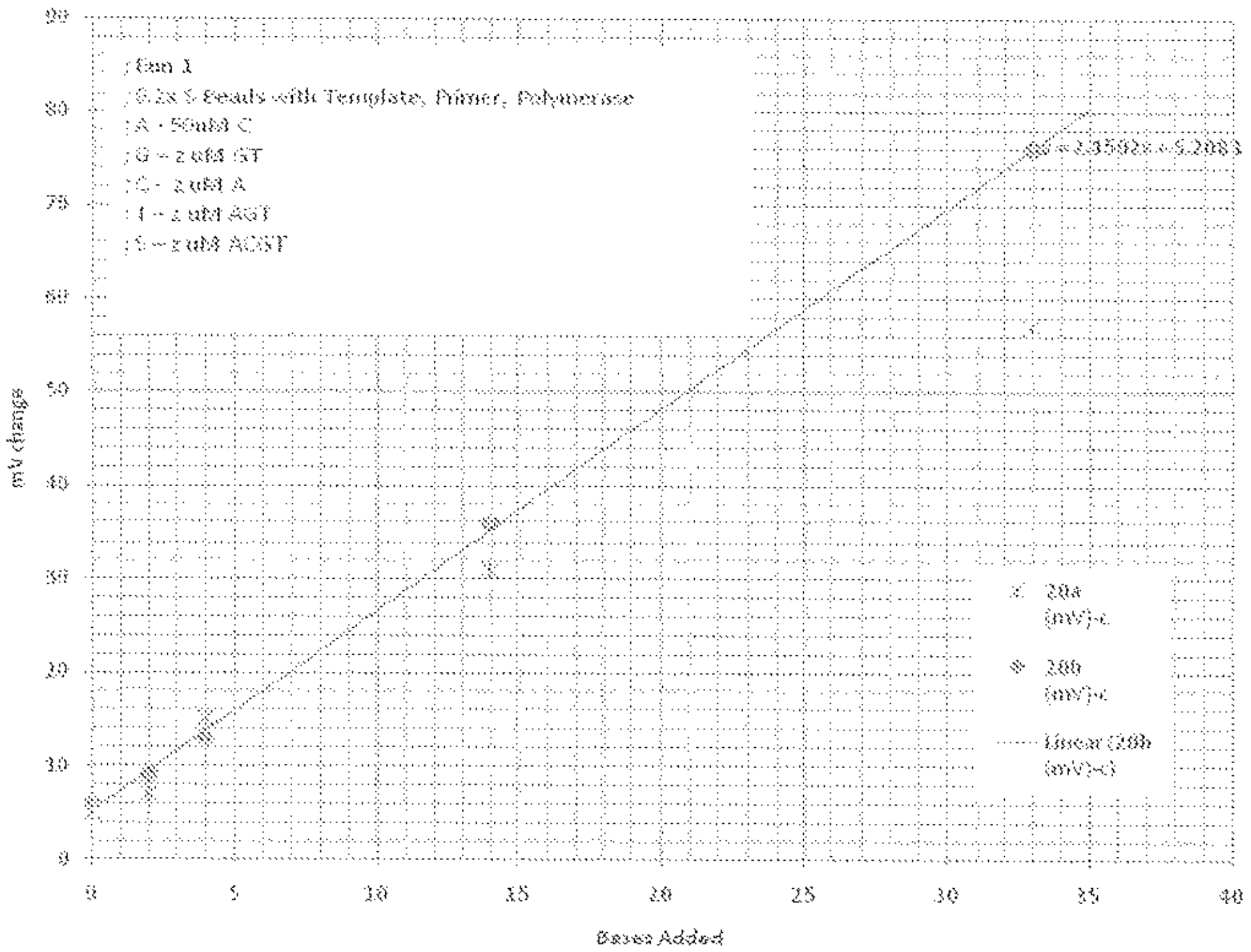

mV change
Bases Added
20a (mV)-c
20b (mV)-c
Linear (20b (mV)-c)

FIG. 16

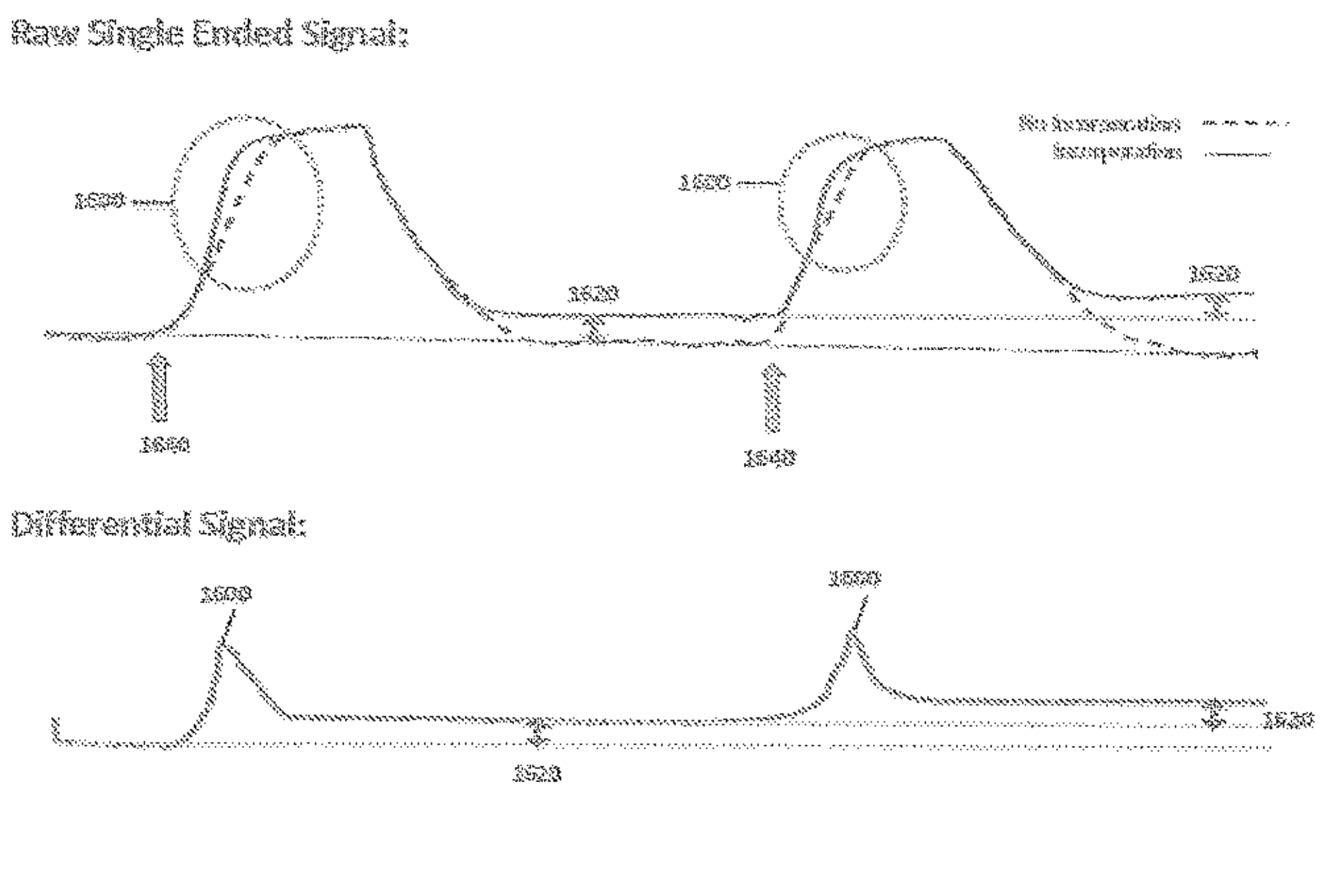

Raw Single Ended Signal:
No Incorporation
Incorporation
1620
1640
Differential Signal:
1620

FIG. 17

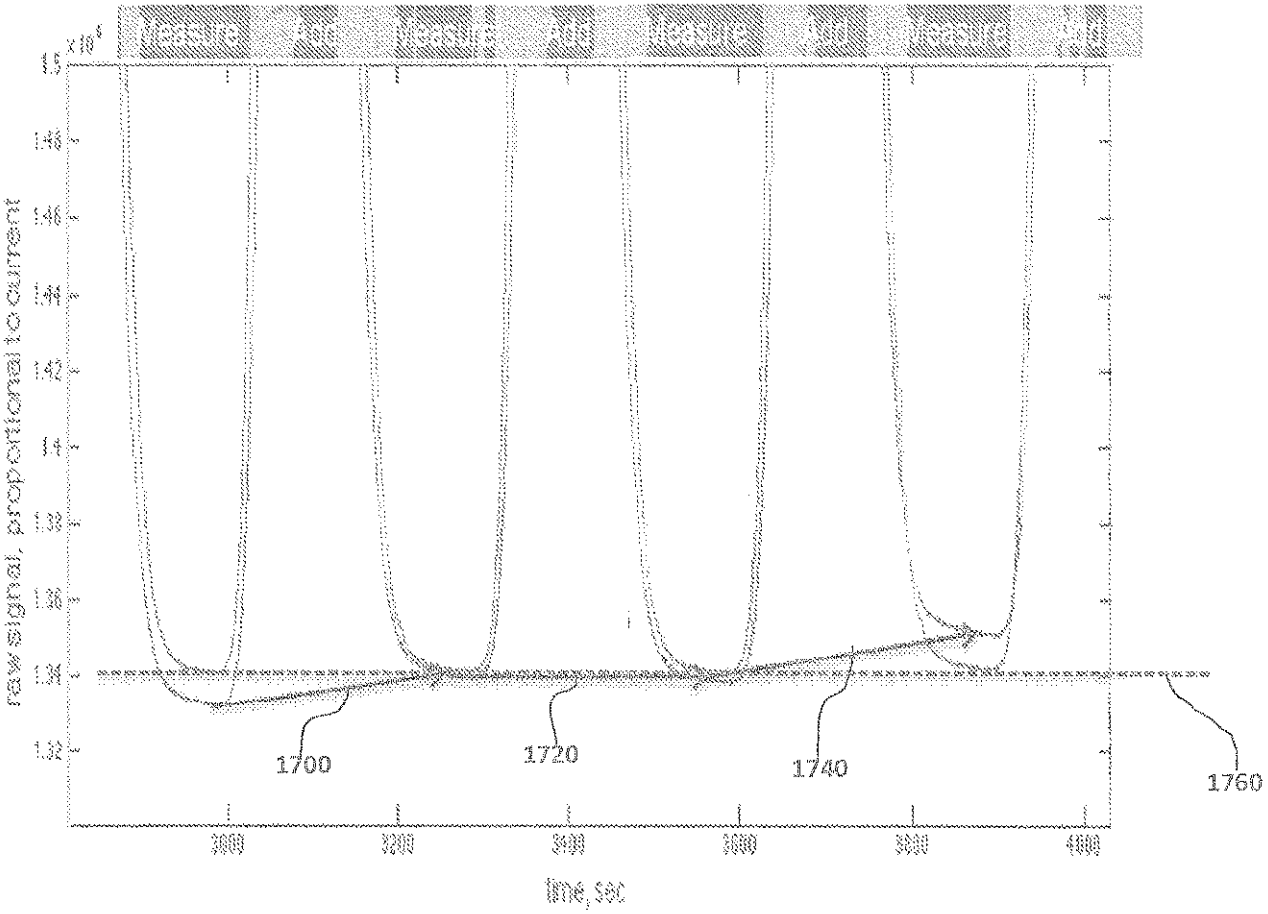

Measure
Add
Measure
Add
Measure
Add
Measure
Add
x10^4
1.5
1.48
1.46
1.44
1.42
1.4
1.38
1.36
1.34
1.32
raw signal, proportional to current
1700
1720
1740
1760
3000
3200
3400
3600
3800
4000
time, sec

FIG. 18A

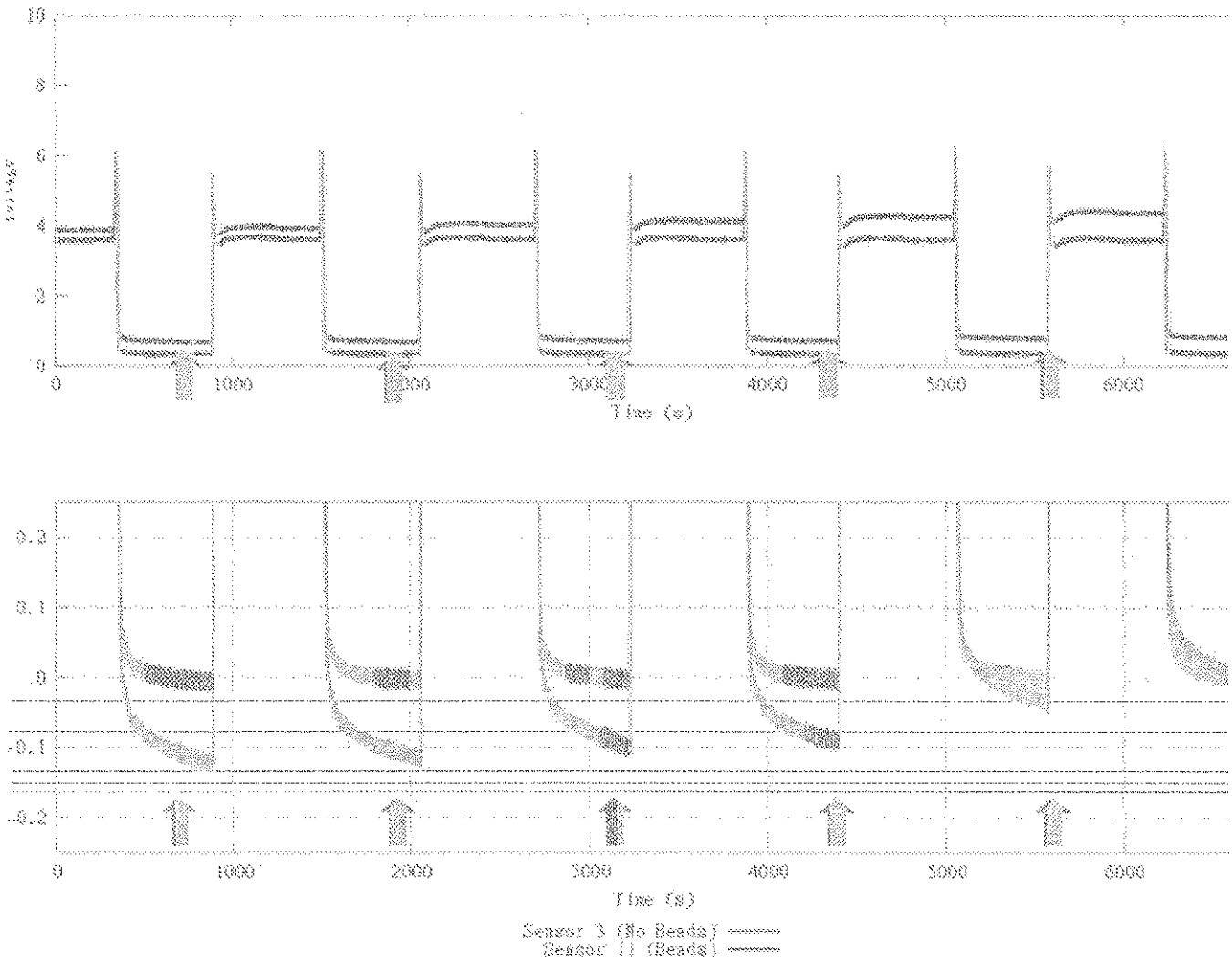

10
8
6
4
2
0
0
1000
2000
3000
4000
5000
6000
Time (s)
0.2
0.1
0
-0.1
-0.2
0
1000
2000
3000
4000
5000
6000
Time (s)
Sensor 3 (No Beads)
Sensor 1 (Beads)

FIG. 18B

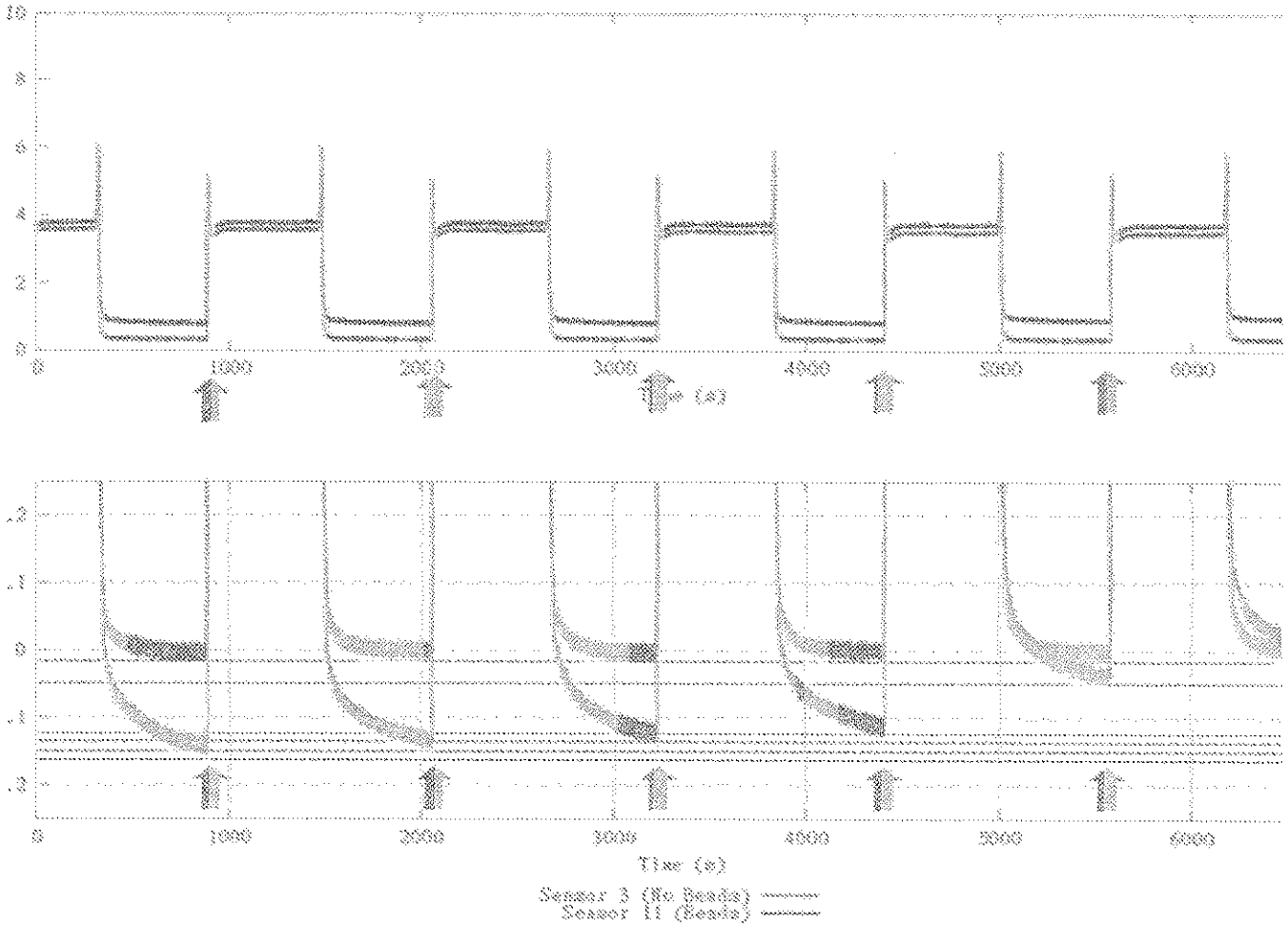


FIG. 19A

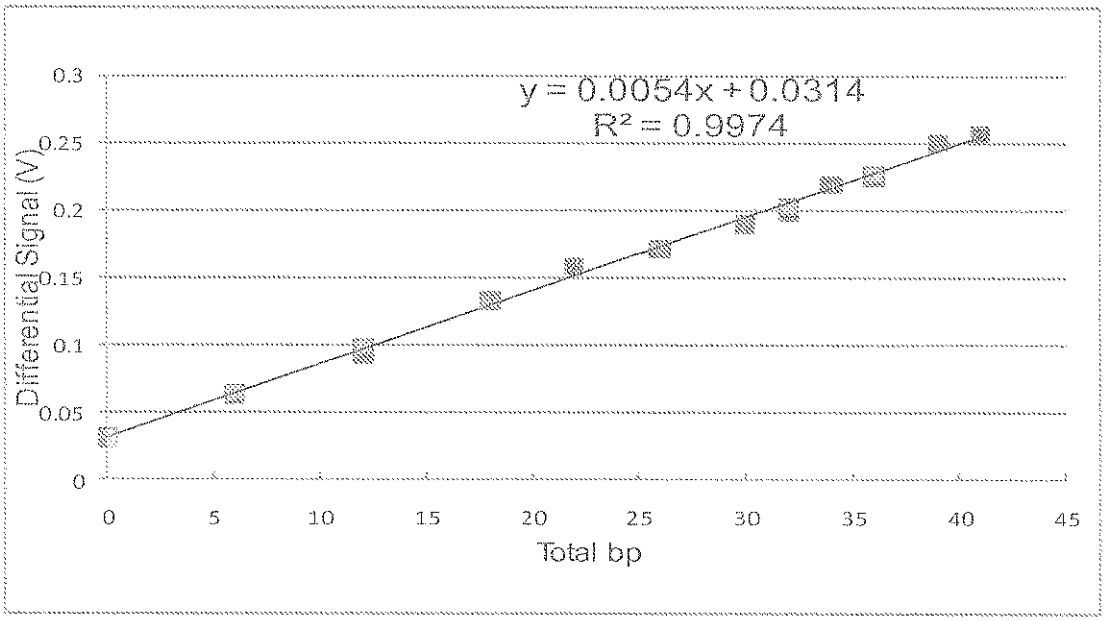


FIG. 19B

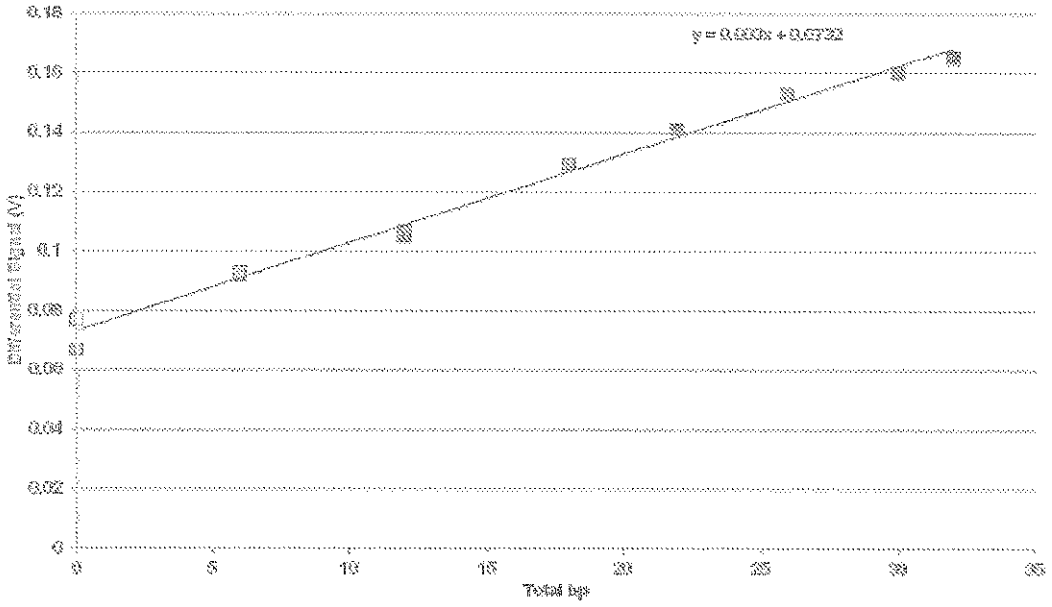


FIG. 19C

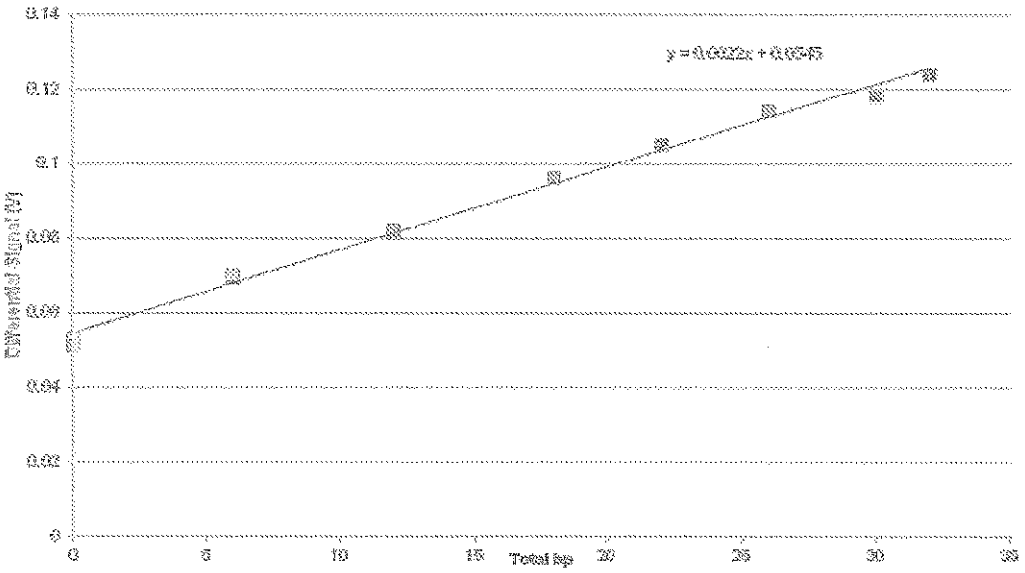


FIG. 20

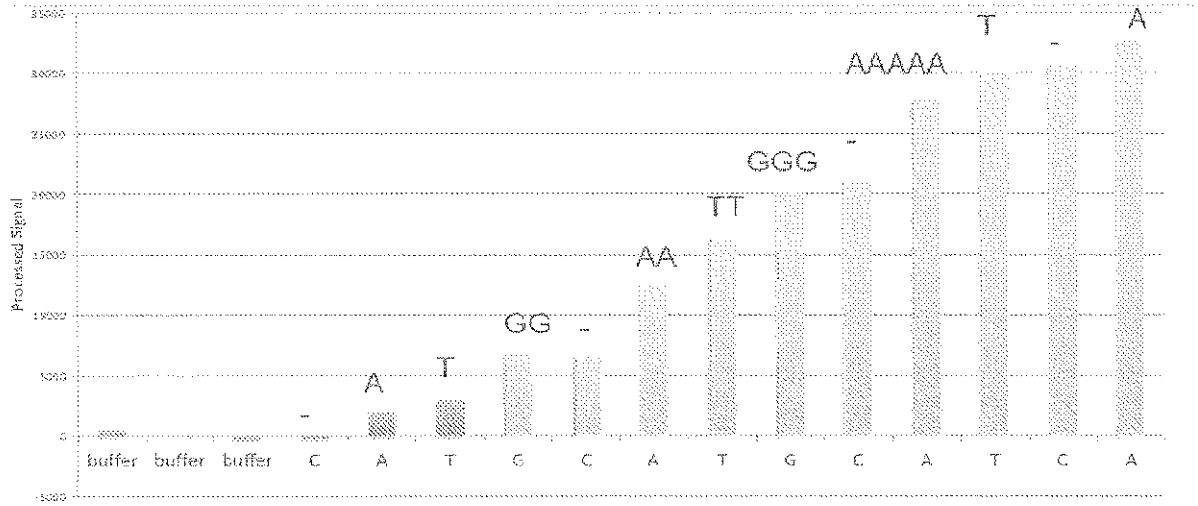

Processed Signal
buffer
buffer
buffer
C
A
T
G
C
A
T
G
C
A
T
C
A
A
T
GG
AA
TT
GGG
AAAAA
T
A

FIG. 21

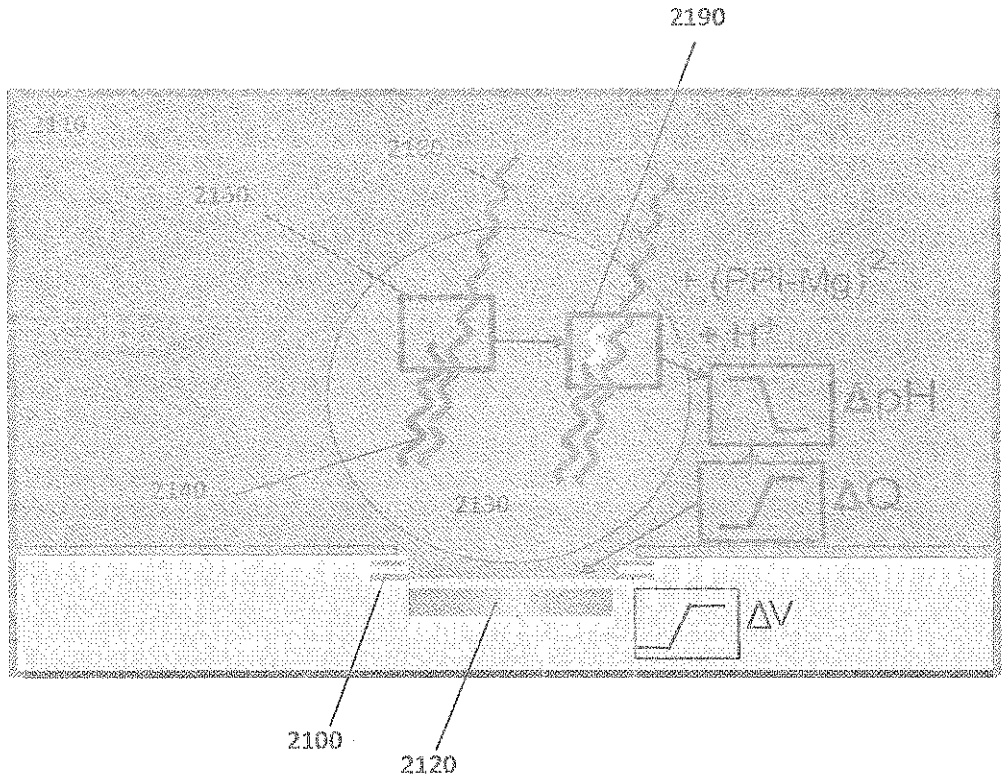

2190
2110
2130
$(PPi-Mg)^{2-}$
H^+
ΔpH
ΔQ
ΔV
2100
2120

FIG. 22A

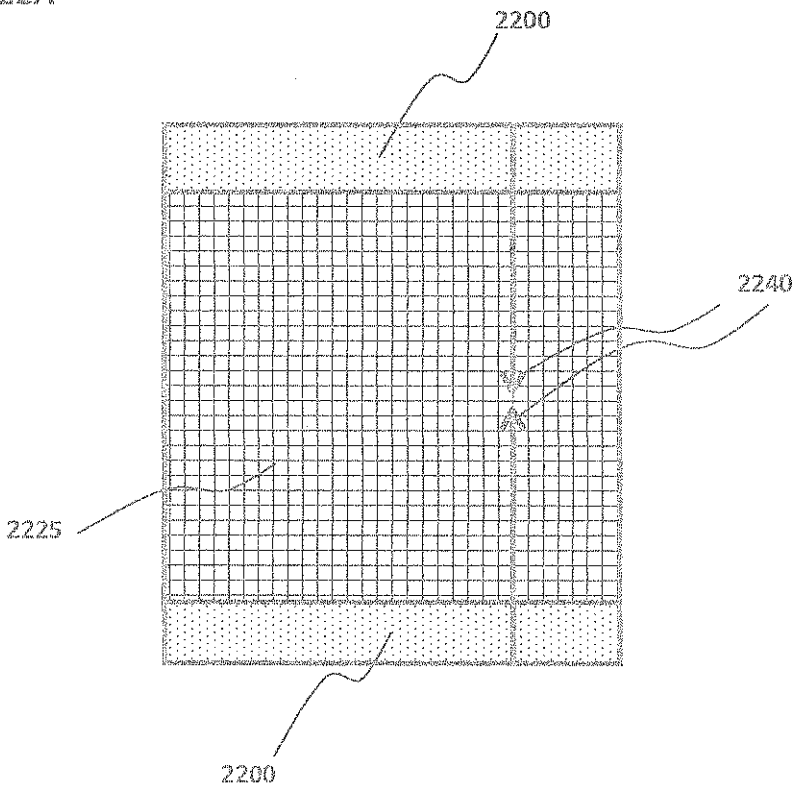


FIG. 22B

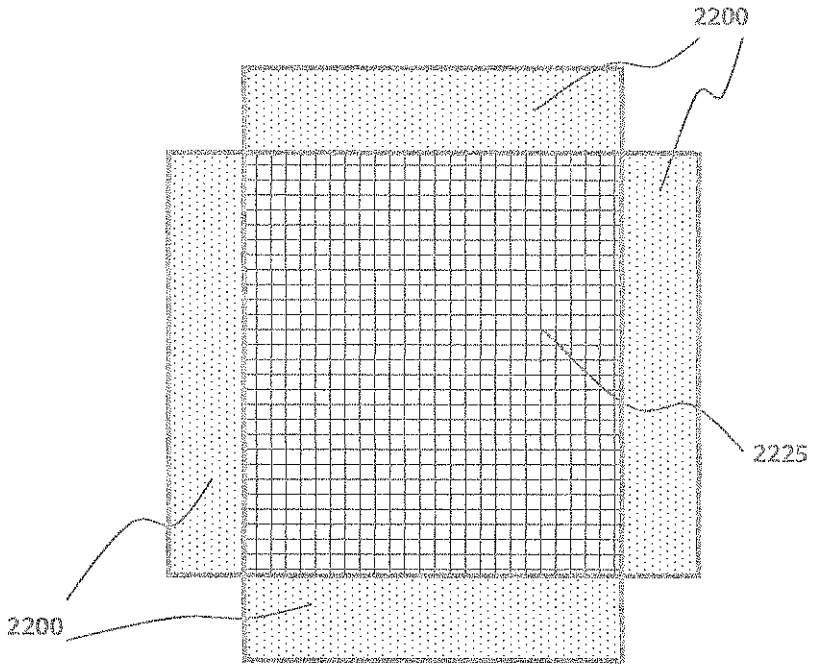


FIG. 23

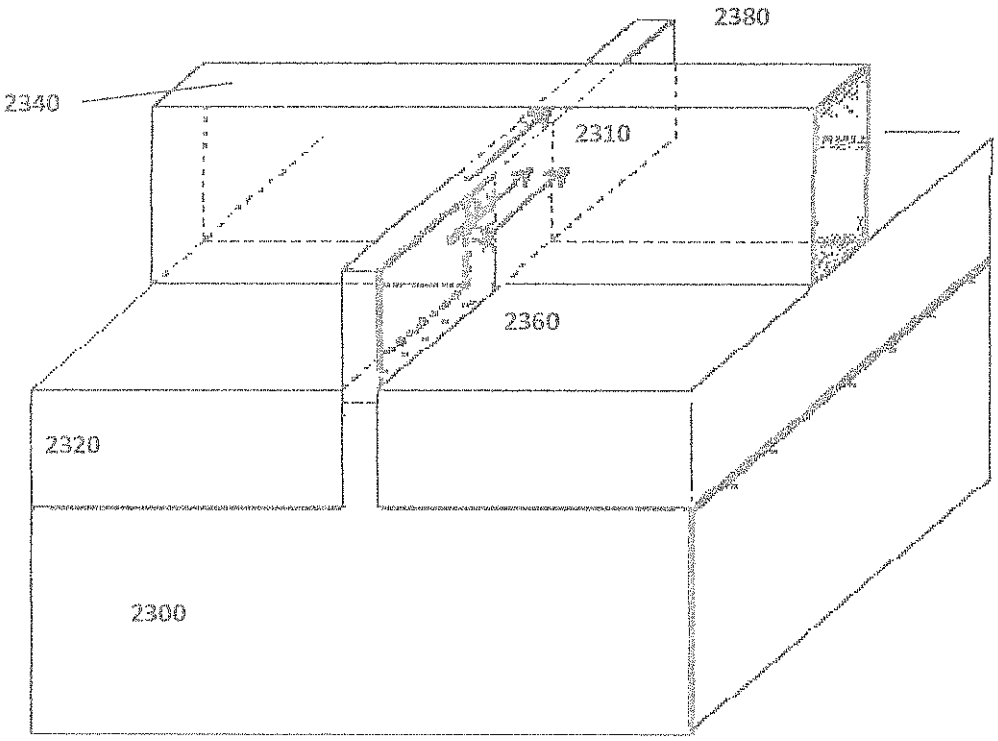


FIG. 24

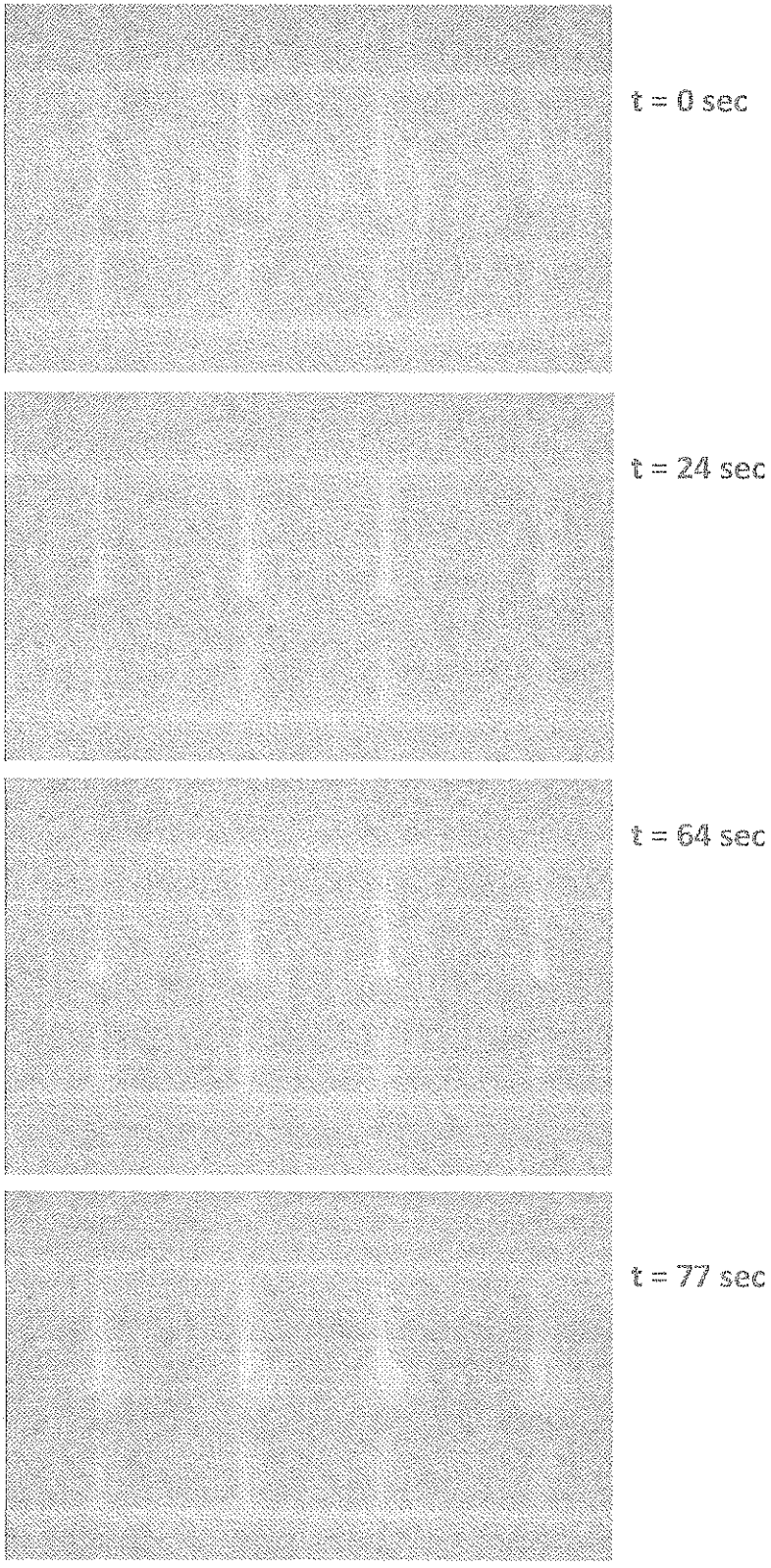


FIG. 25

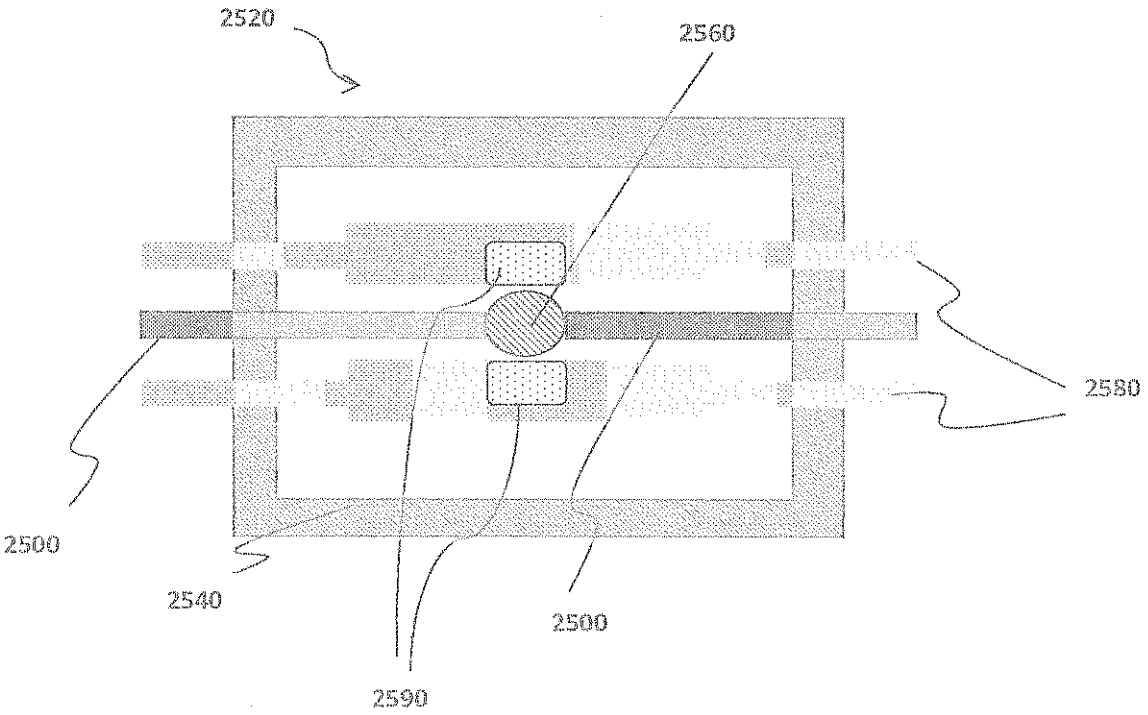


FIG. 26

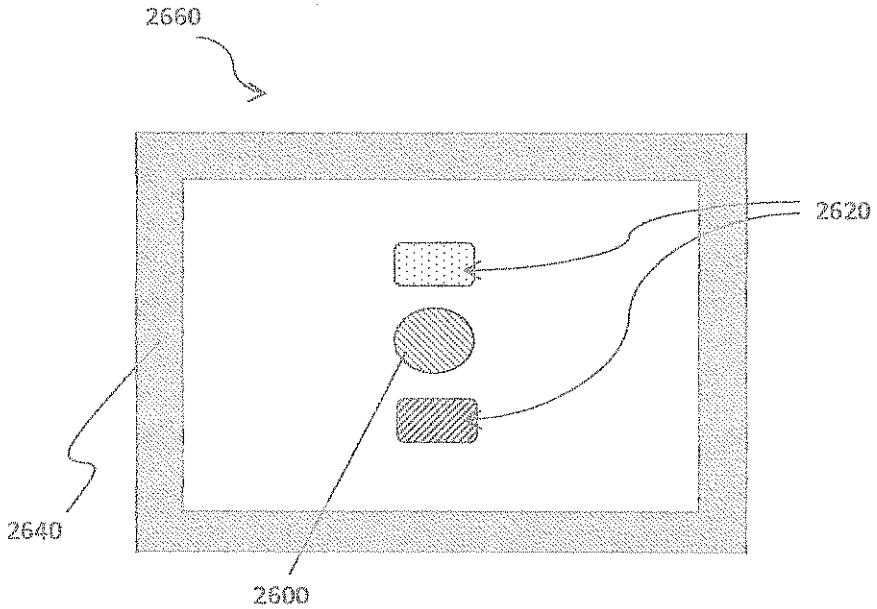


FIG. 27A

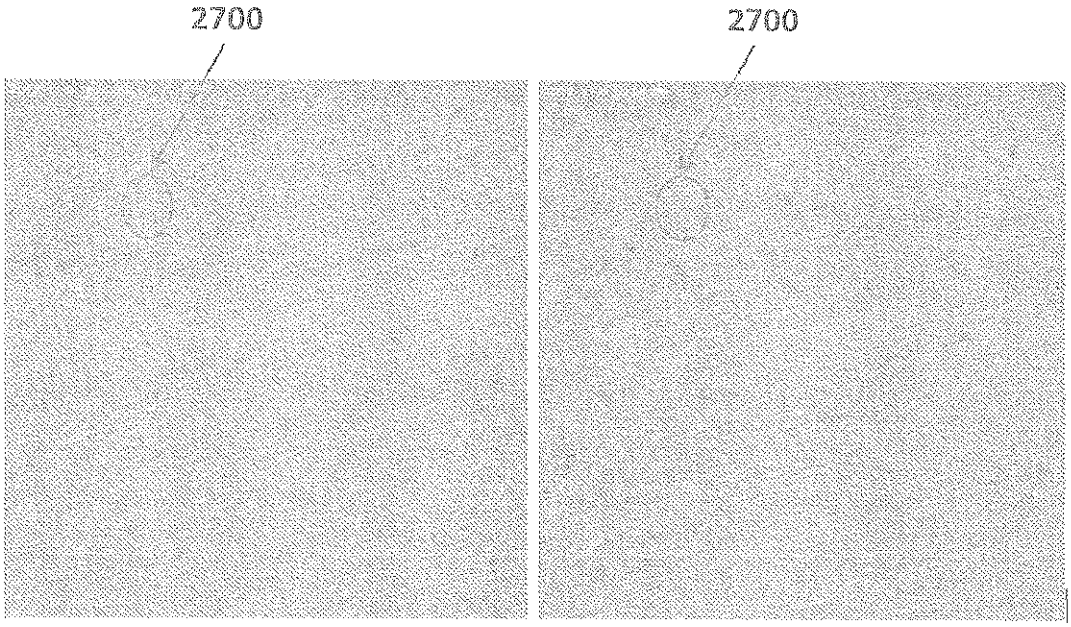


FIG. 27B

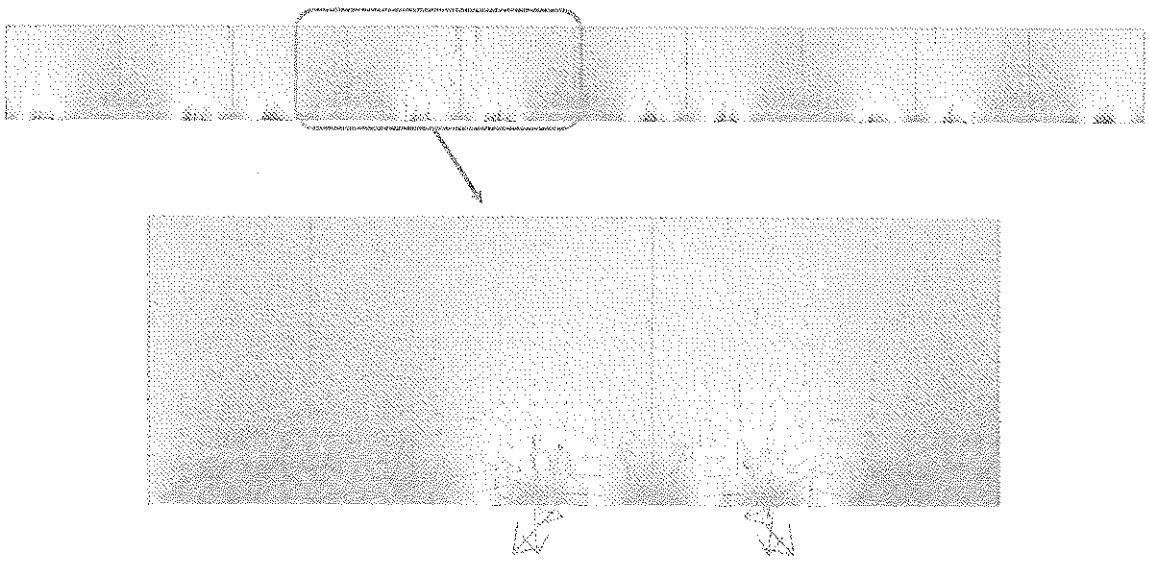


FIG. 27C

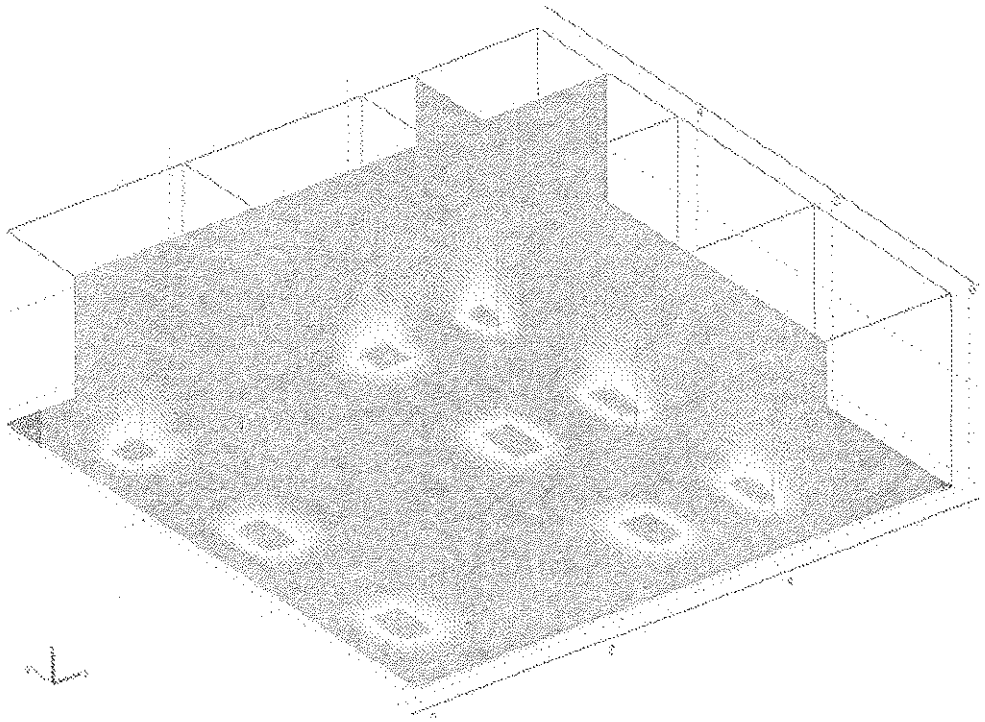


FIG. 28

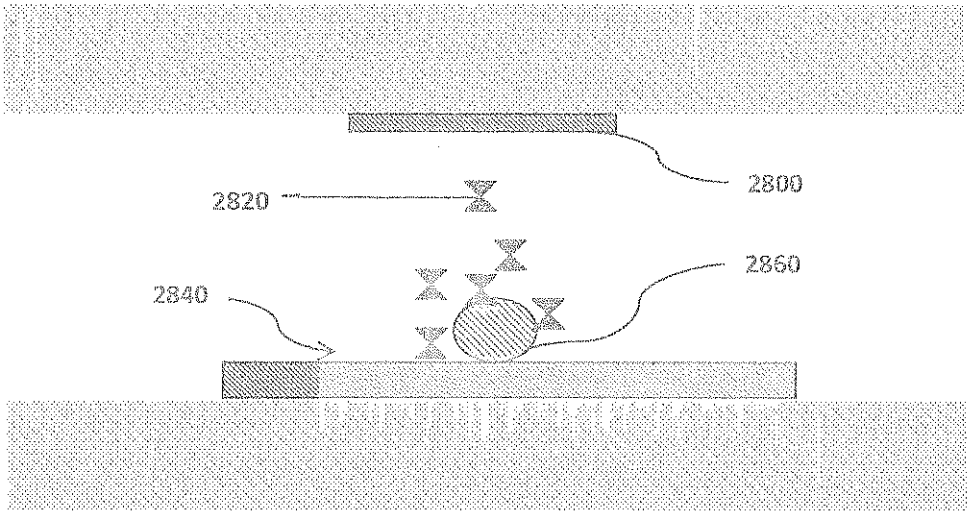


FIG. 29

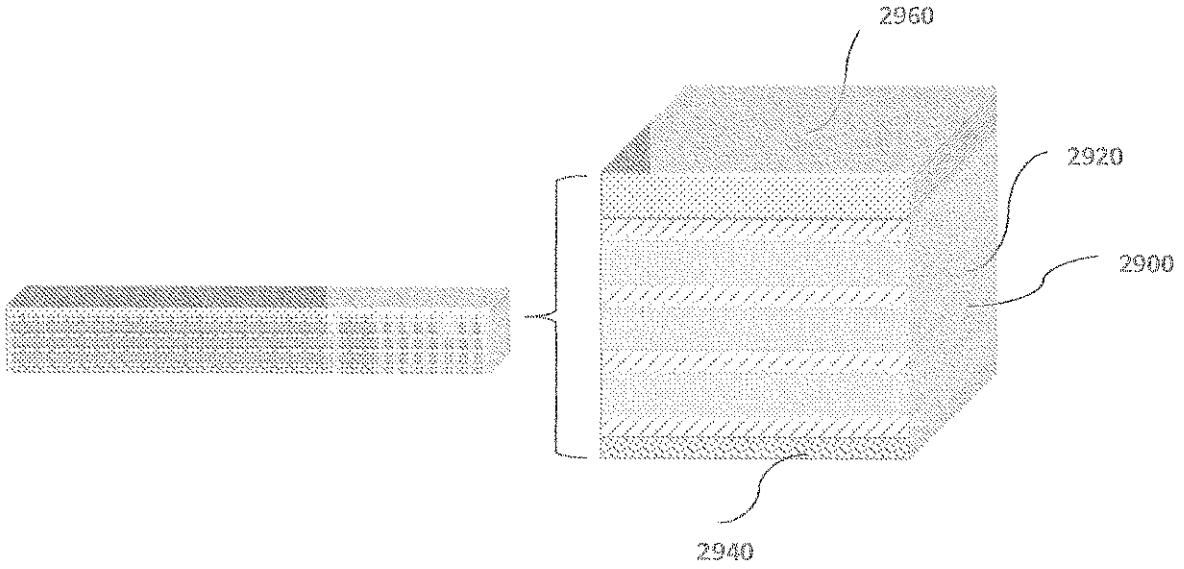


FIG. 30

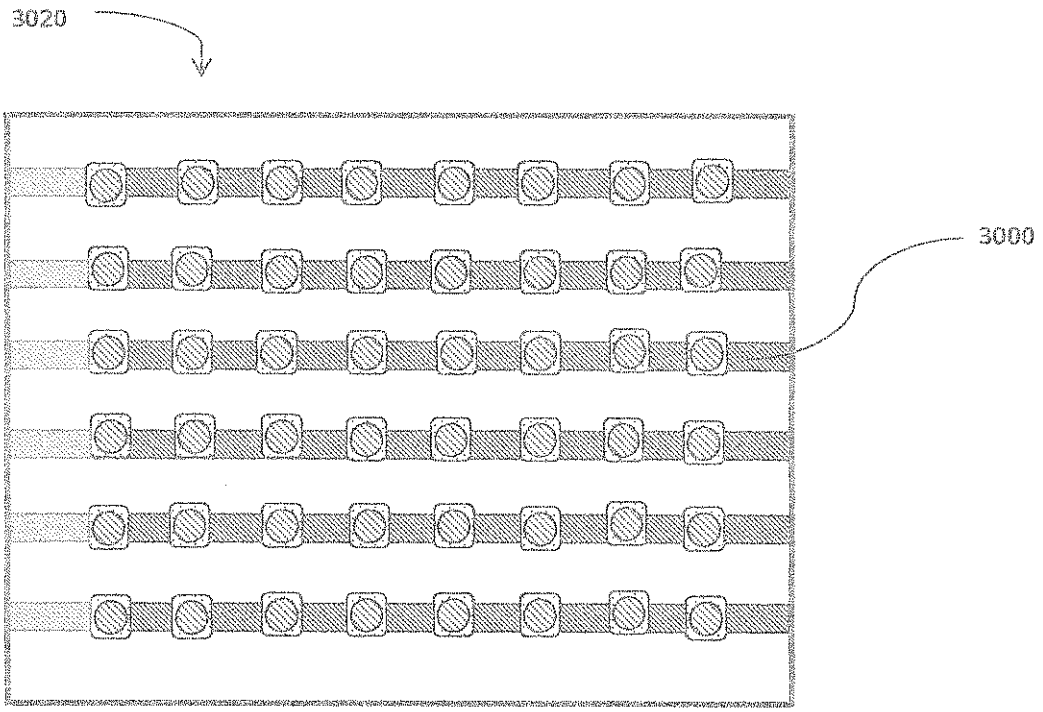


FIG. 31

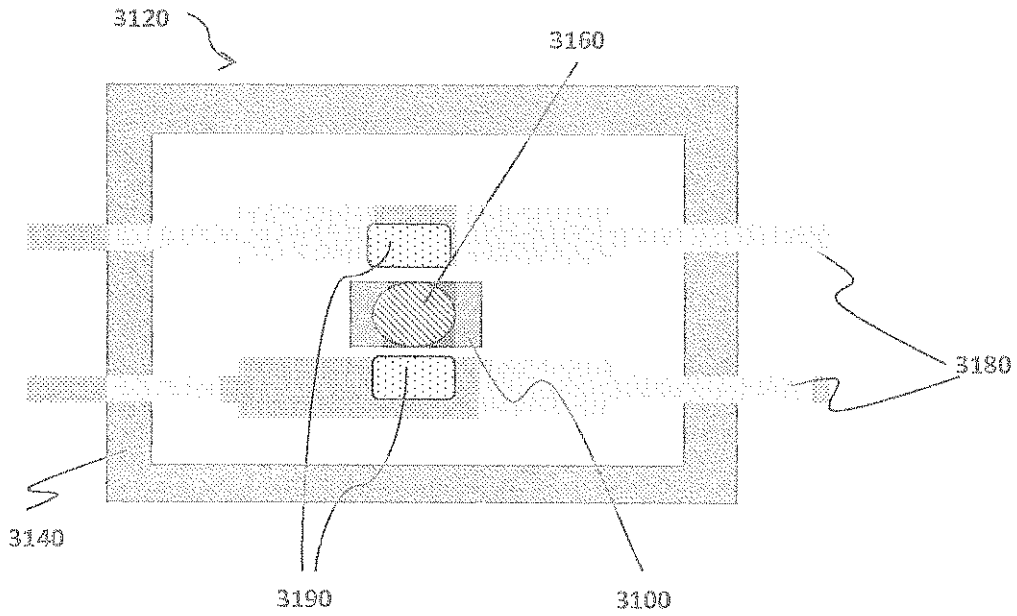
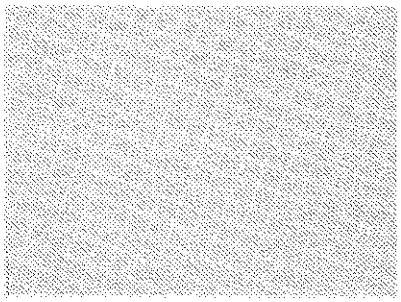
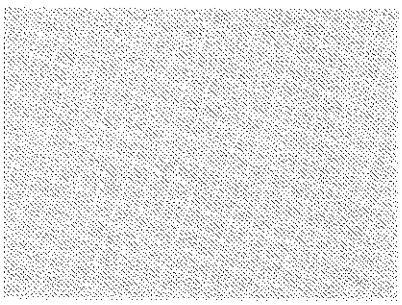


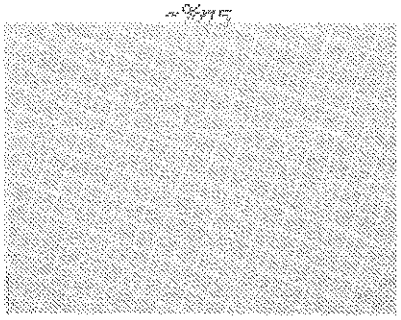
FIG. 32



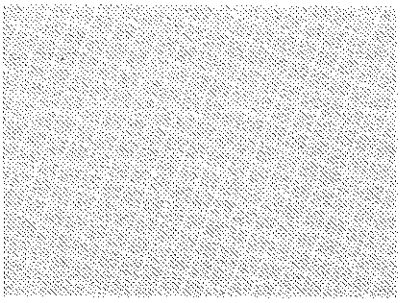
Size: 116 um, Gap: 2.5 um, Single bead: ~%75



Size: 116 um, Gap: 2 um, Single bead: ~%80



Size: 116 um, Gap: 1.75 um, Single bead: ~%80



Size: 116 um, Gap: 1.25 um, Single bead: ~%90

FIG. 33A

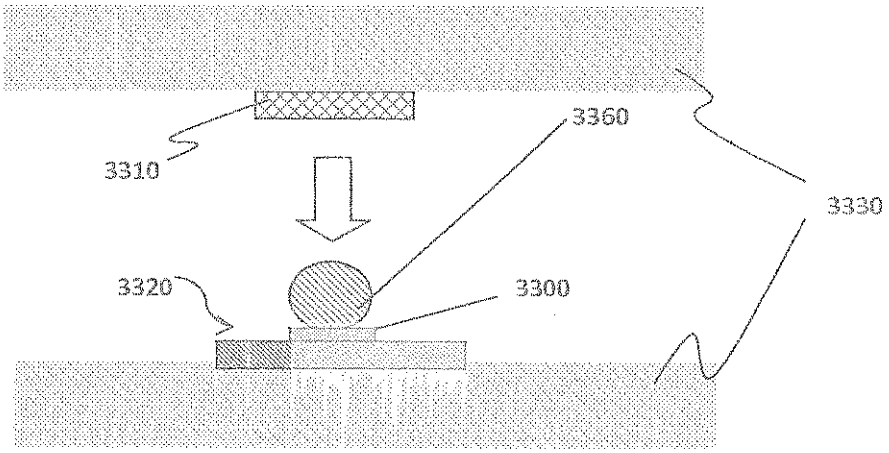


FIG. 33B

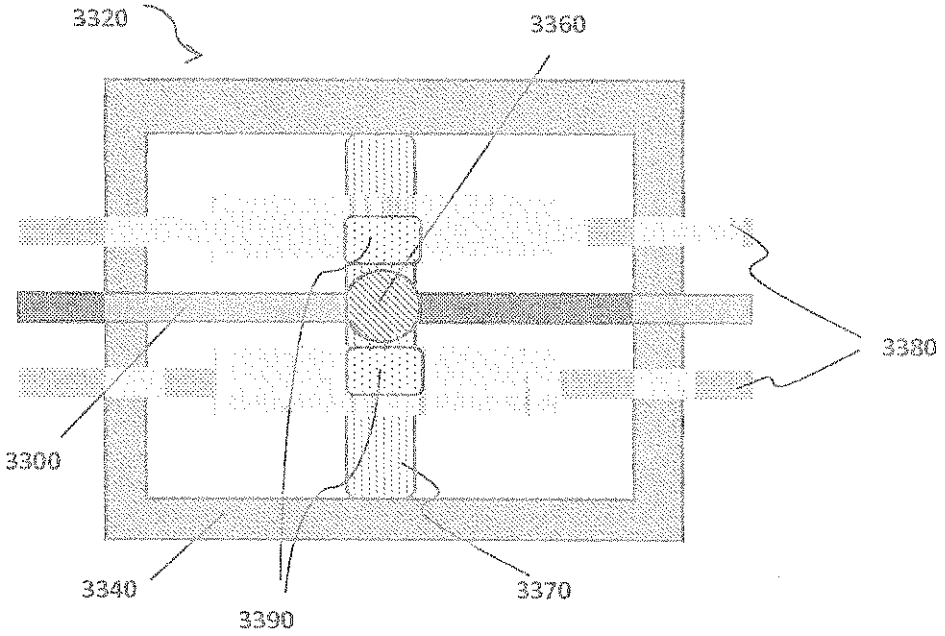


FIG. 33C

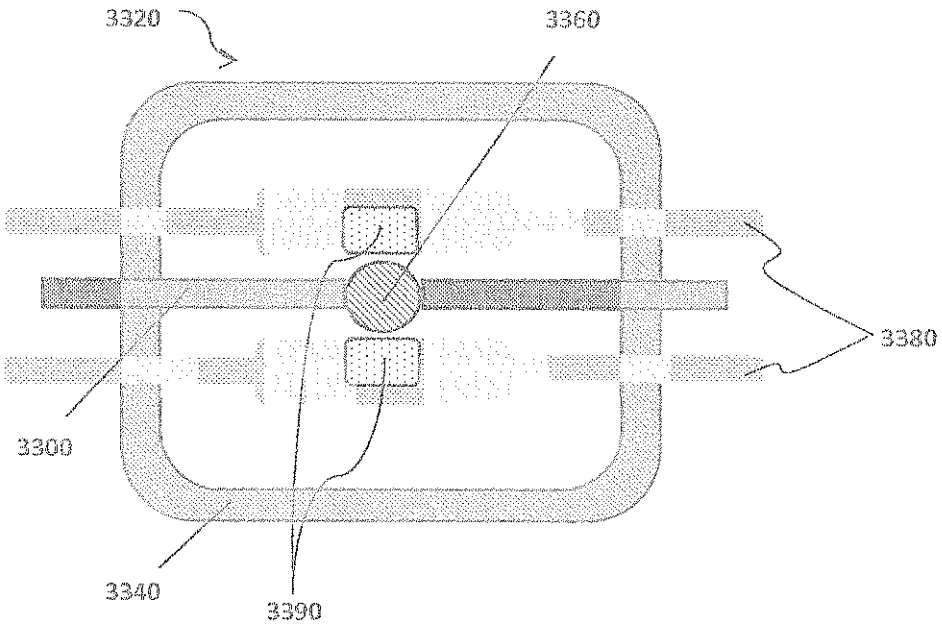


FIG. 33D

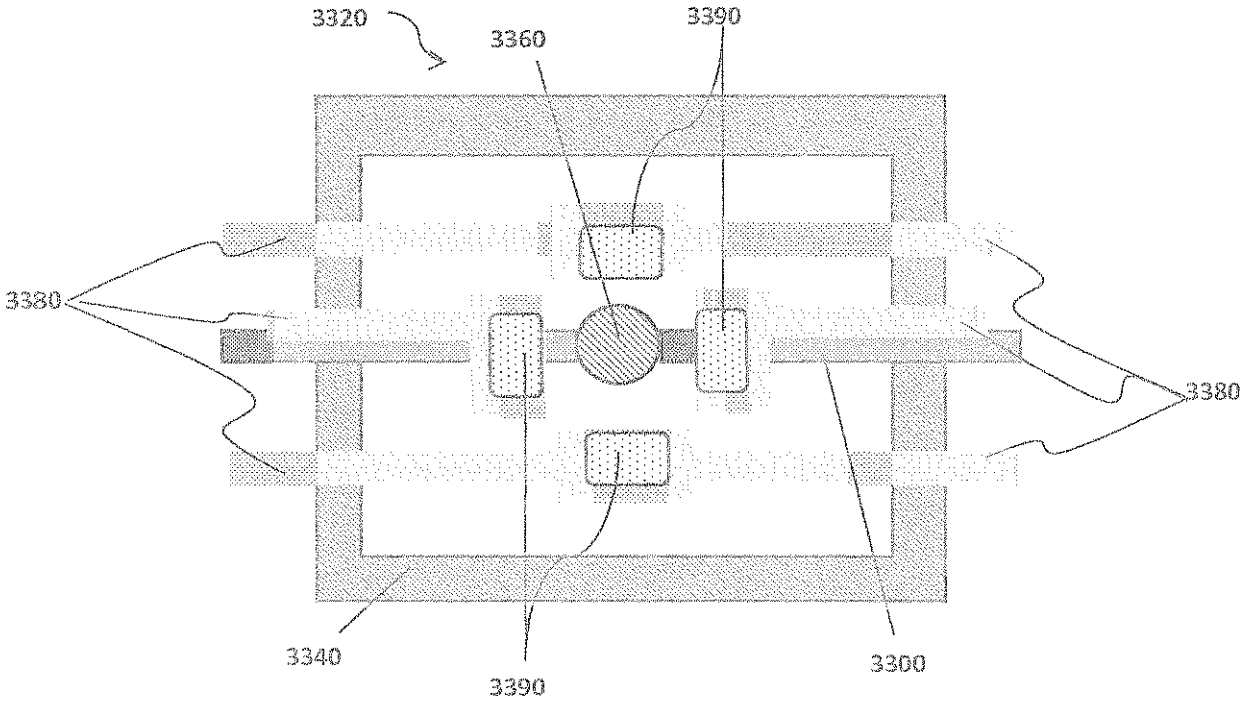


FIG. 33E

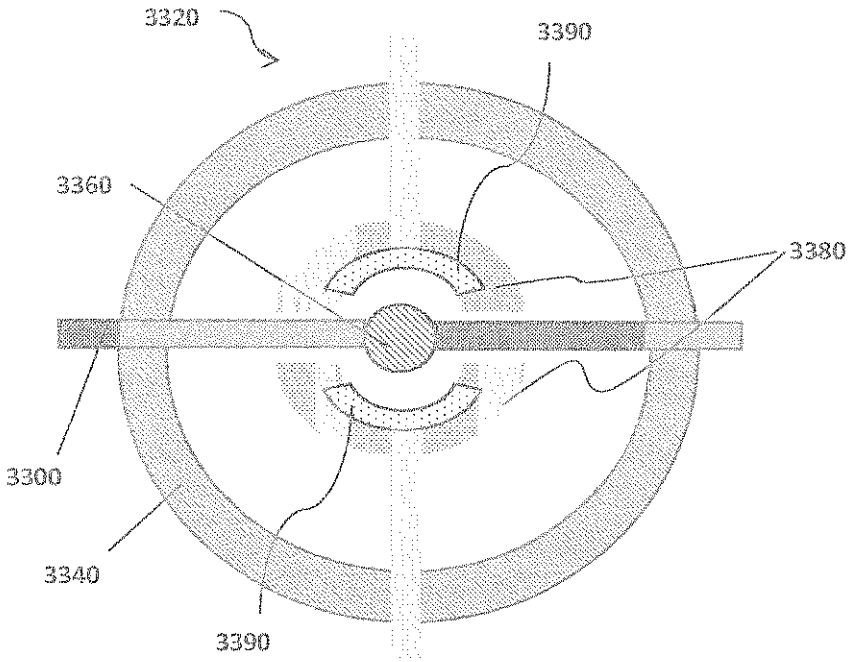


FIG. 33F

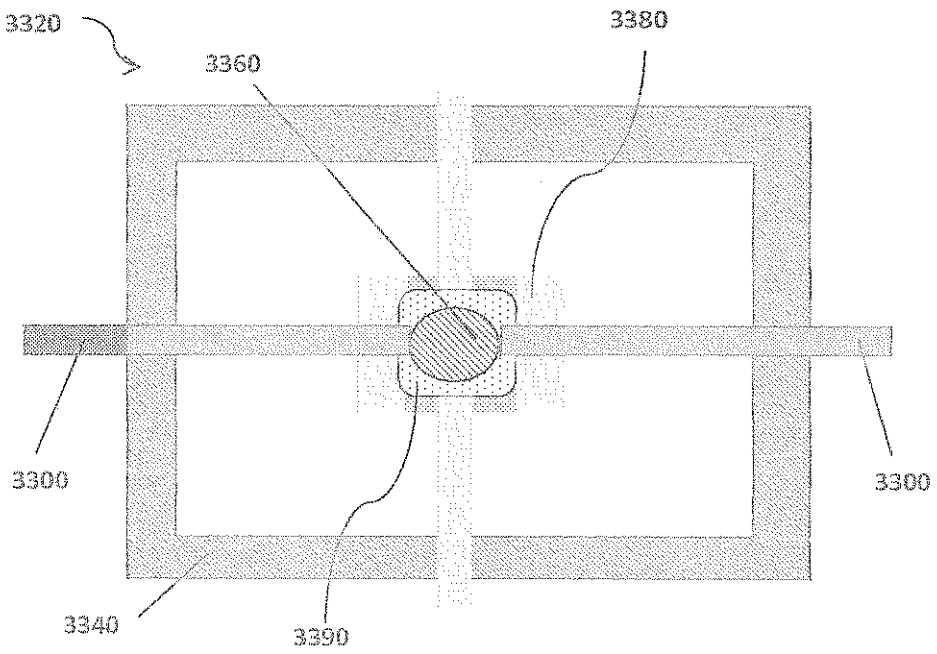


FIG. 33G

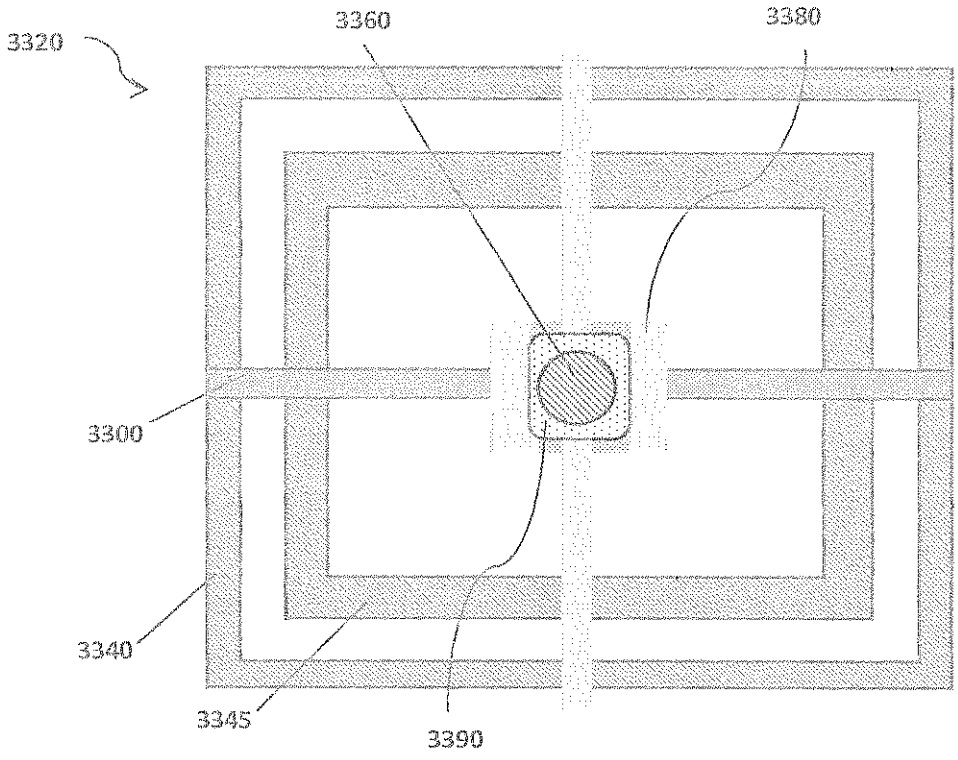


FIG. 33H

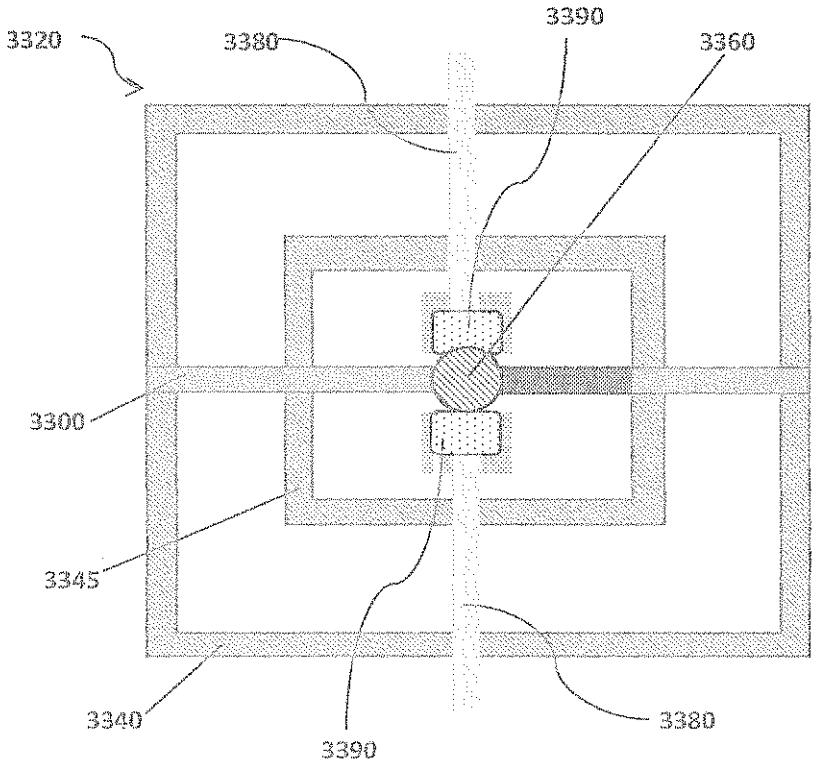


FIG. 33I

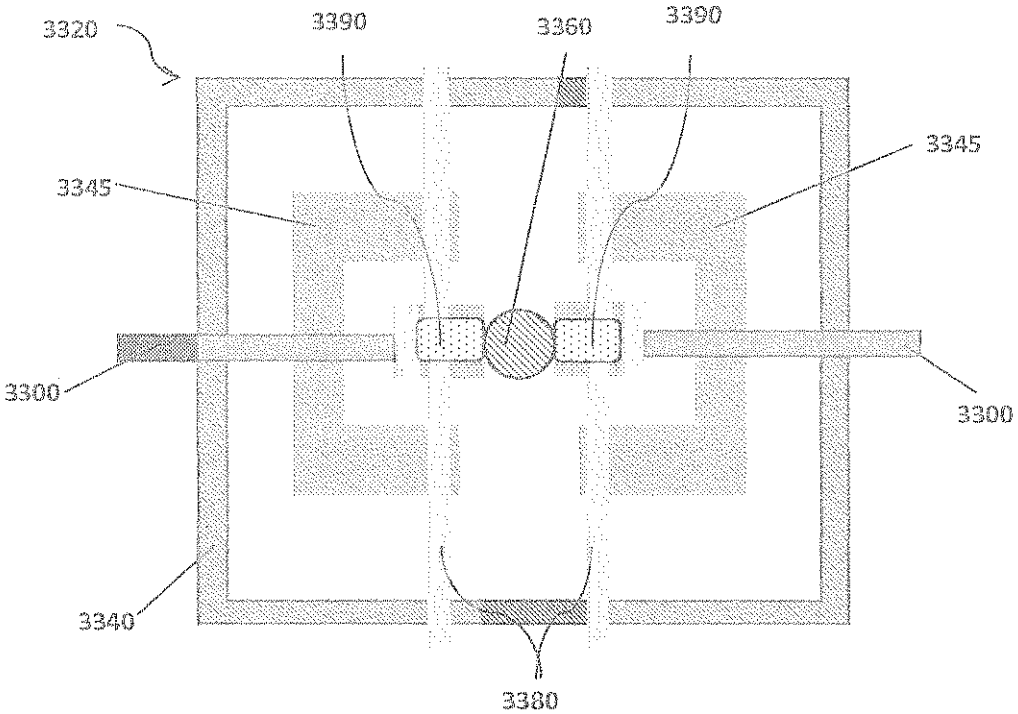


FIG. 33J

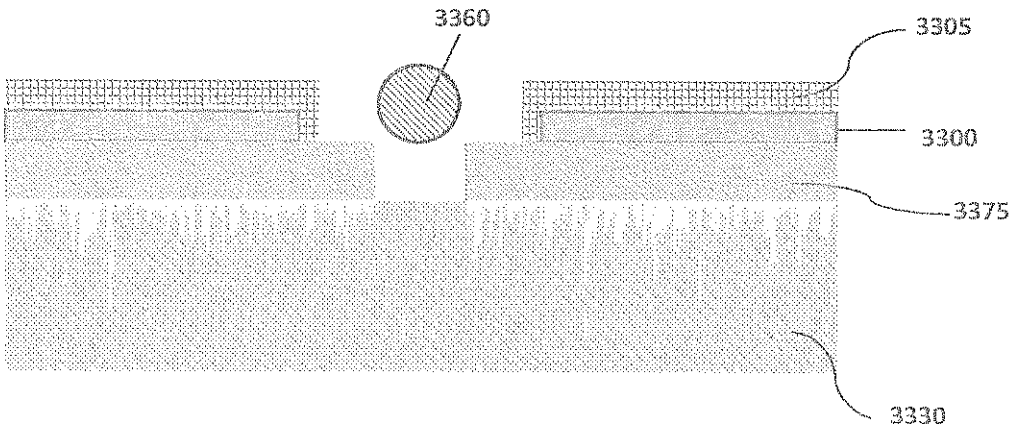


FIG. 33K

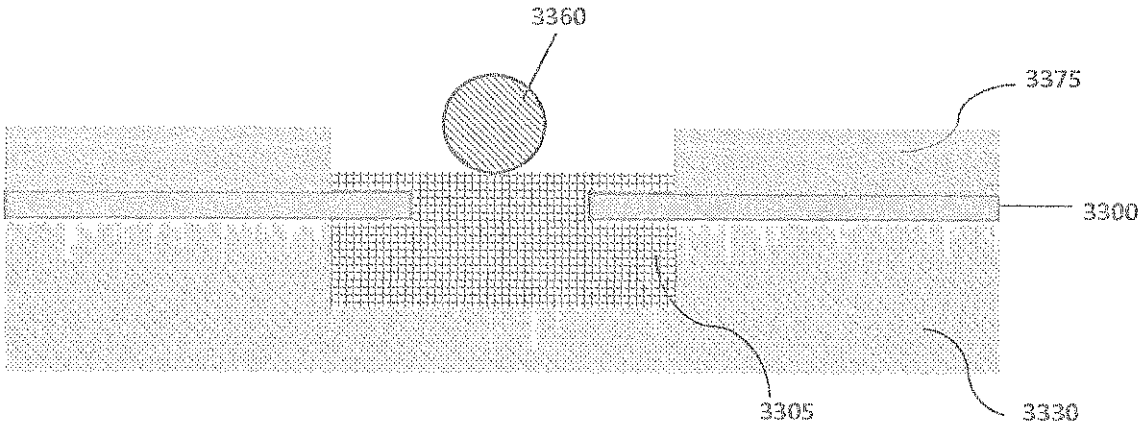


FIG. 33L

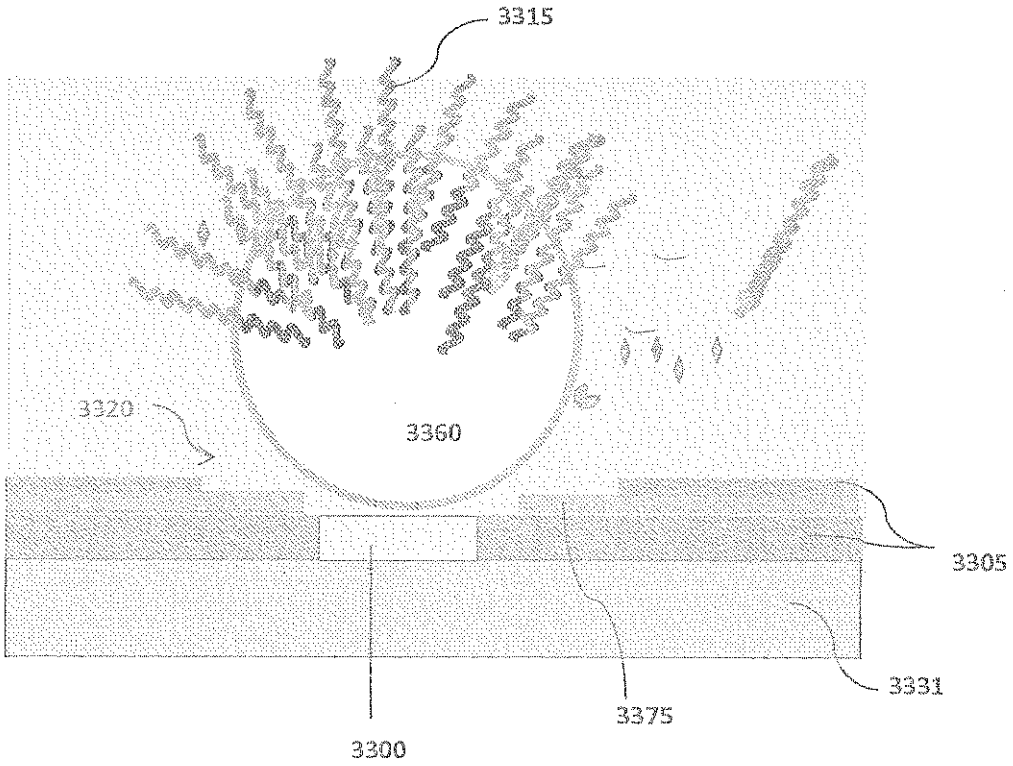


FIG. 33M

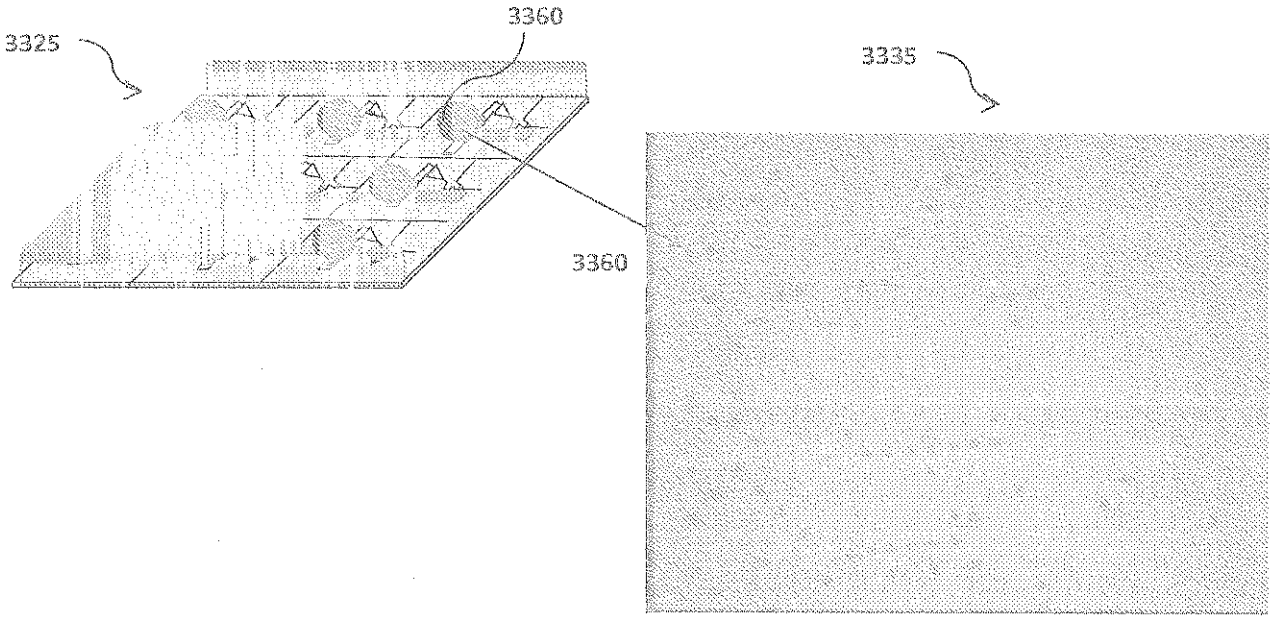


FIG. 33N

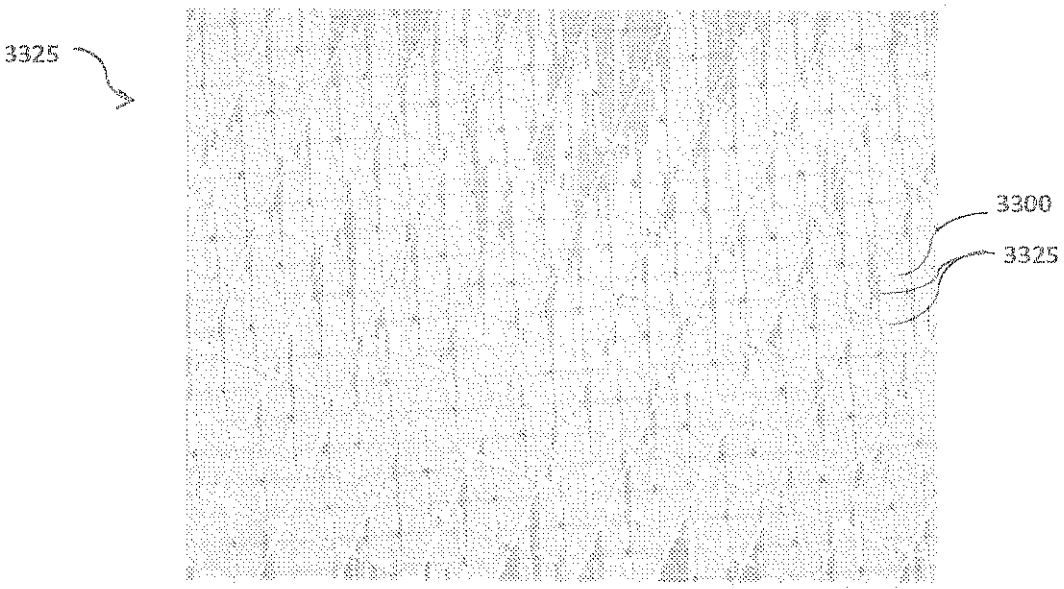


FIG. 34A

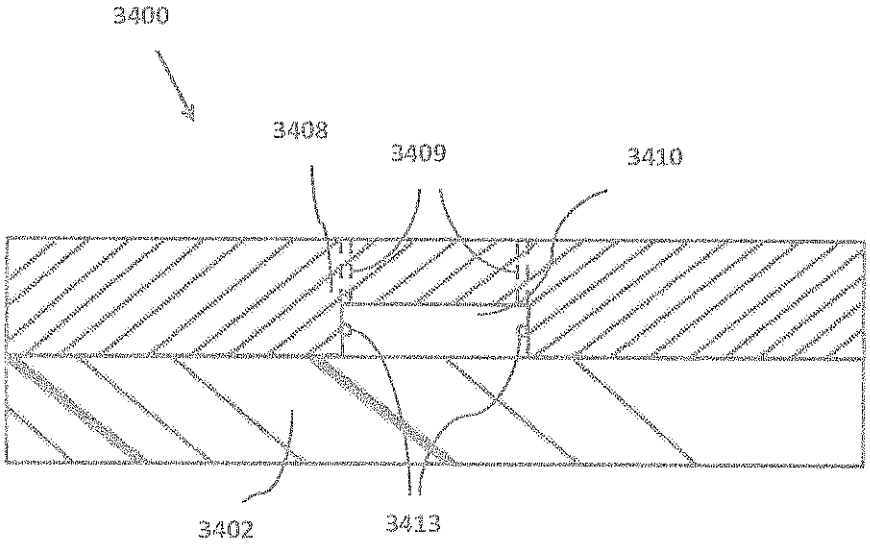


FIG. 34B

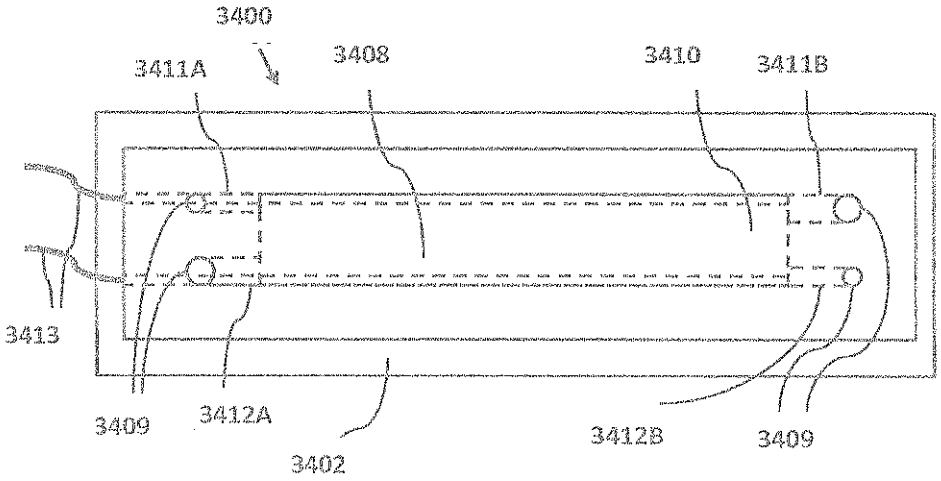


FIG. 34C

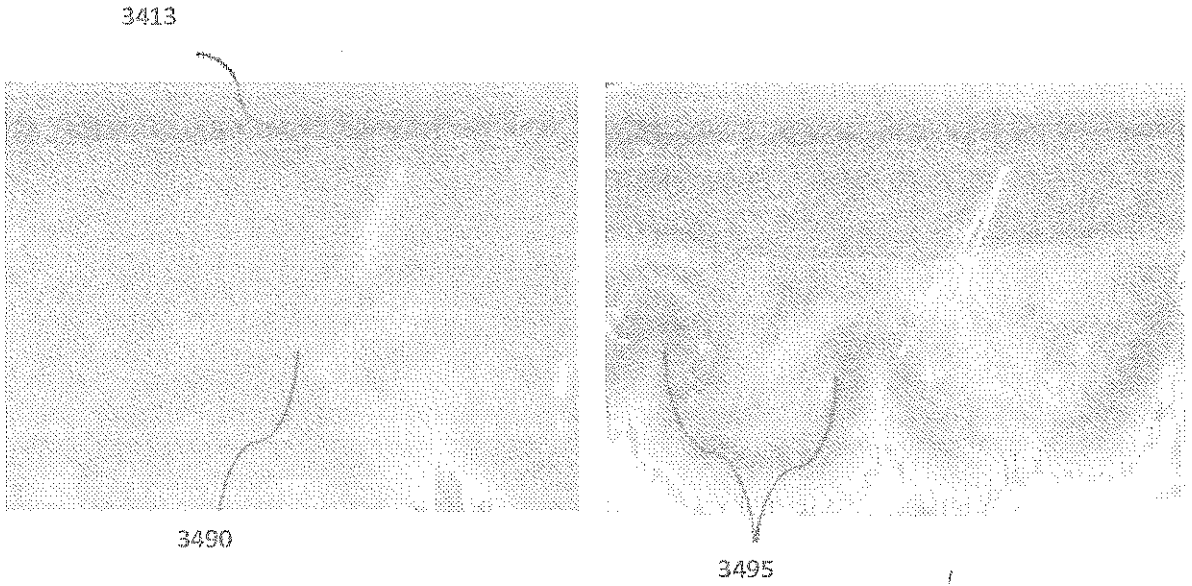


FIG. 34D

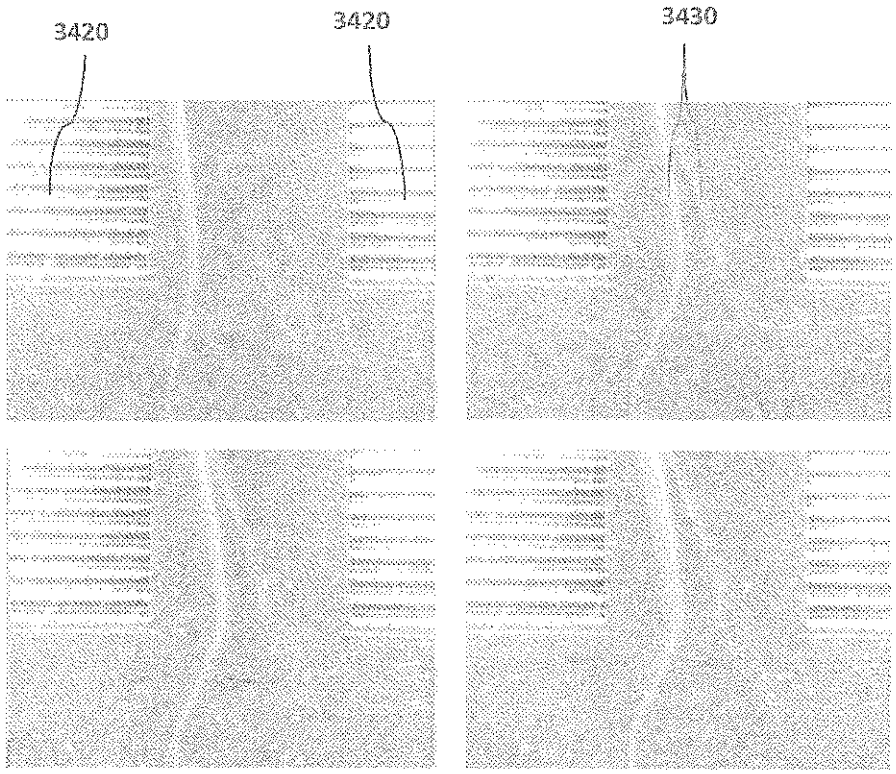


FIG. 34E

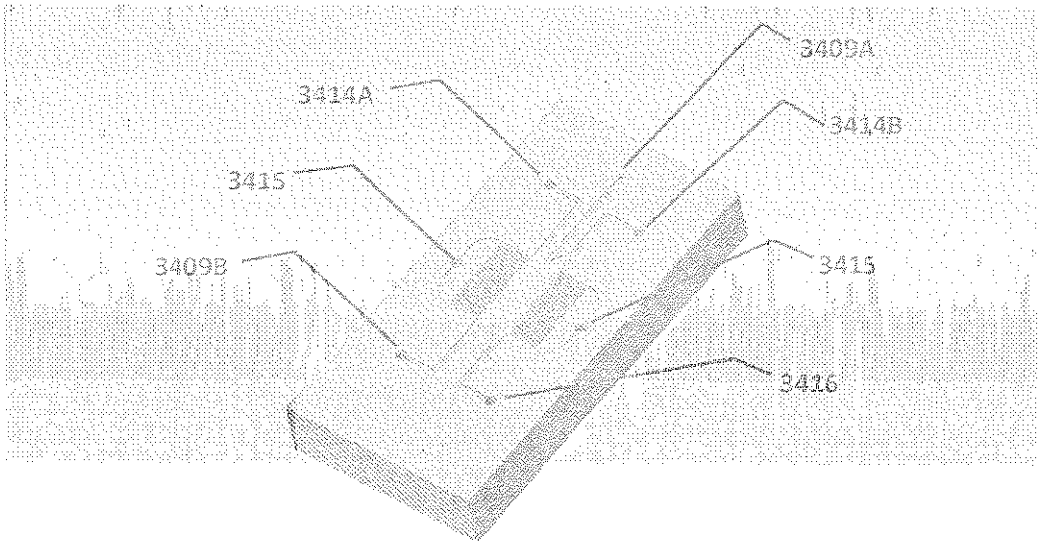


FIG. 35

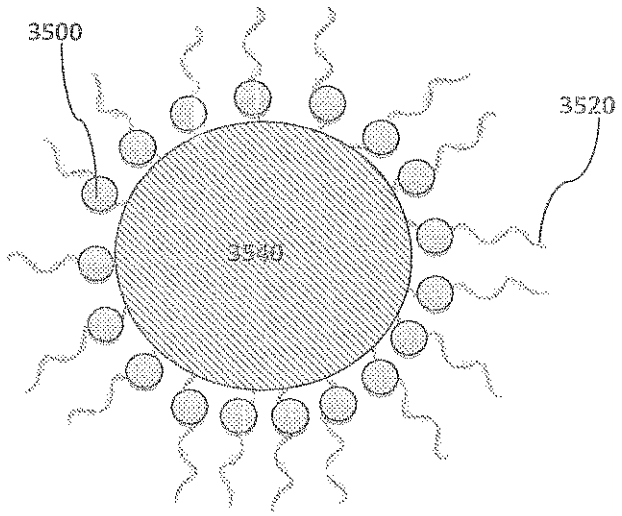


FIG. 36A

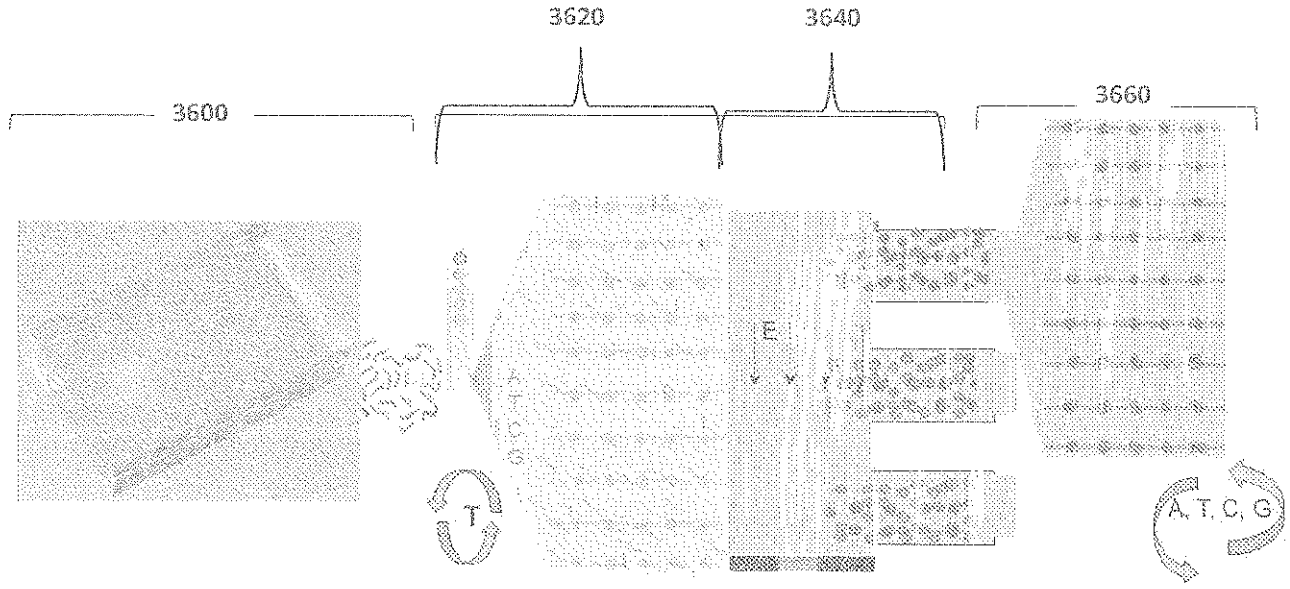


FIG. 36B

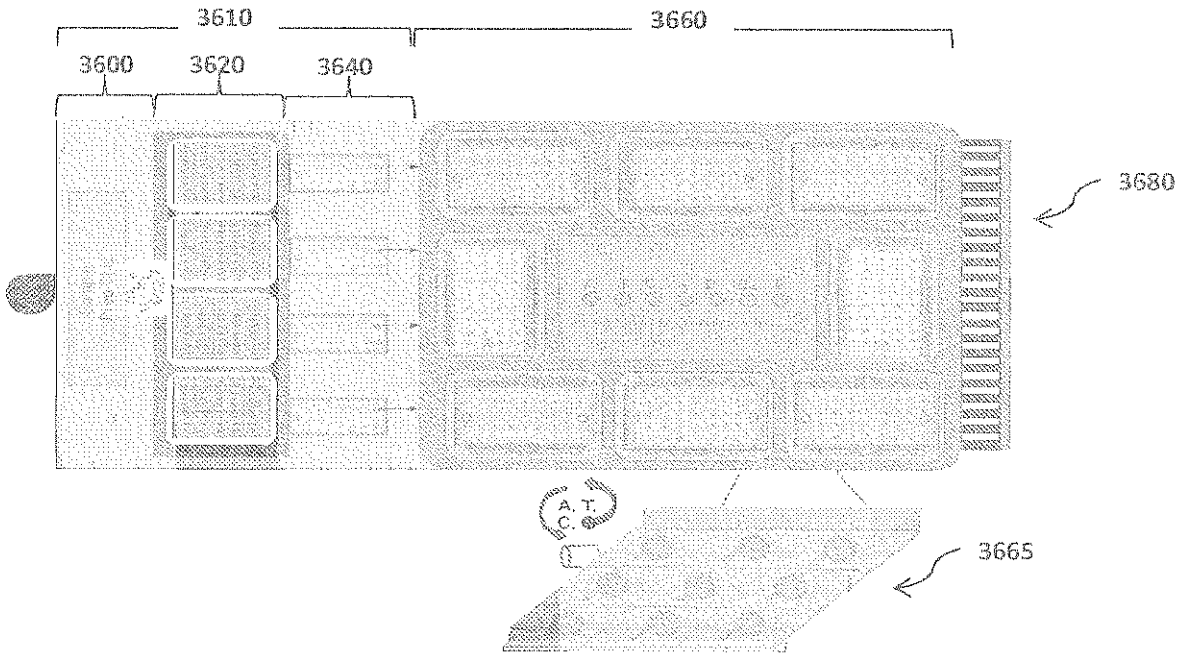


FIG. 37

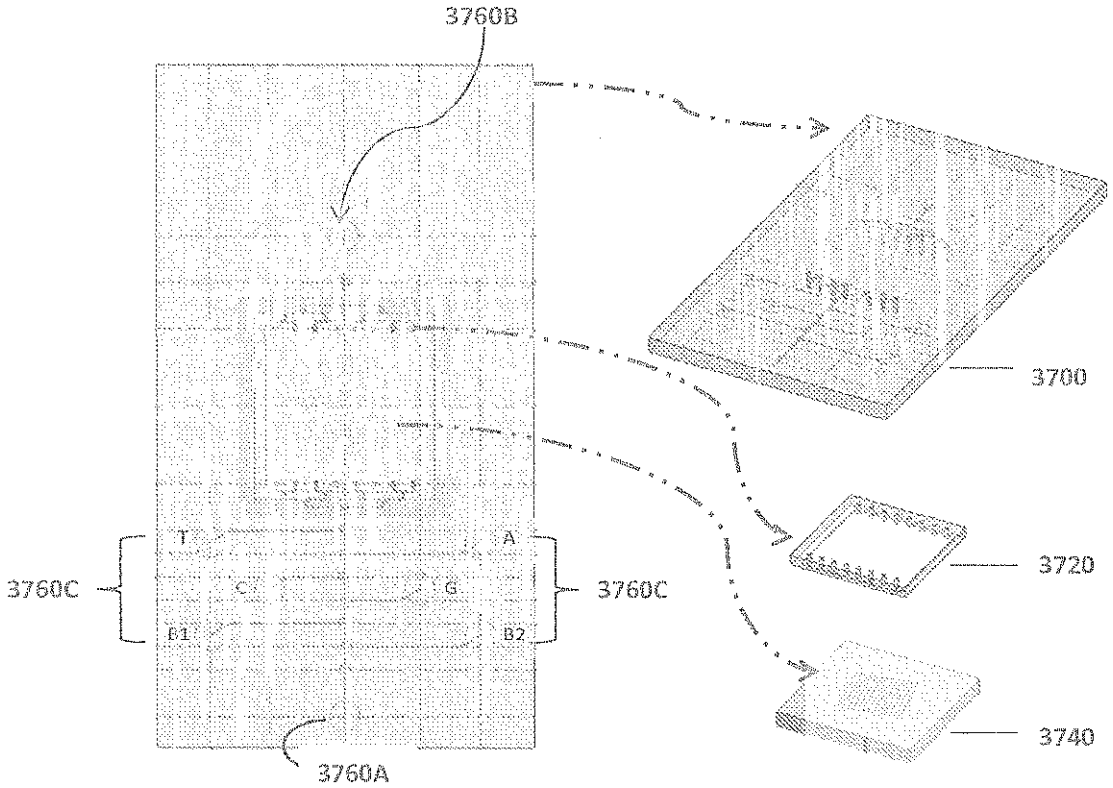


FIG. 38A

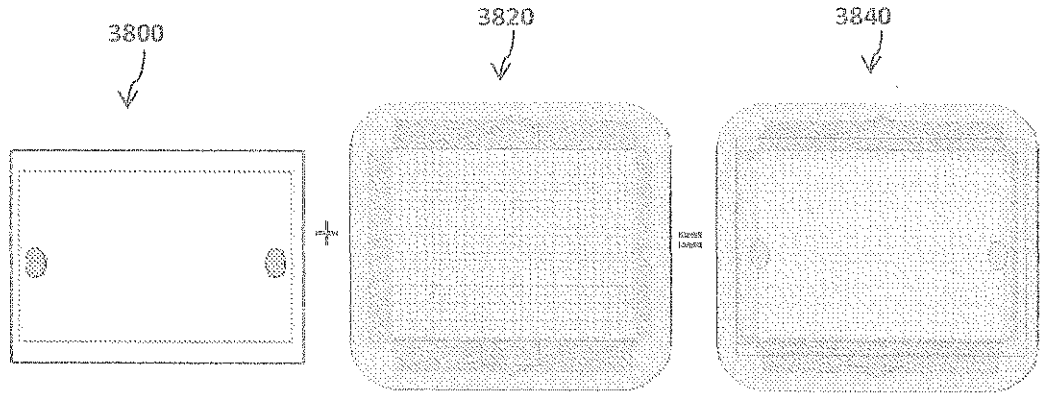


FIG. 38B

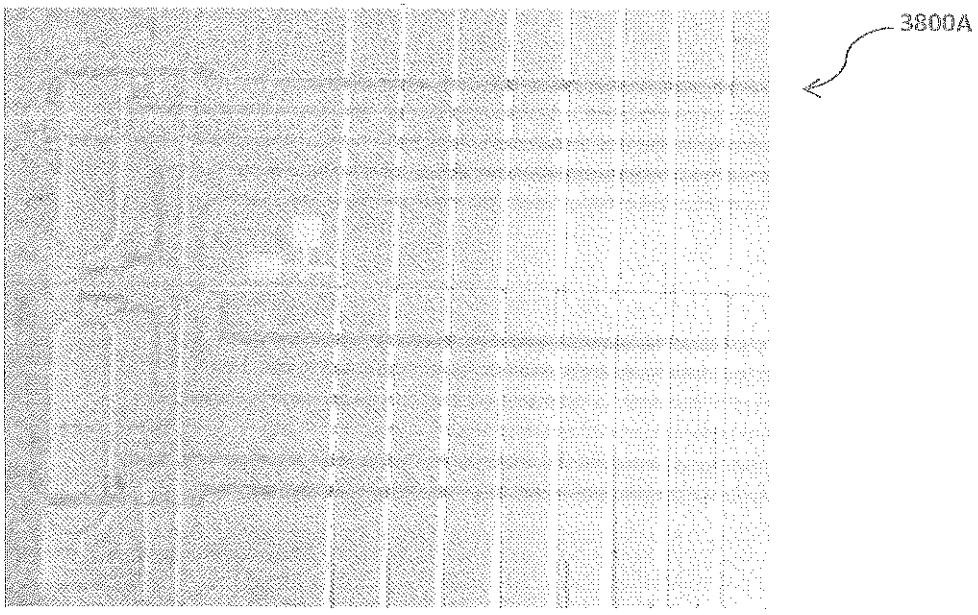


FIG. 38C

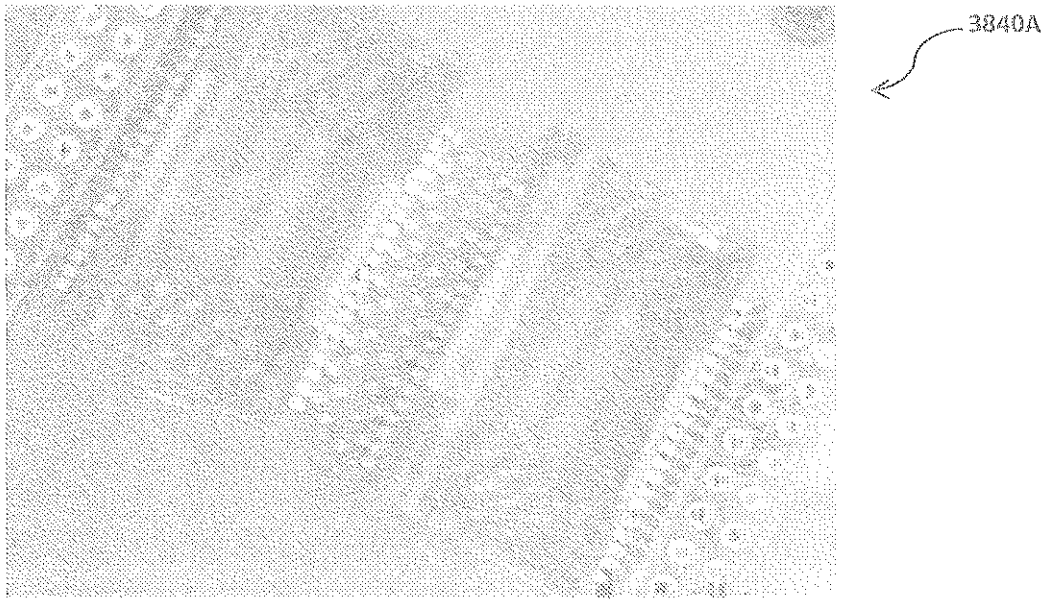


FIG. 39

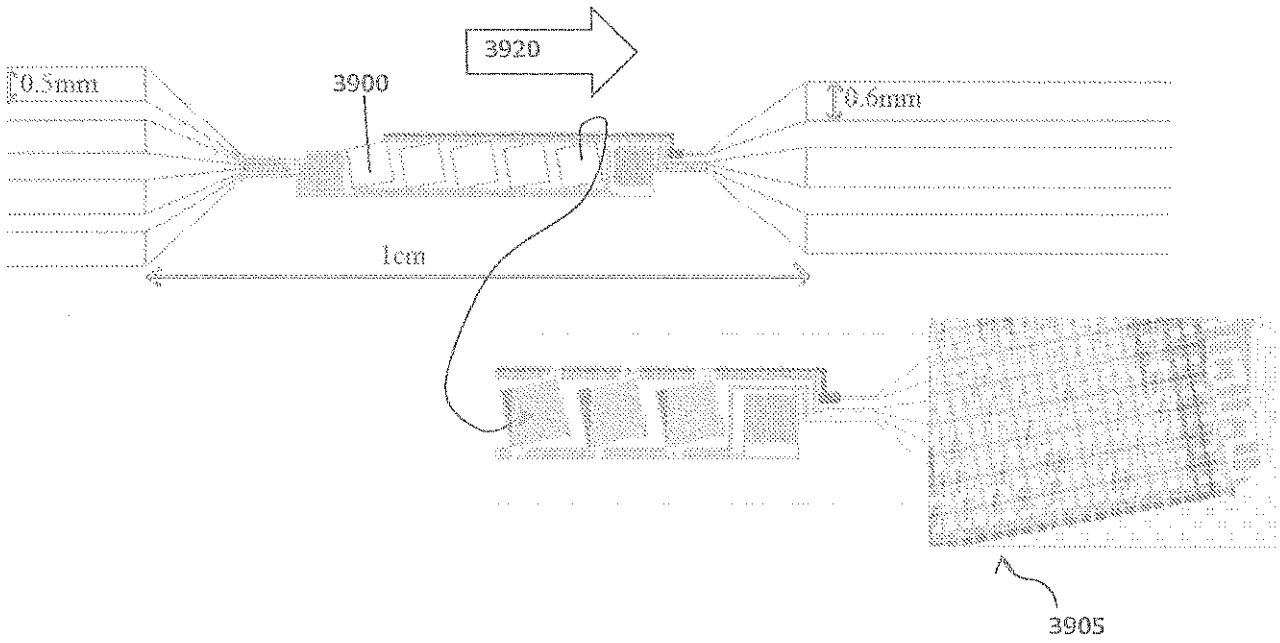


FIG. 40

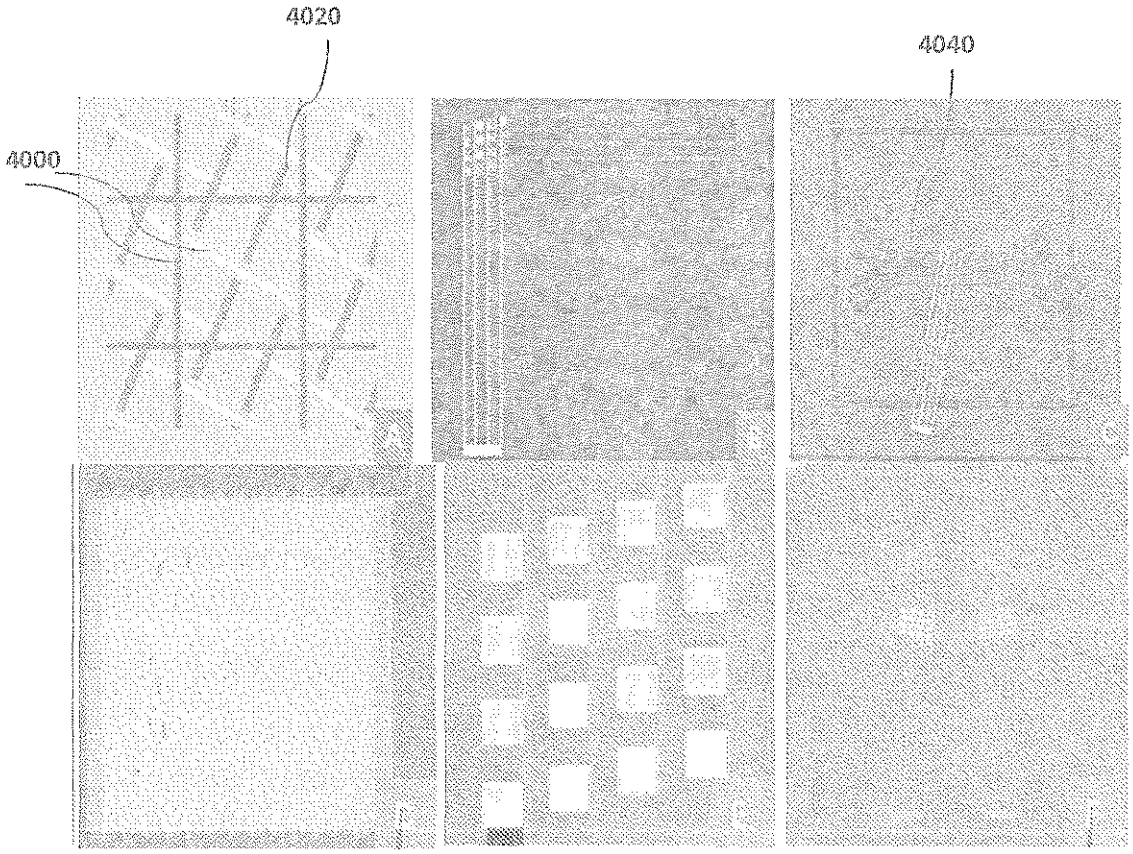


FIG. 41

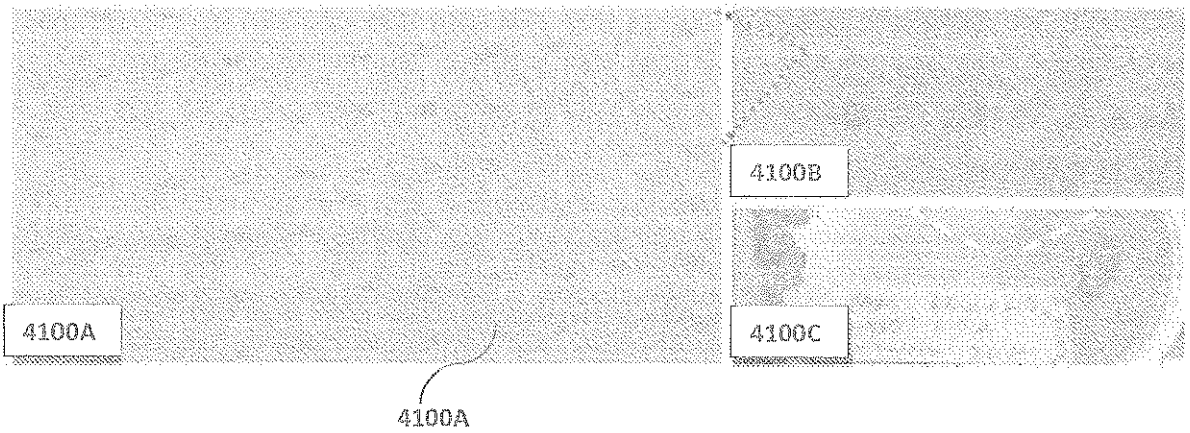


FIG. 42

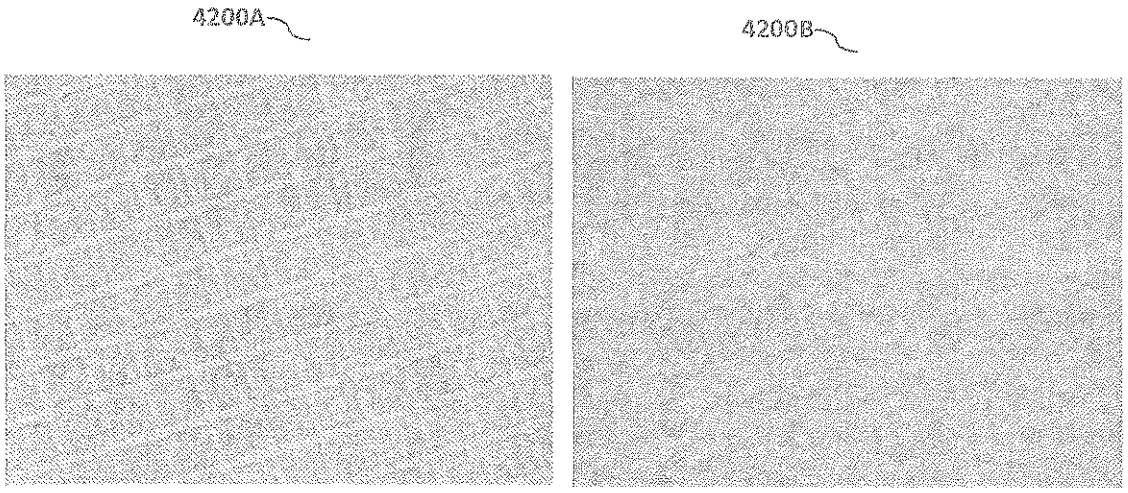


FIG. 43A

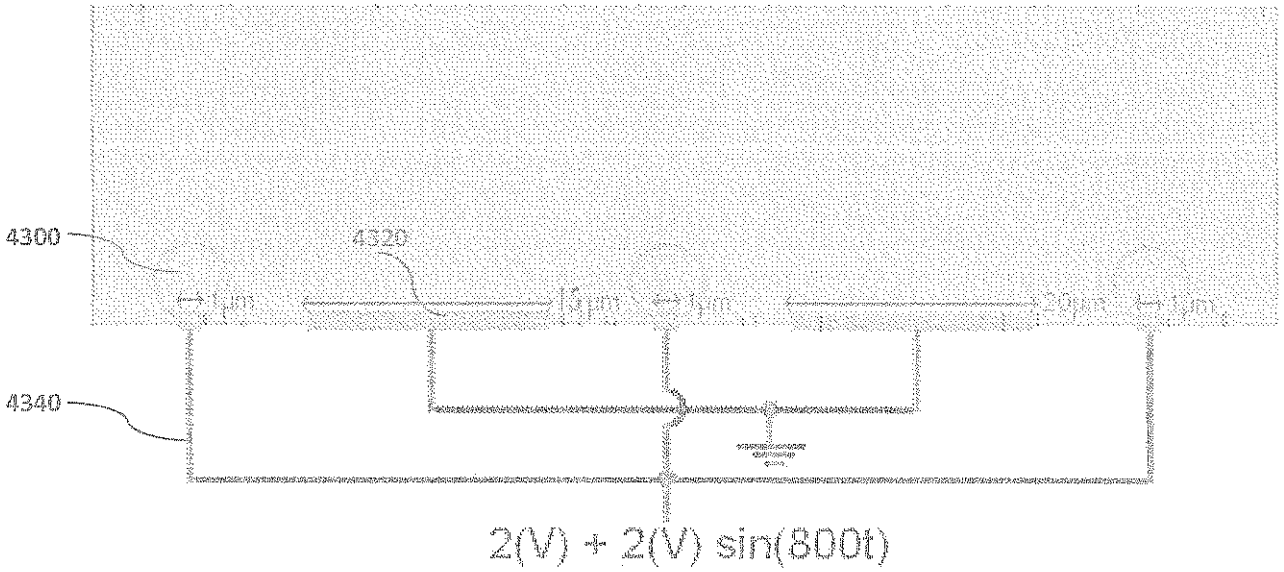


FIG. 43B

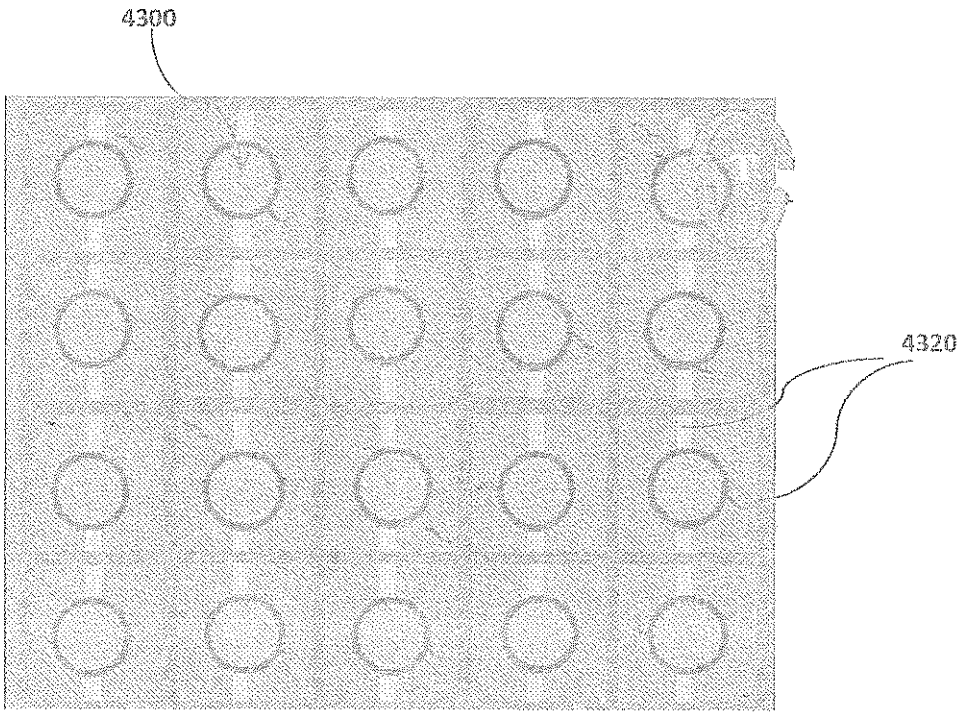


FIG. 44A

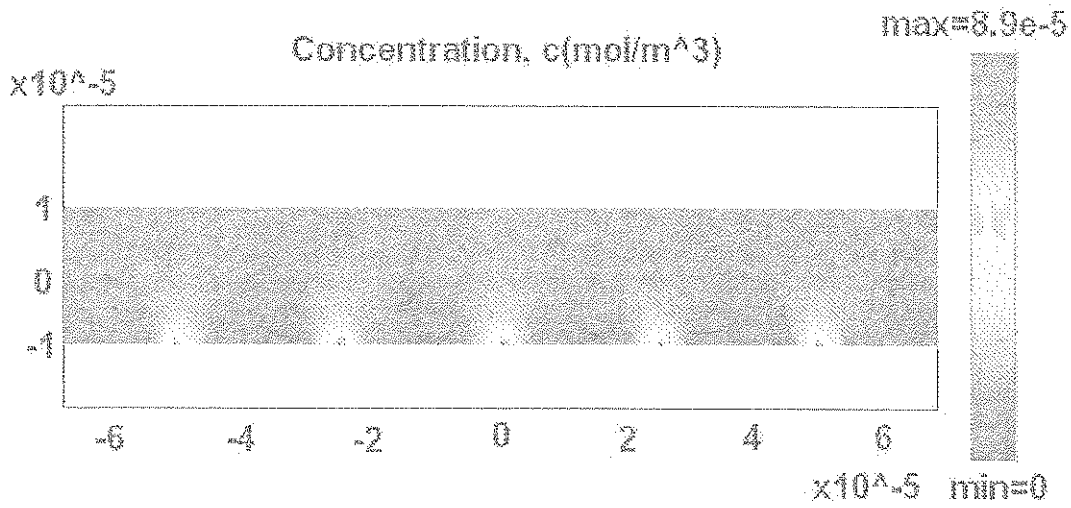


FIG. 44B

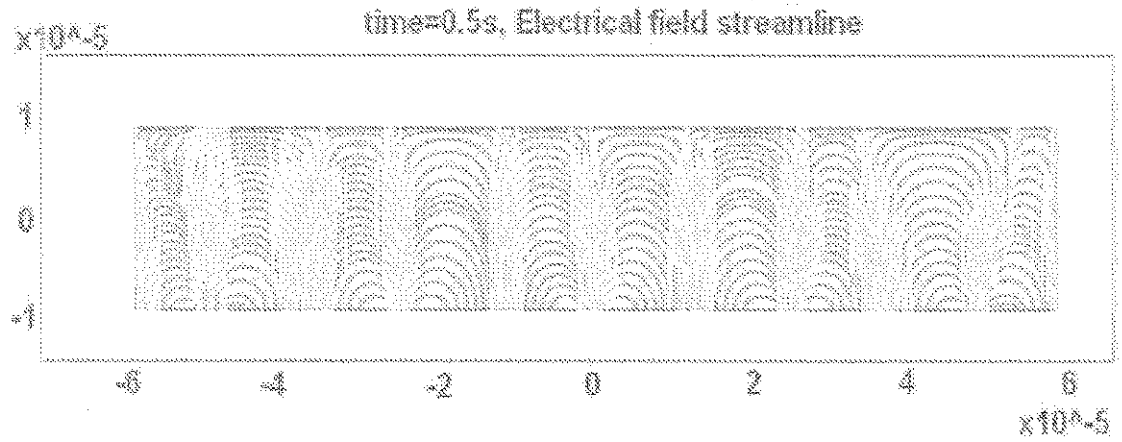


FIG. 44C

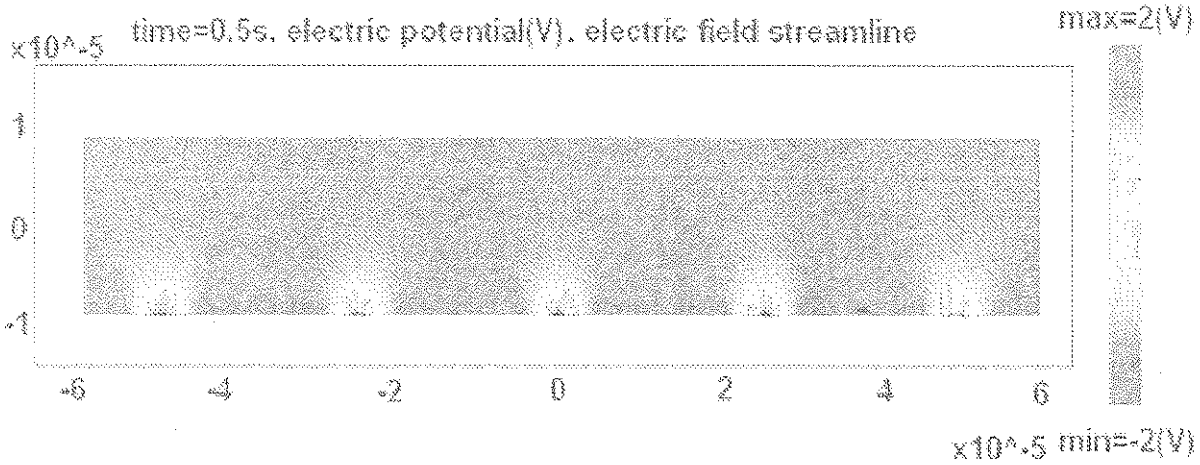


FIG. 44D

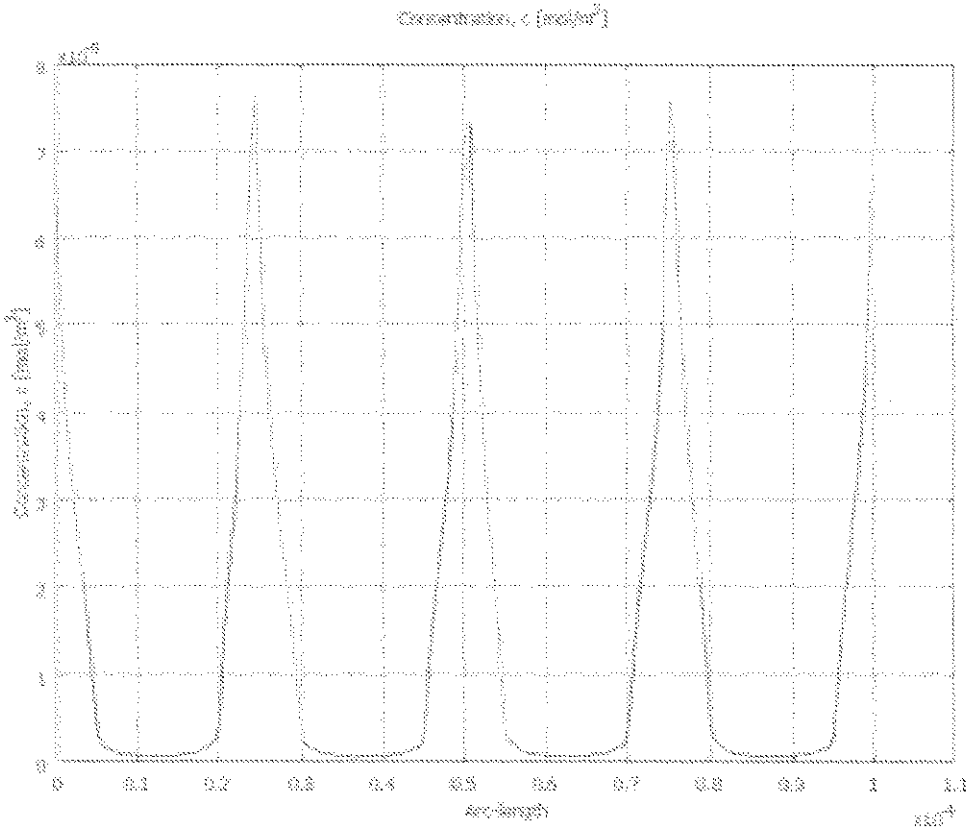


FIG. 45

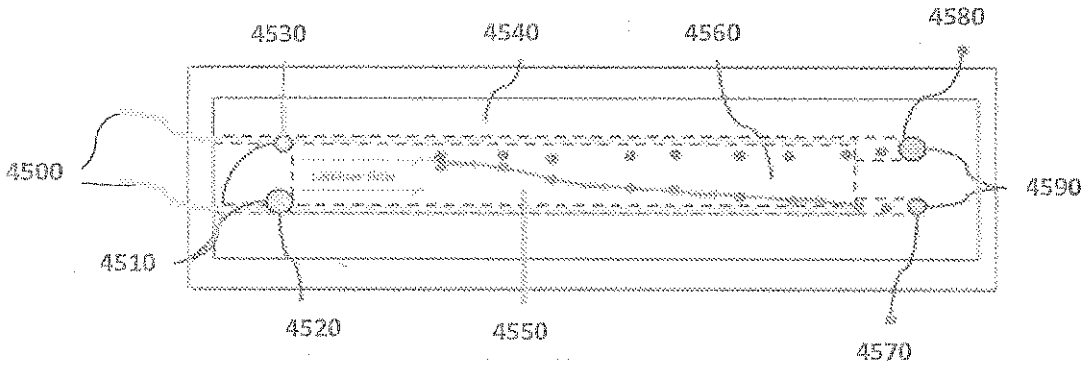


FIG. 46A

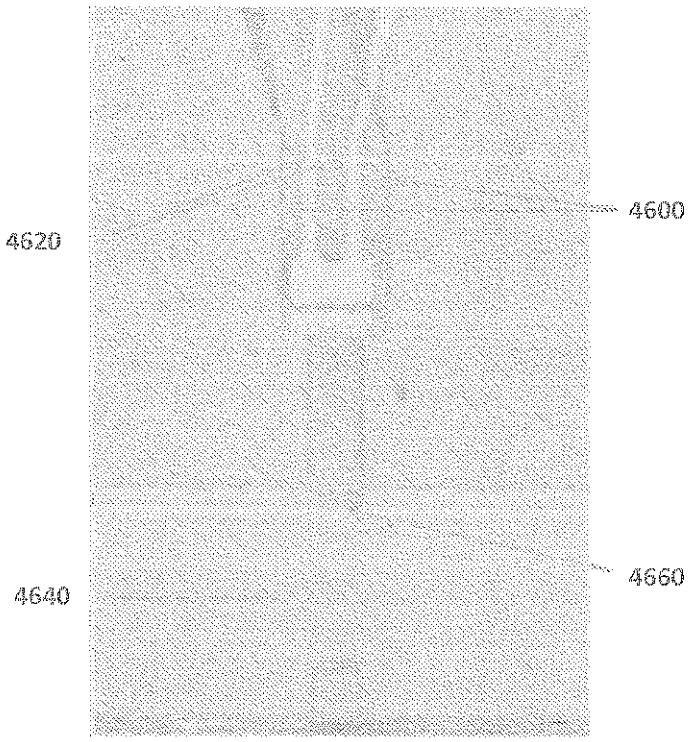


FIG. 46B

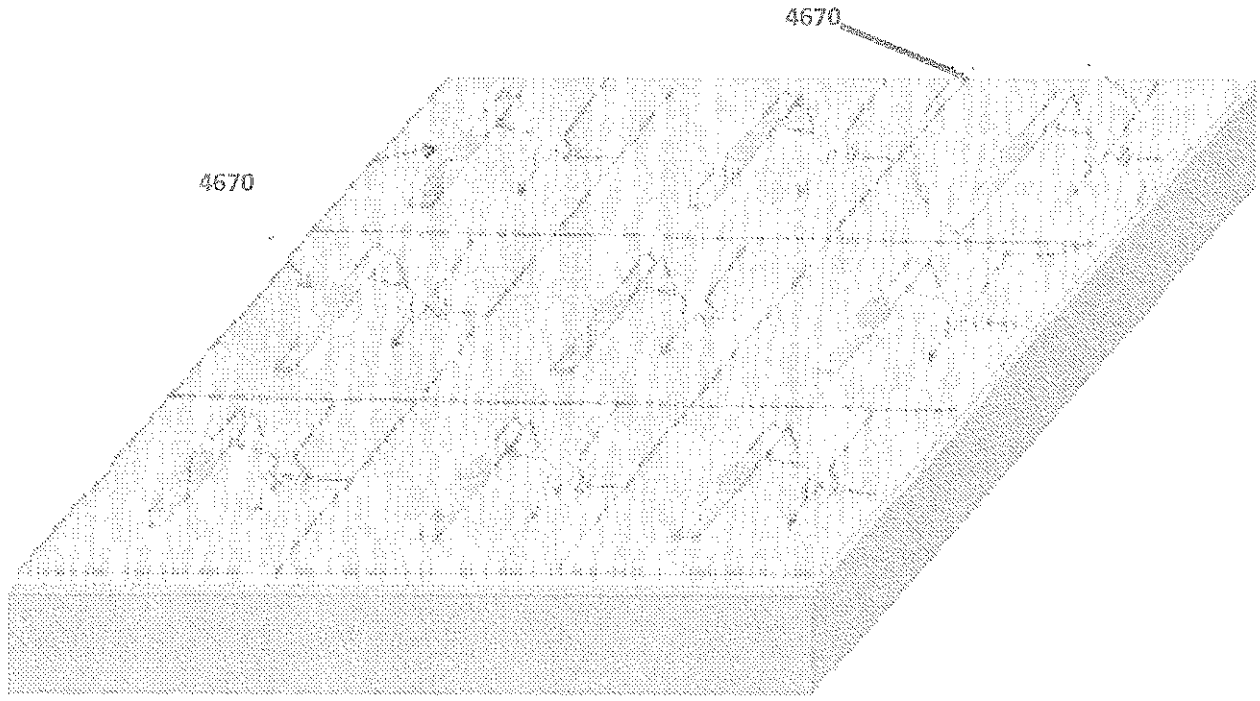


FIG. 46C

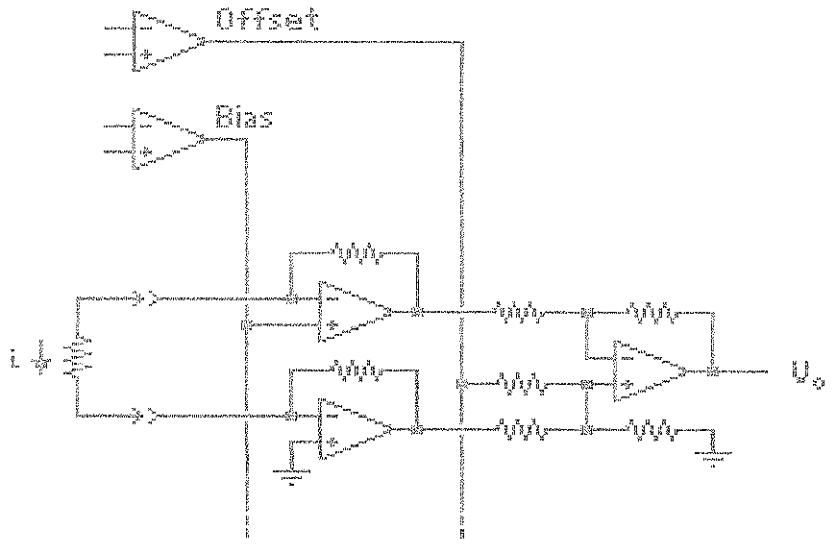


FIG. 47A

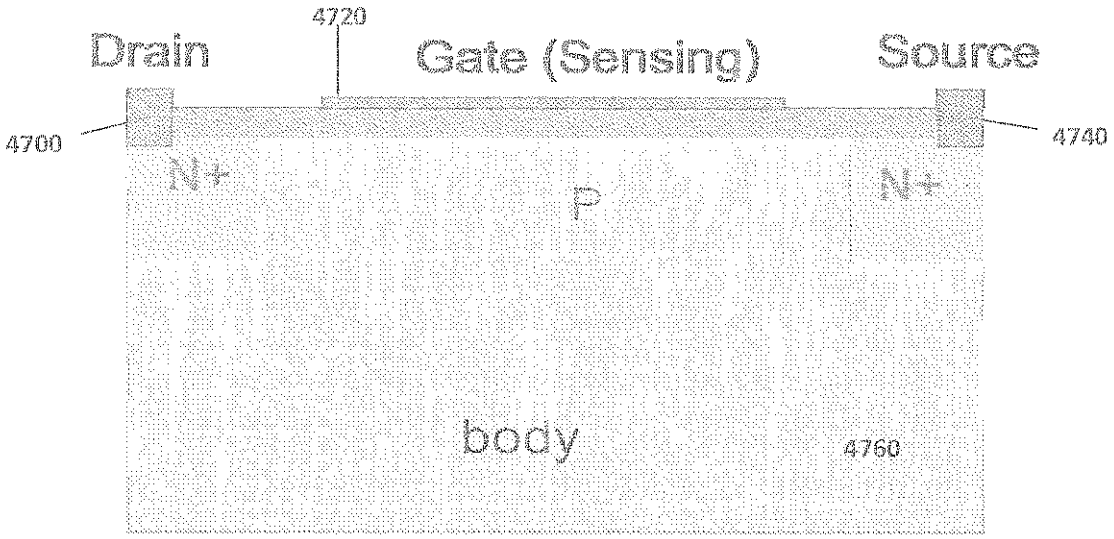


FIG. 47B

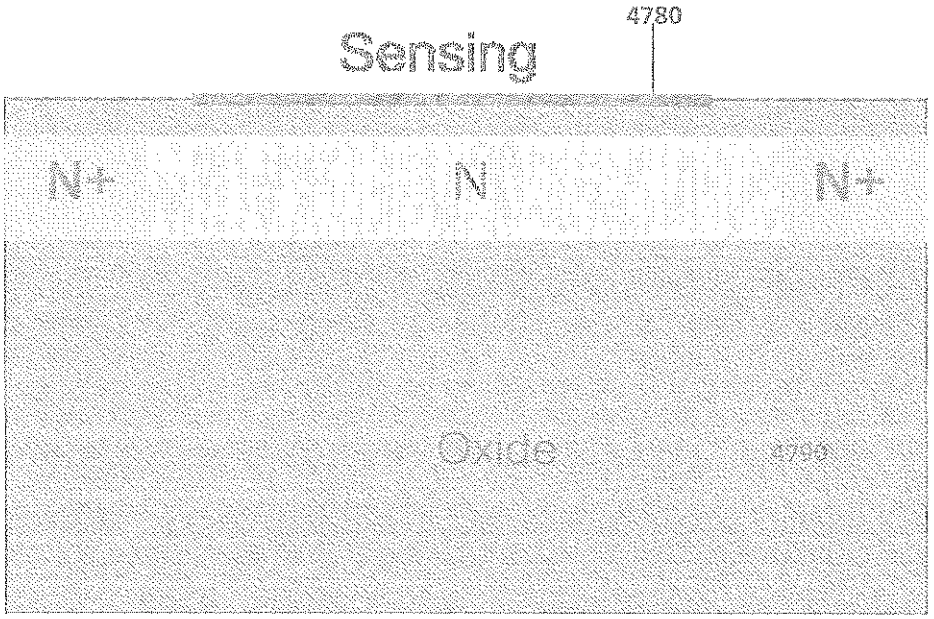


FIG. 47C

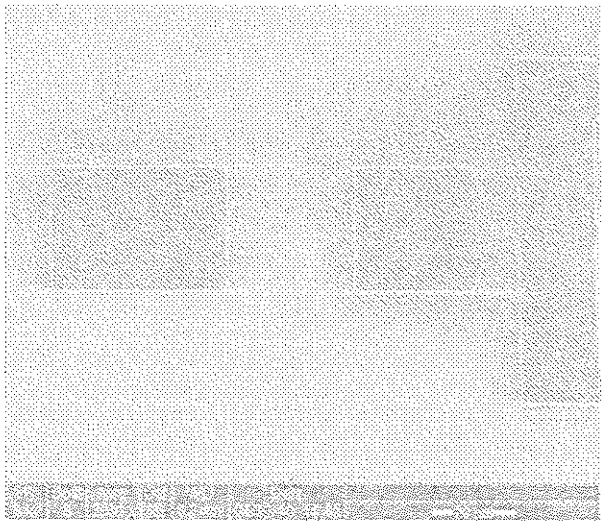


FIG. 47D

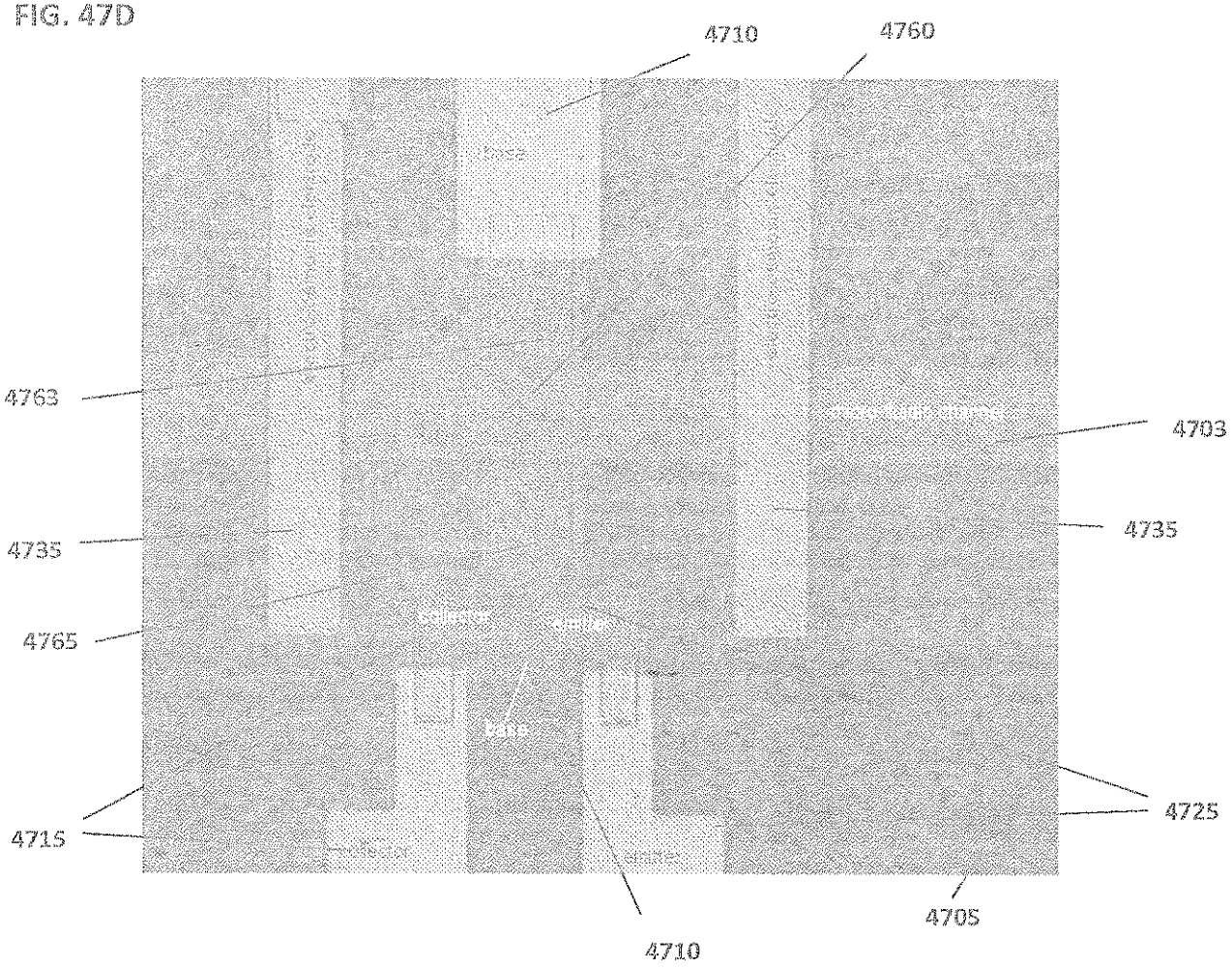


FIG. 48

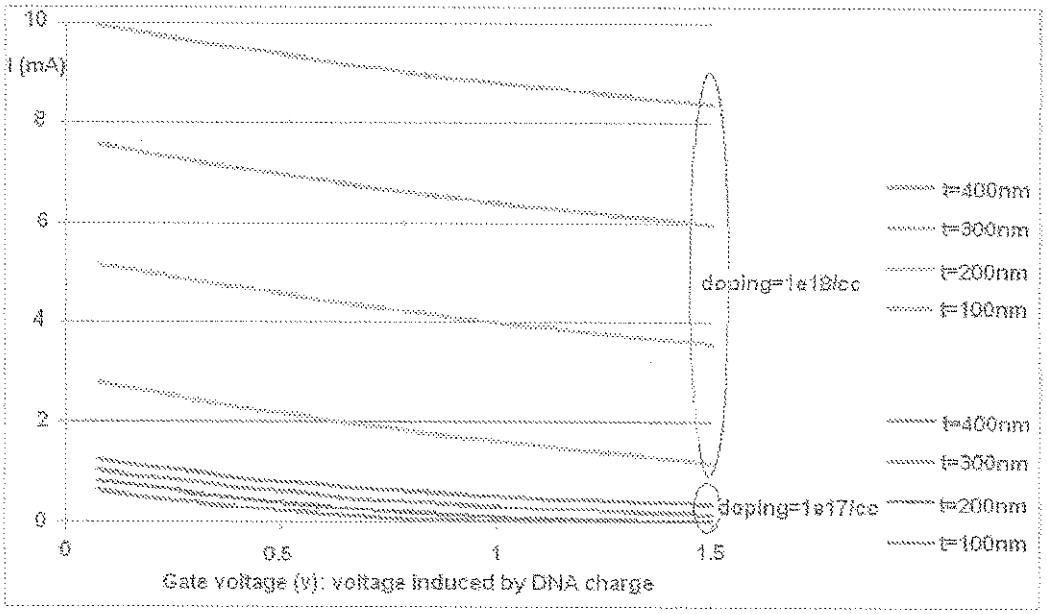


FIG. 49A

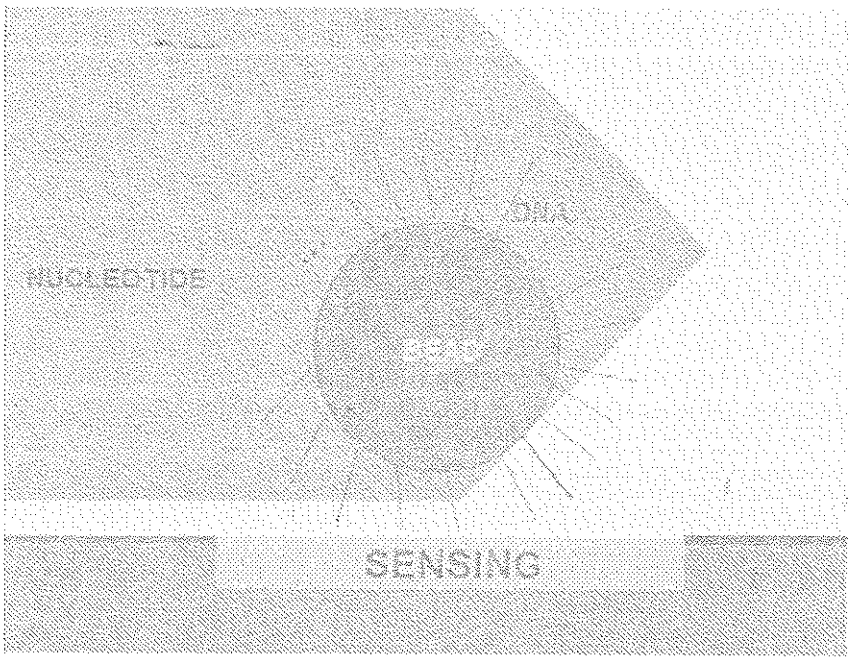


FIG. 49B

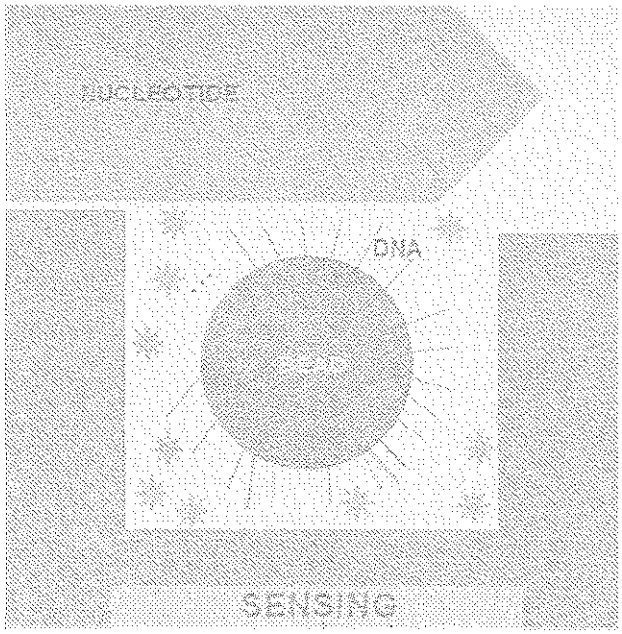


FIG. 50A

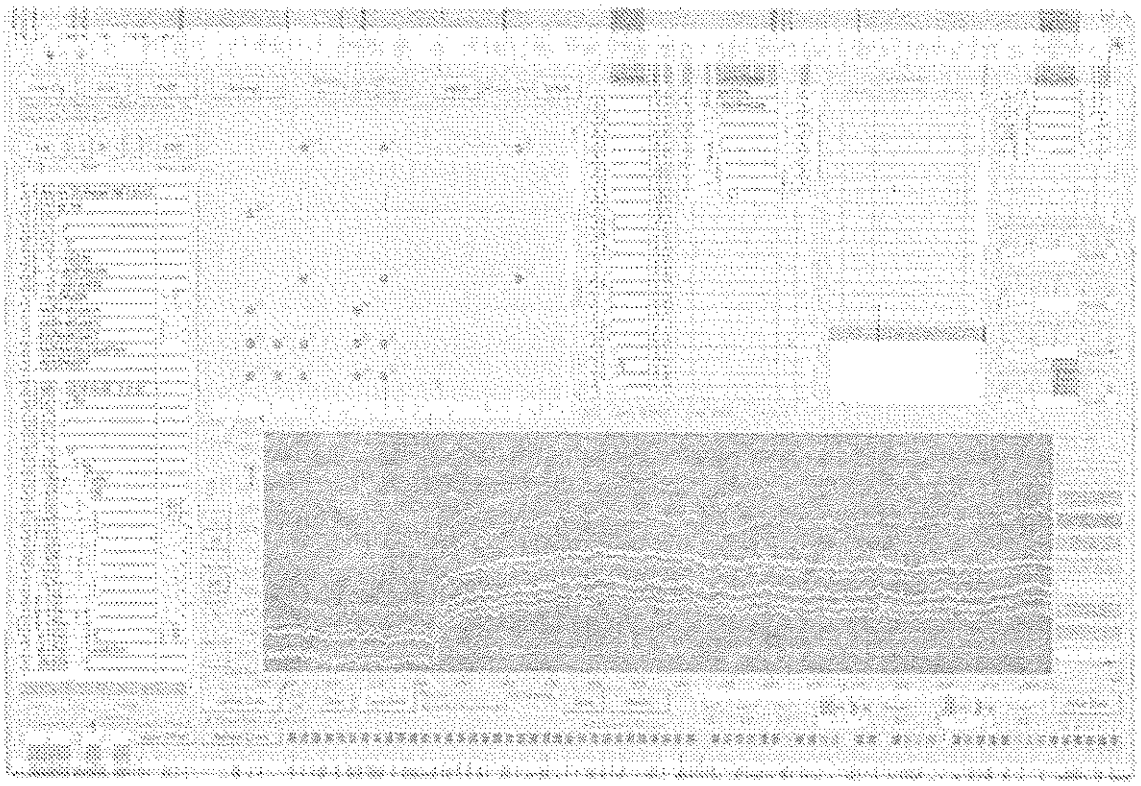


FIG. 50B

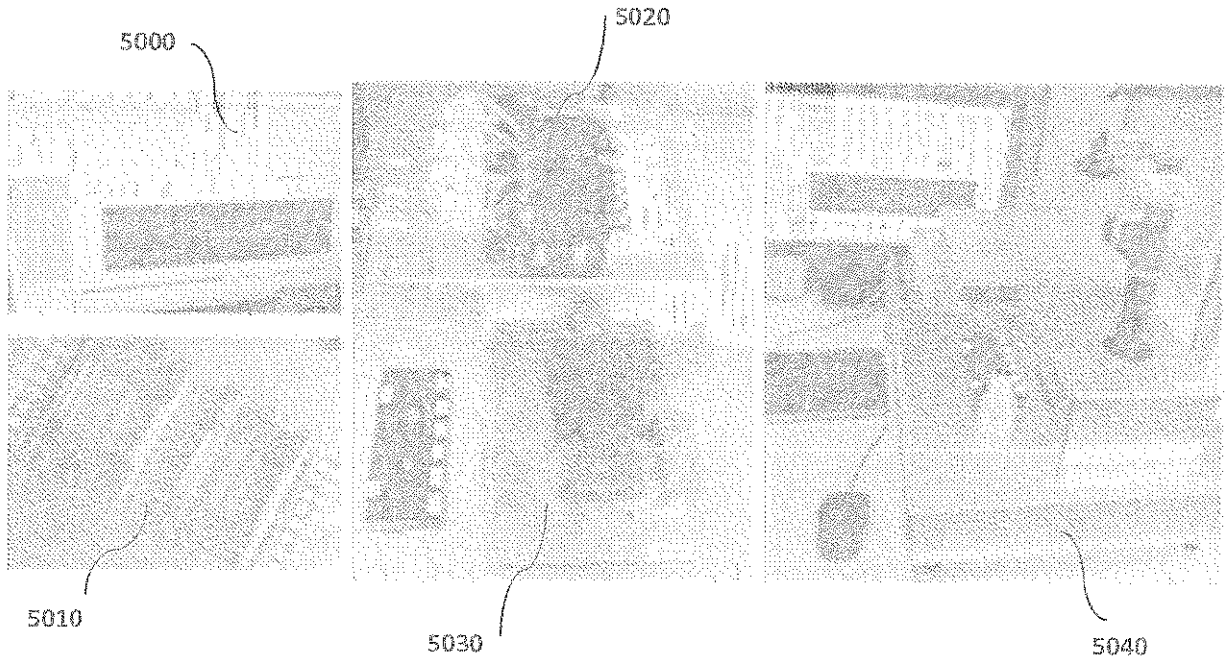


FIG. 51

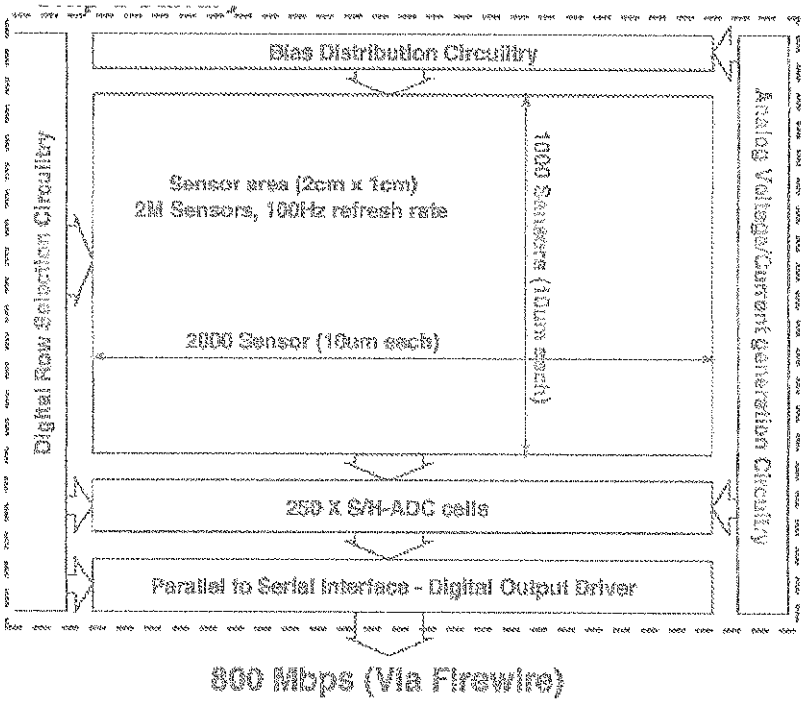


FIG. 52

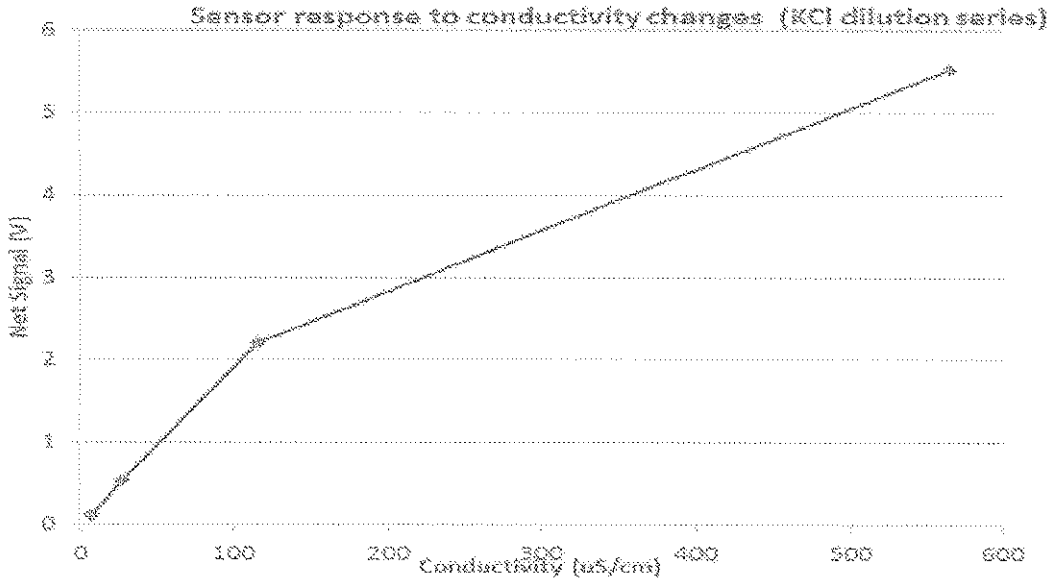


FIG. 53A

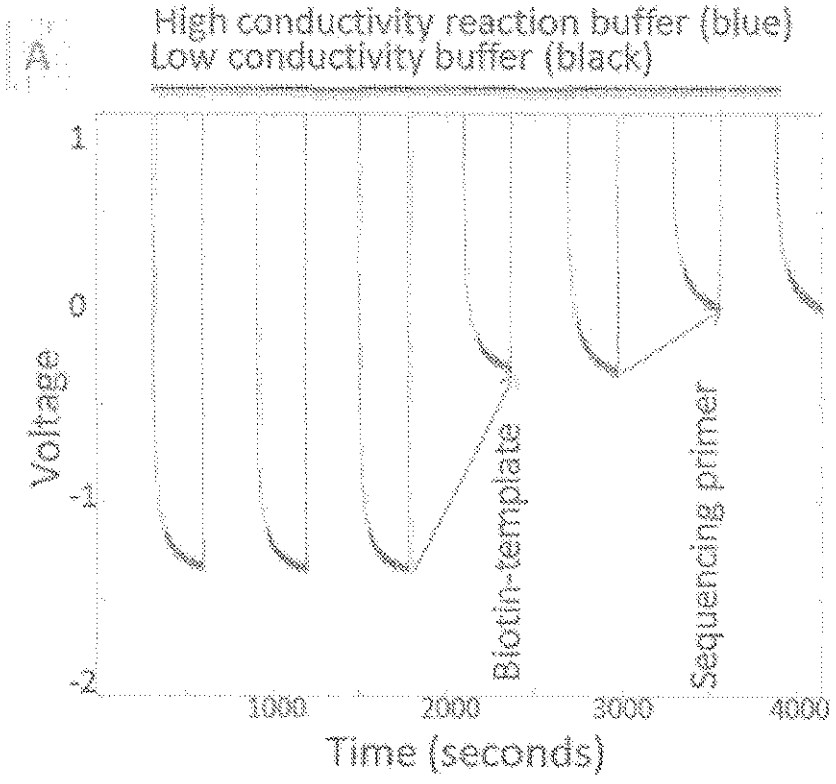


FIG. 53B

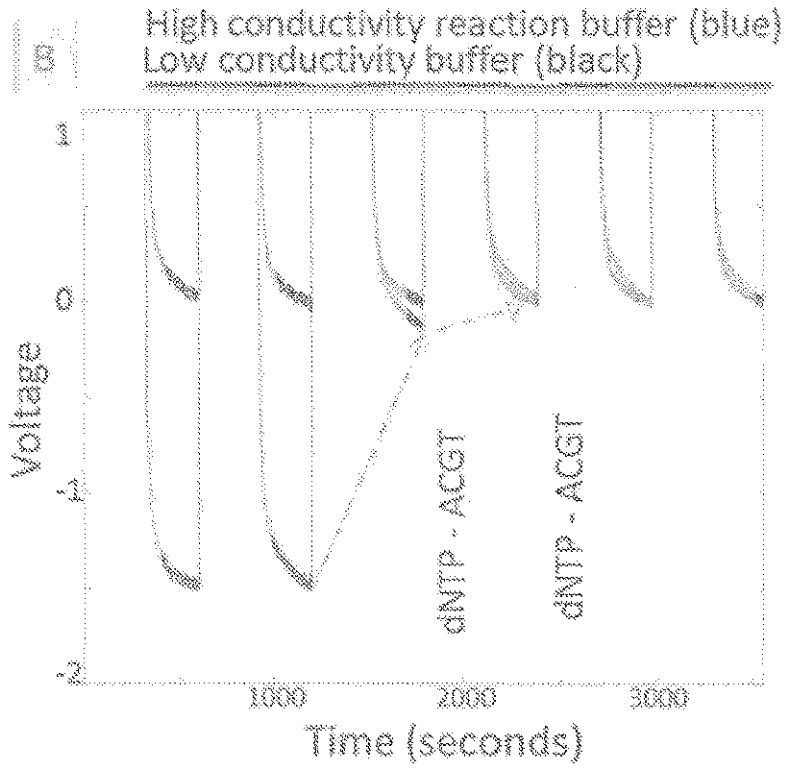


FIG. 54A

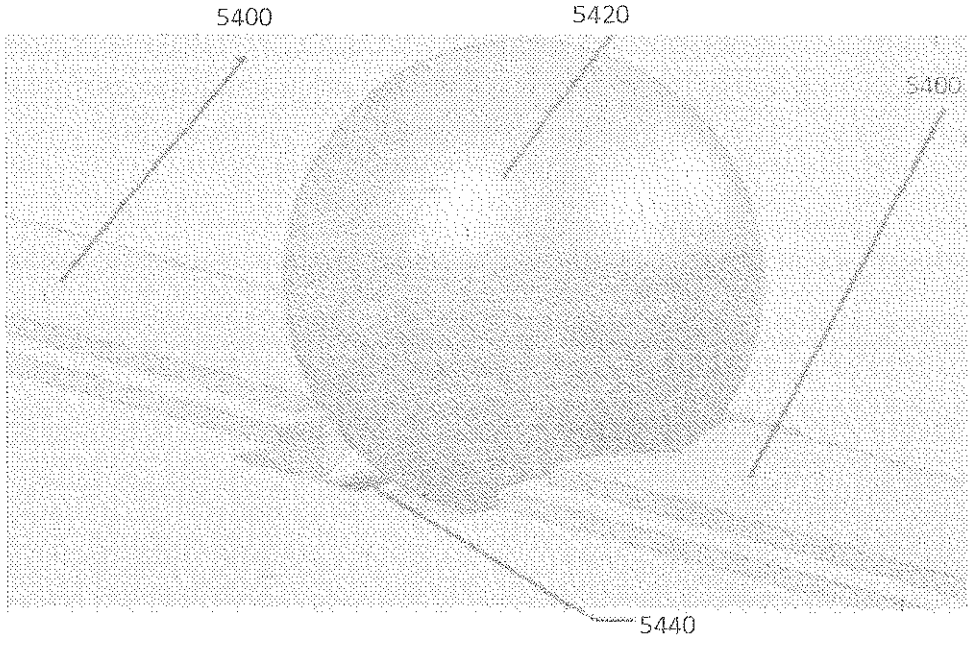


FIG. 54B

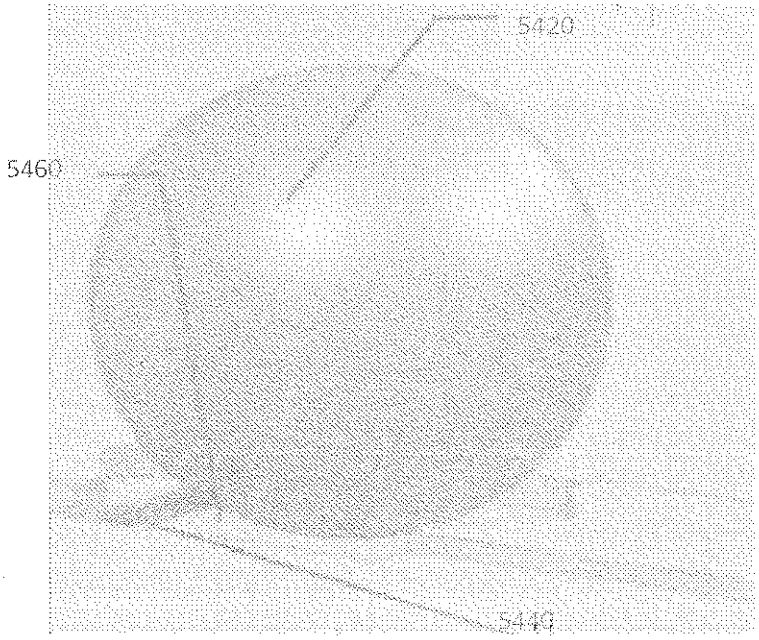


FIG. 54C

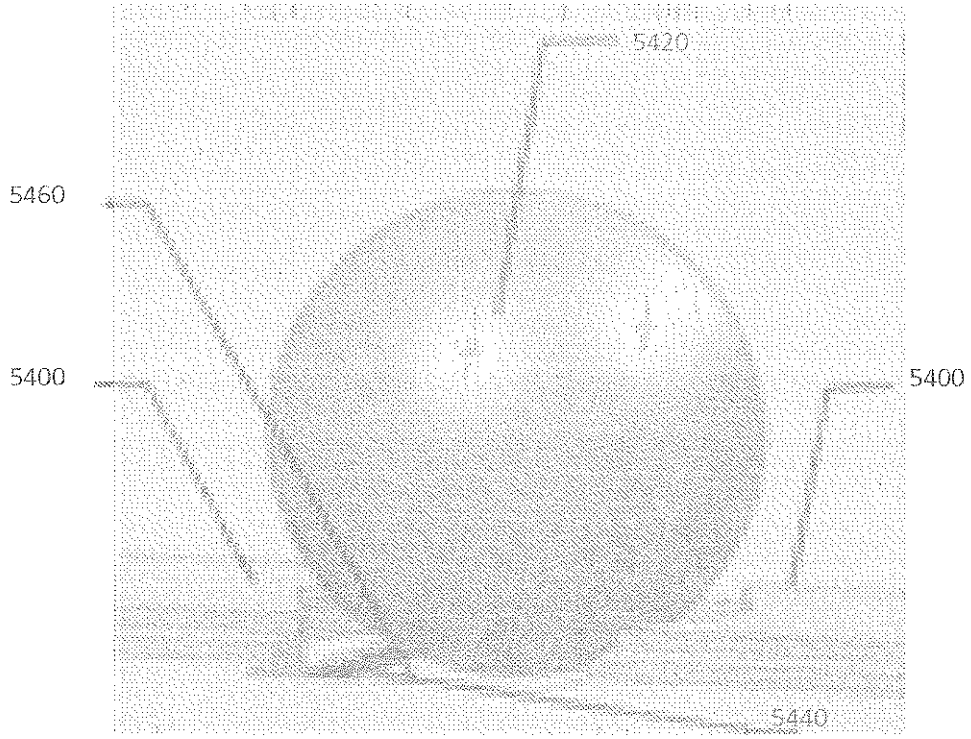


FIG. 55A

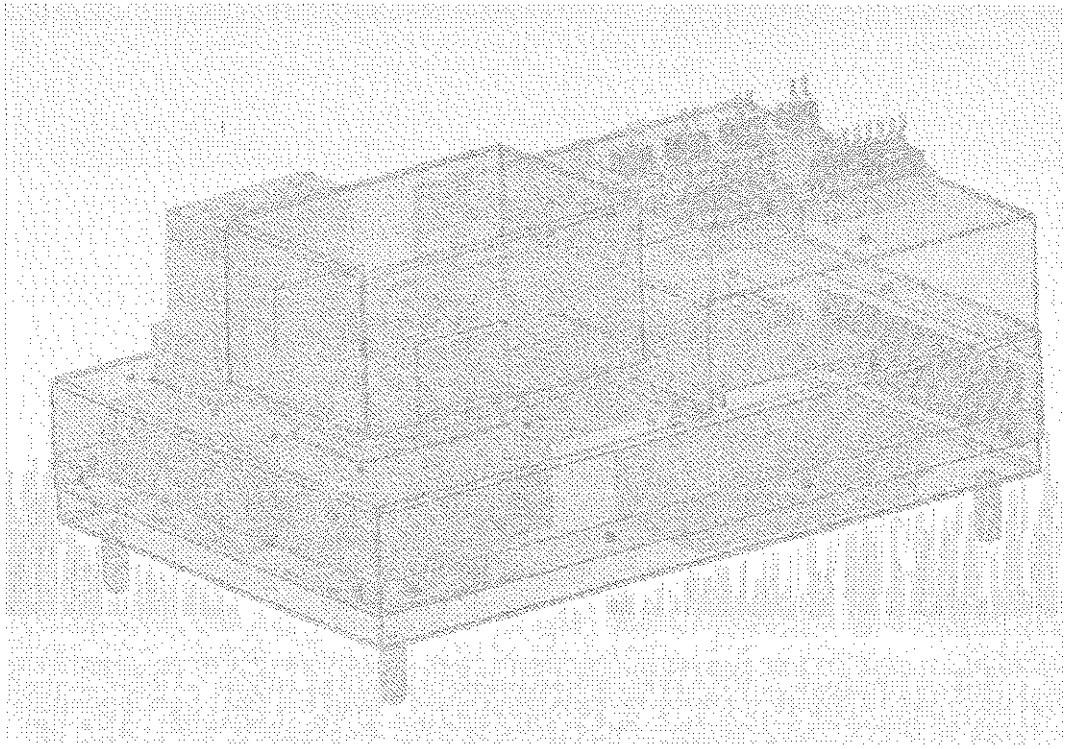


FIG. 55B

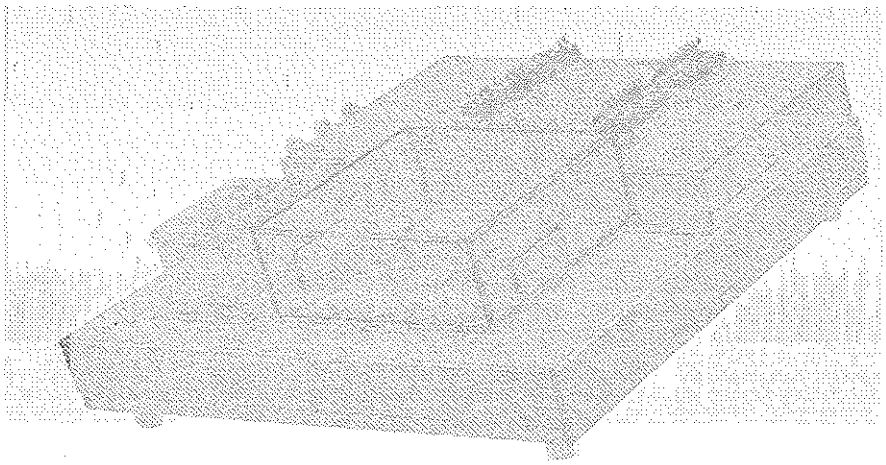


FIG. 56

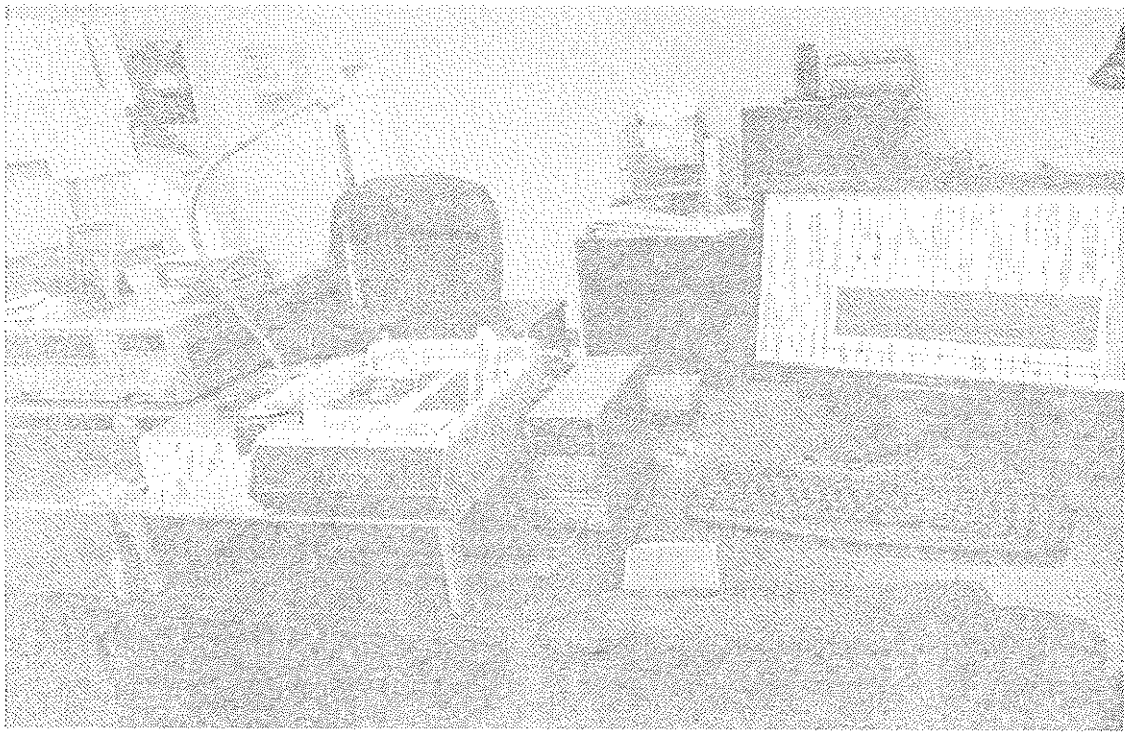


FIG. 57

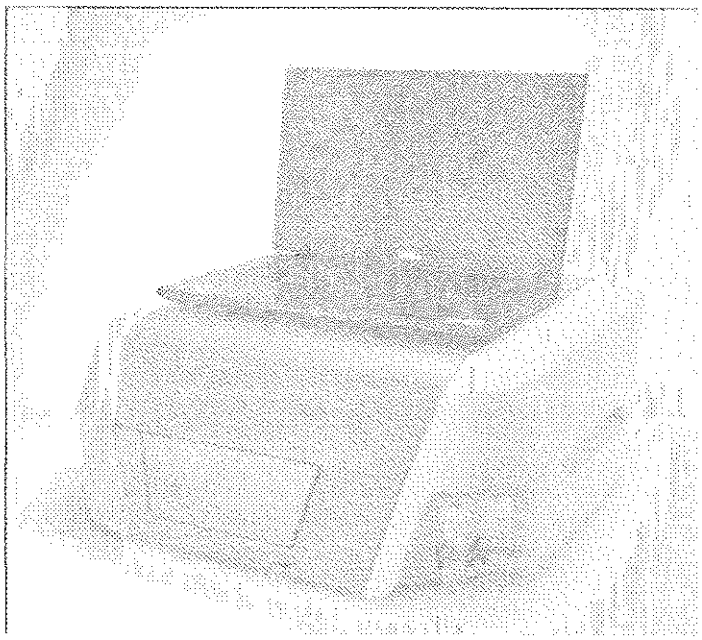


FIG. 58

