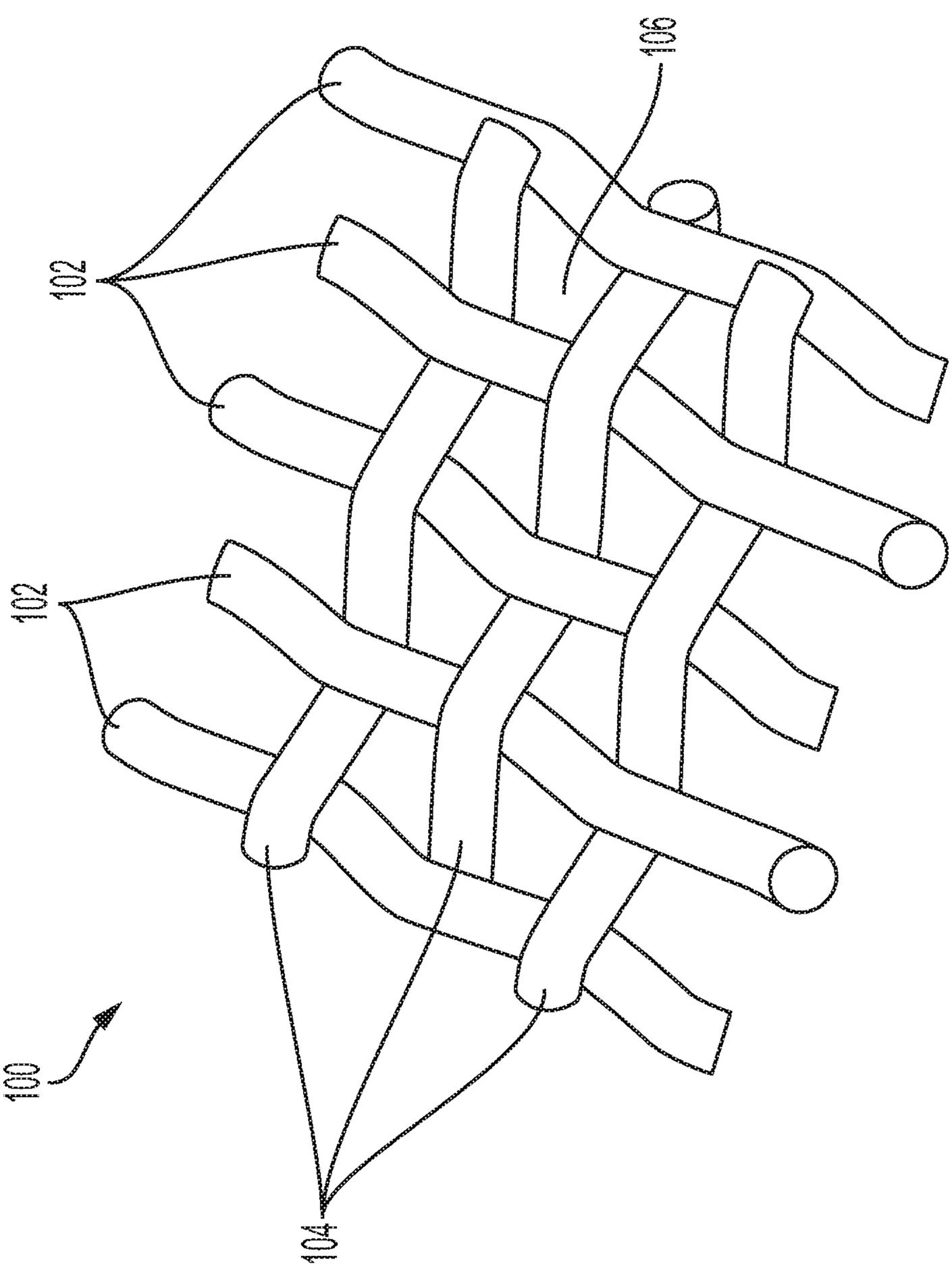


FIGURE 1A

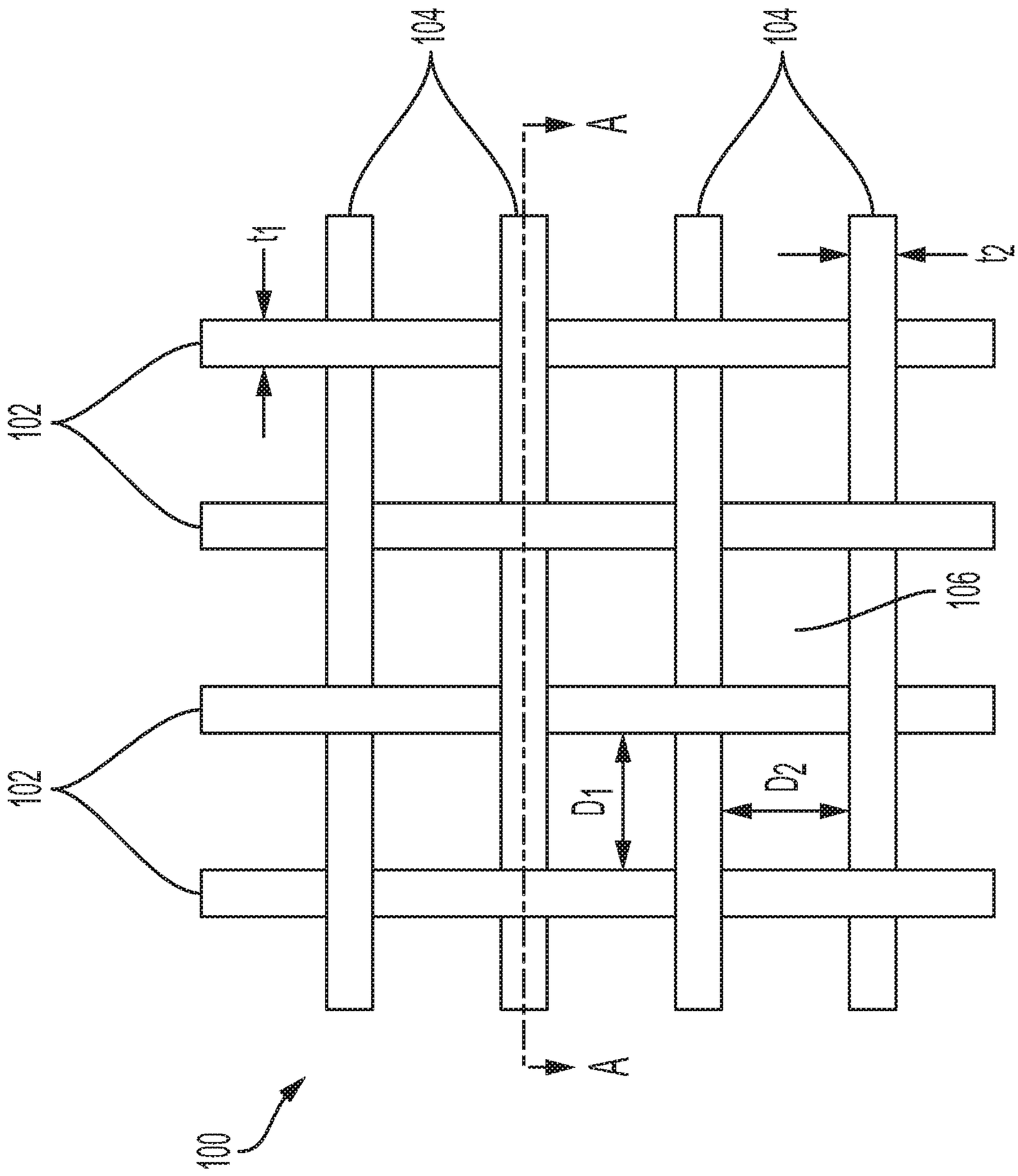


FIGURE 1B

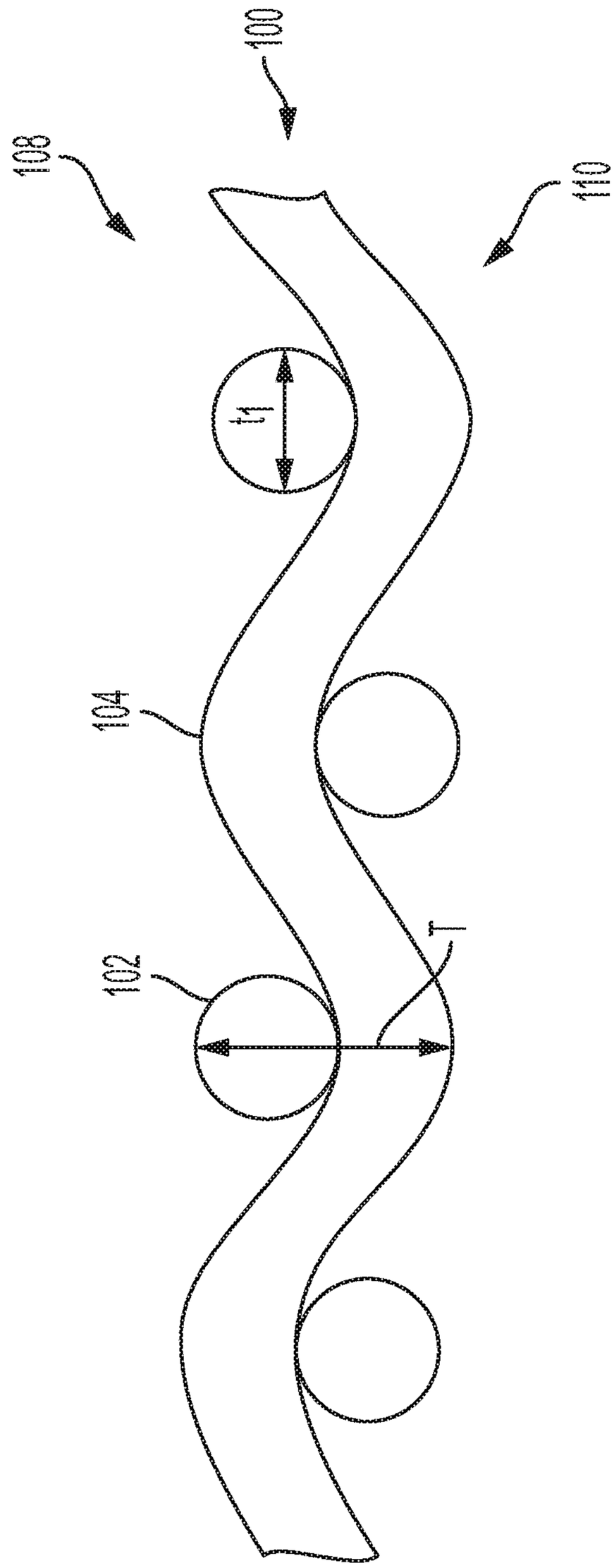


FIGURE 1C

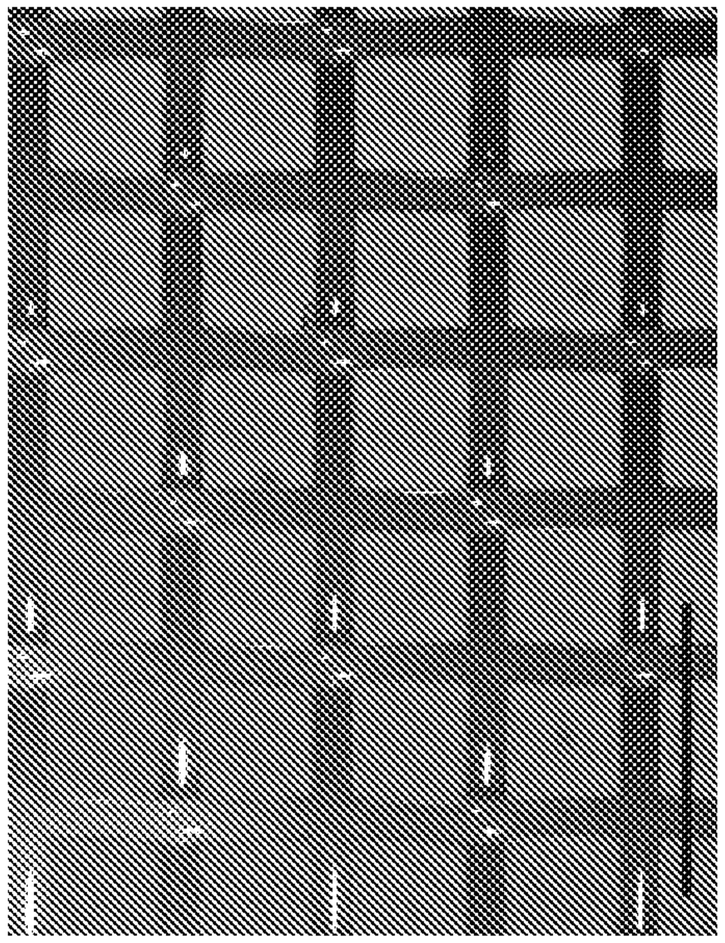


FIGURE 2A

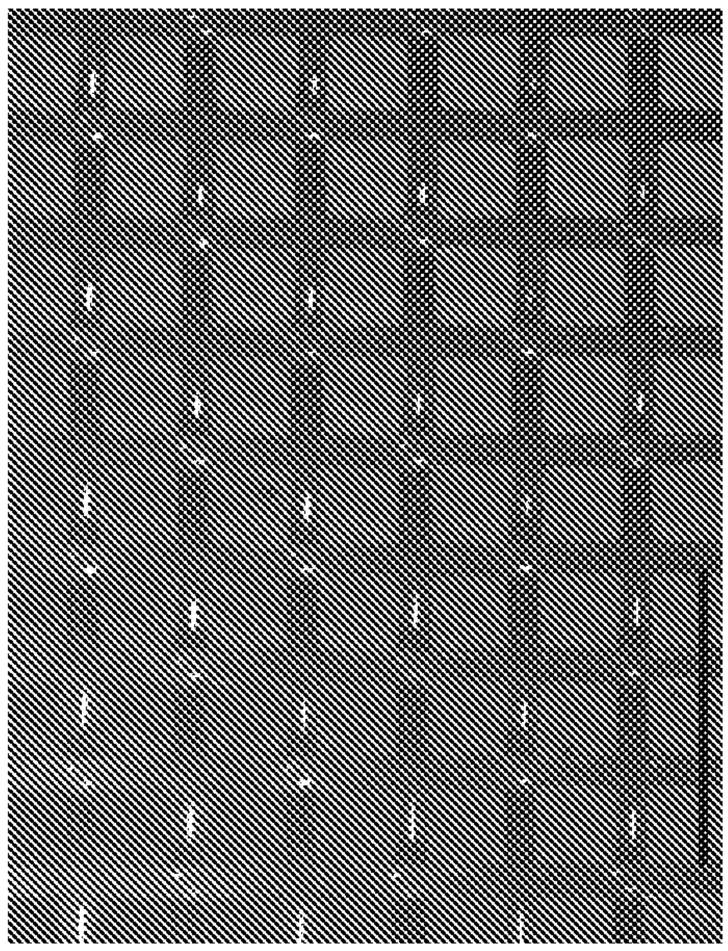


FIGURE 2B

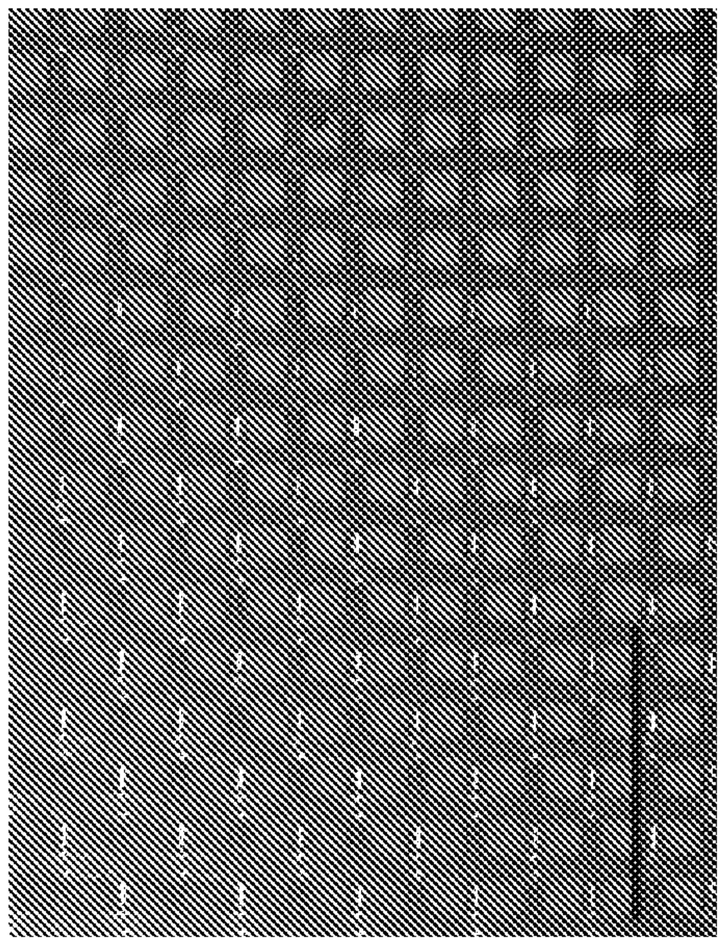


FIGURE 2C

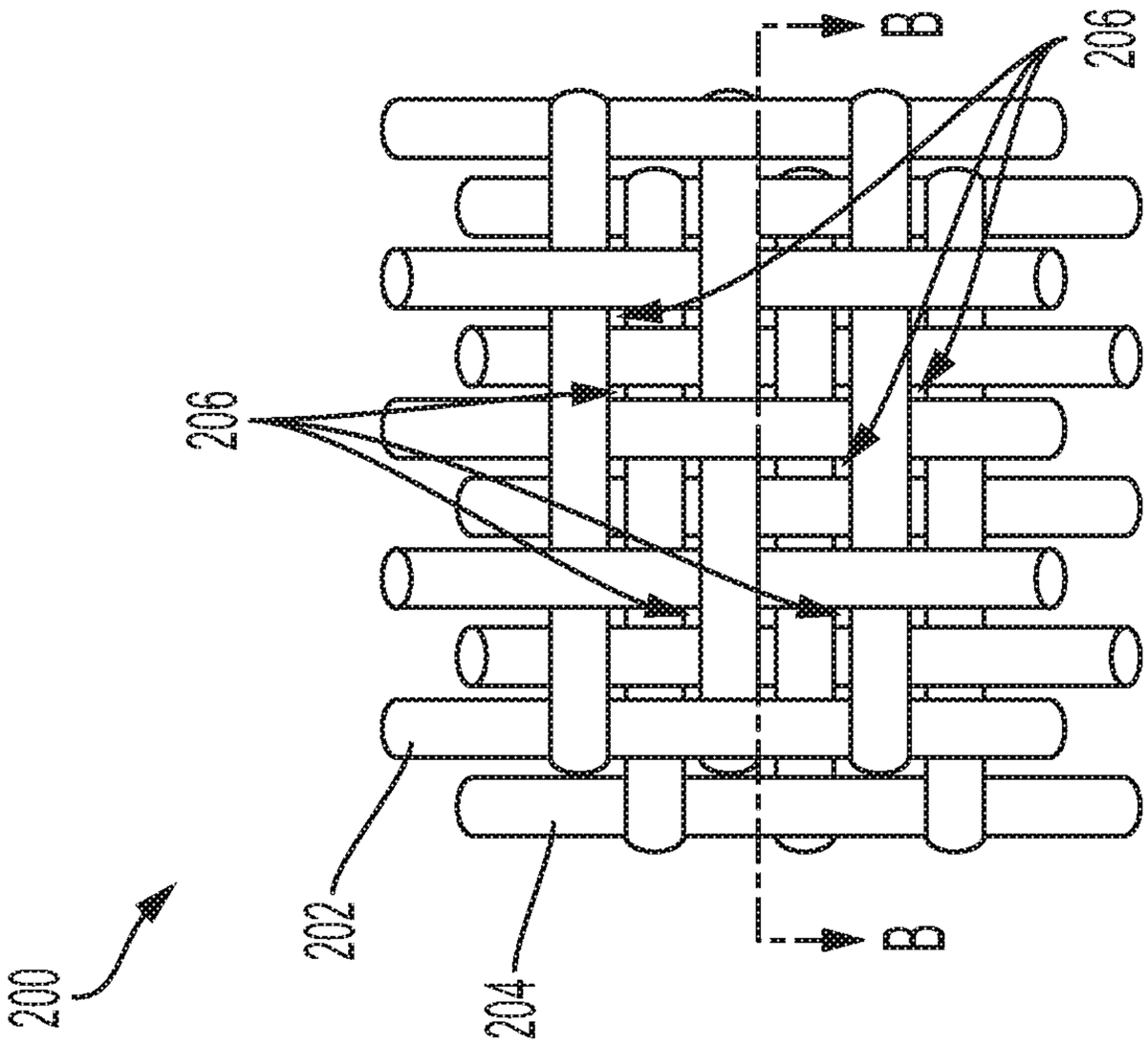


FIGURE 3B

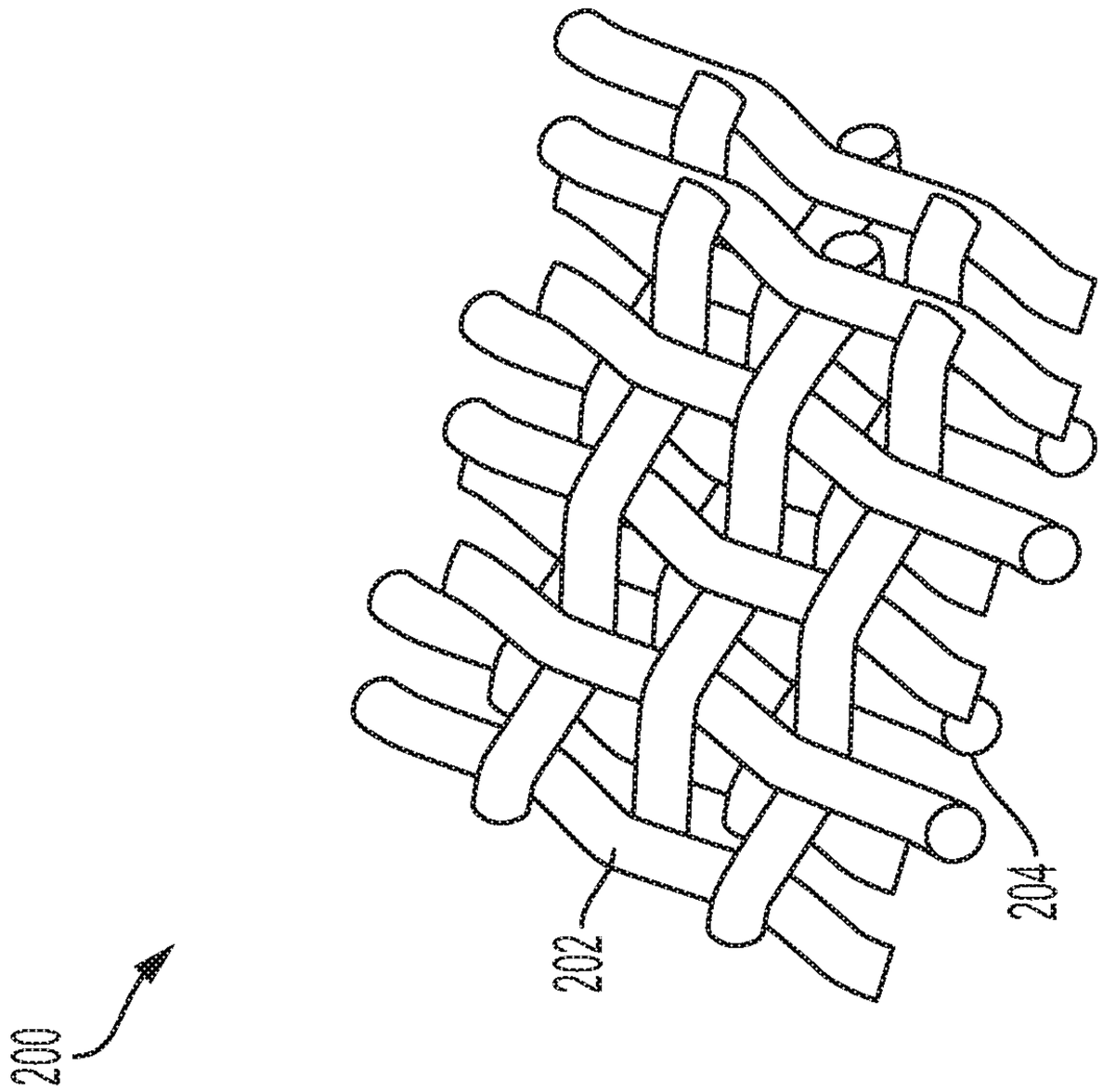


FIGURE 3A

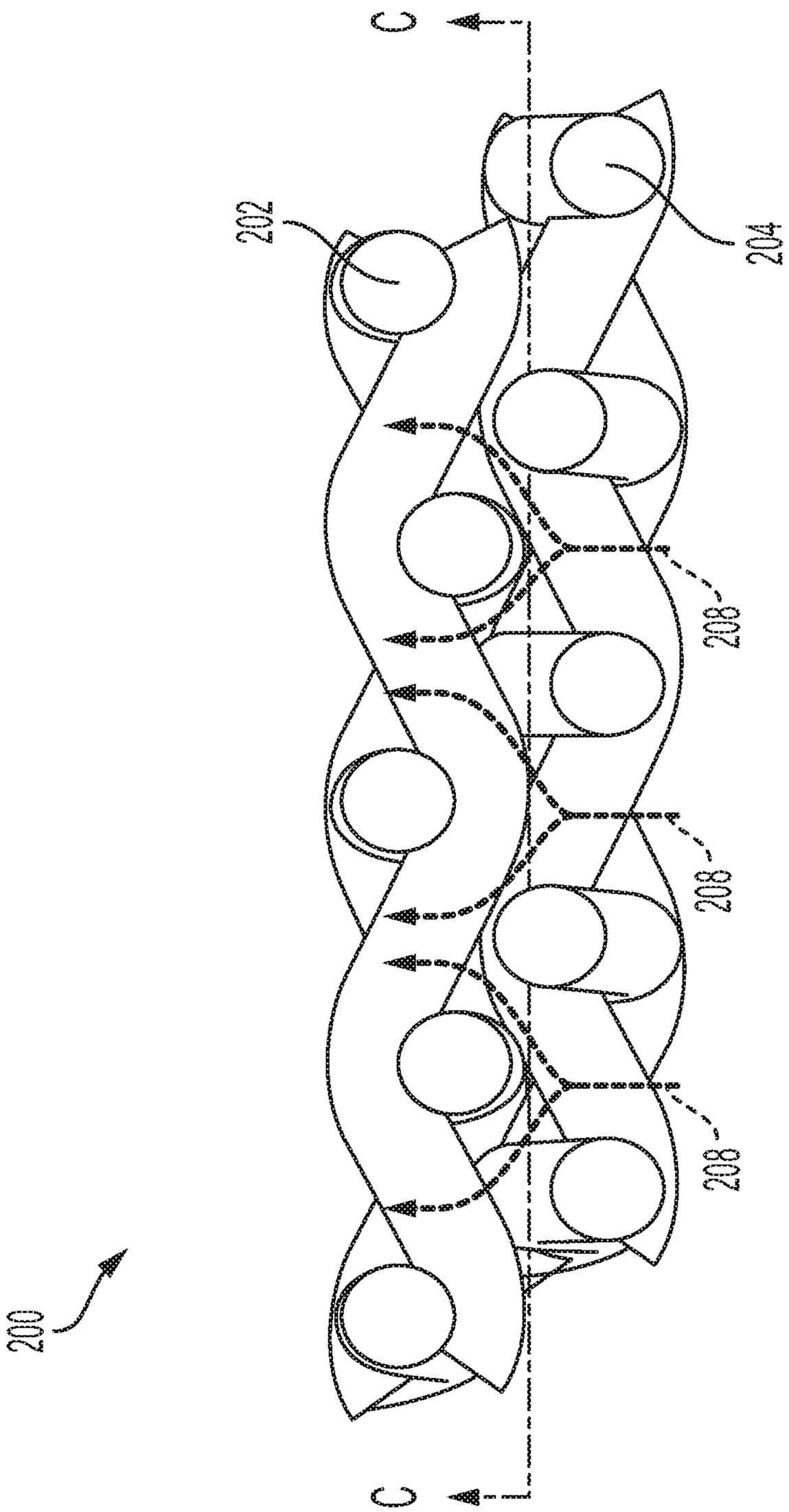


FIGURE 4

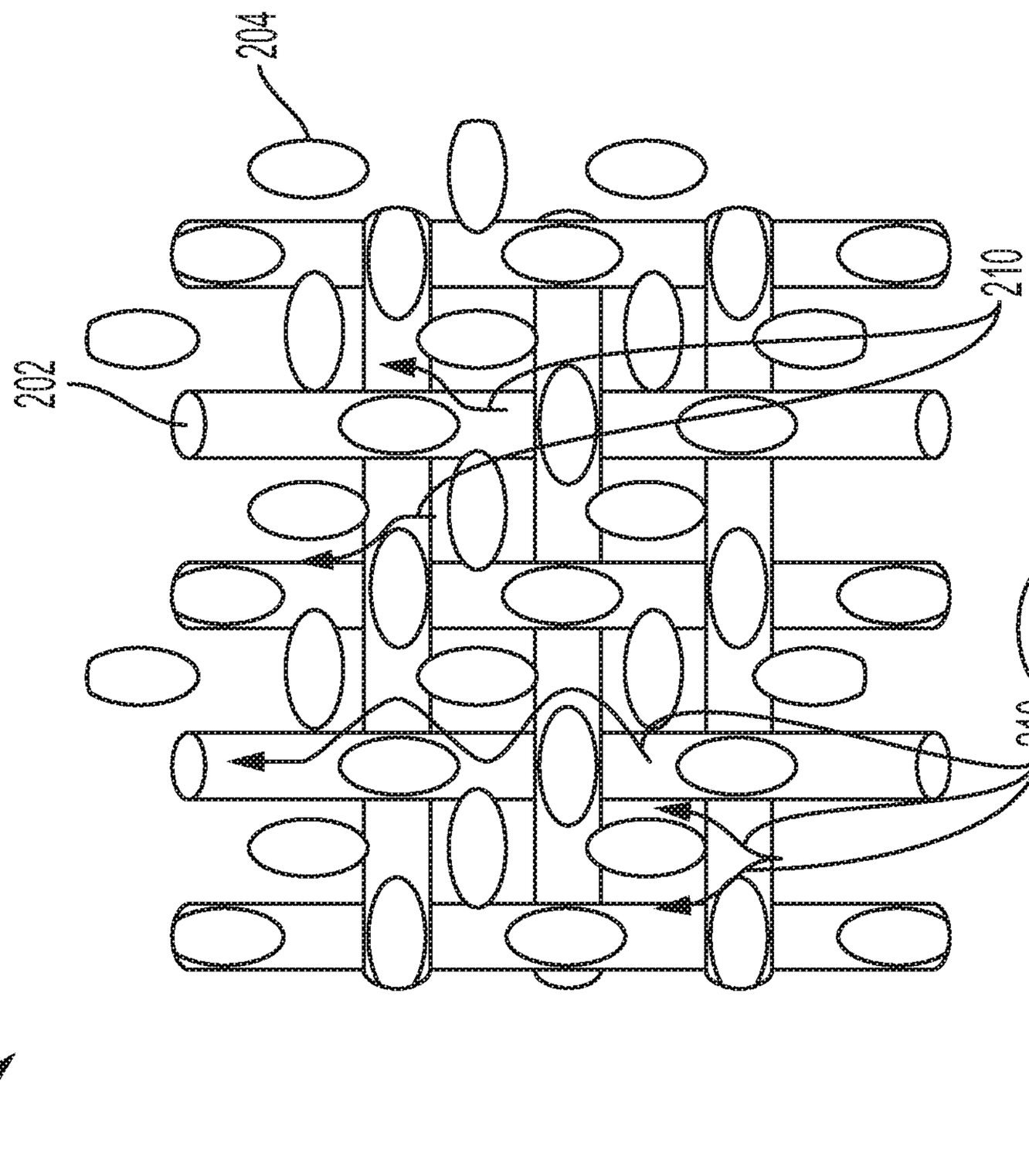


FIGURE 5

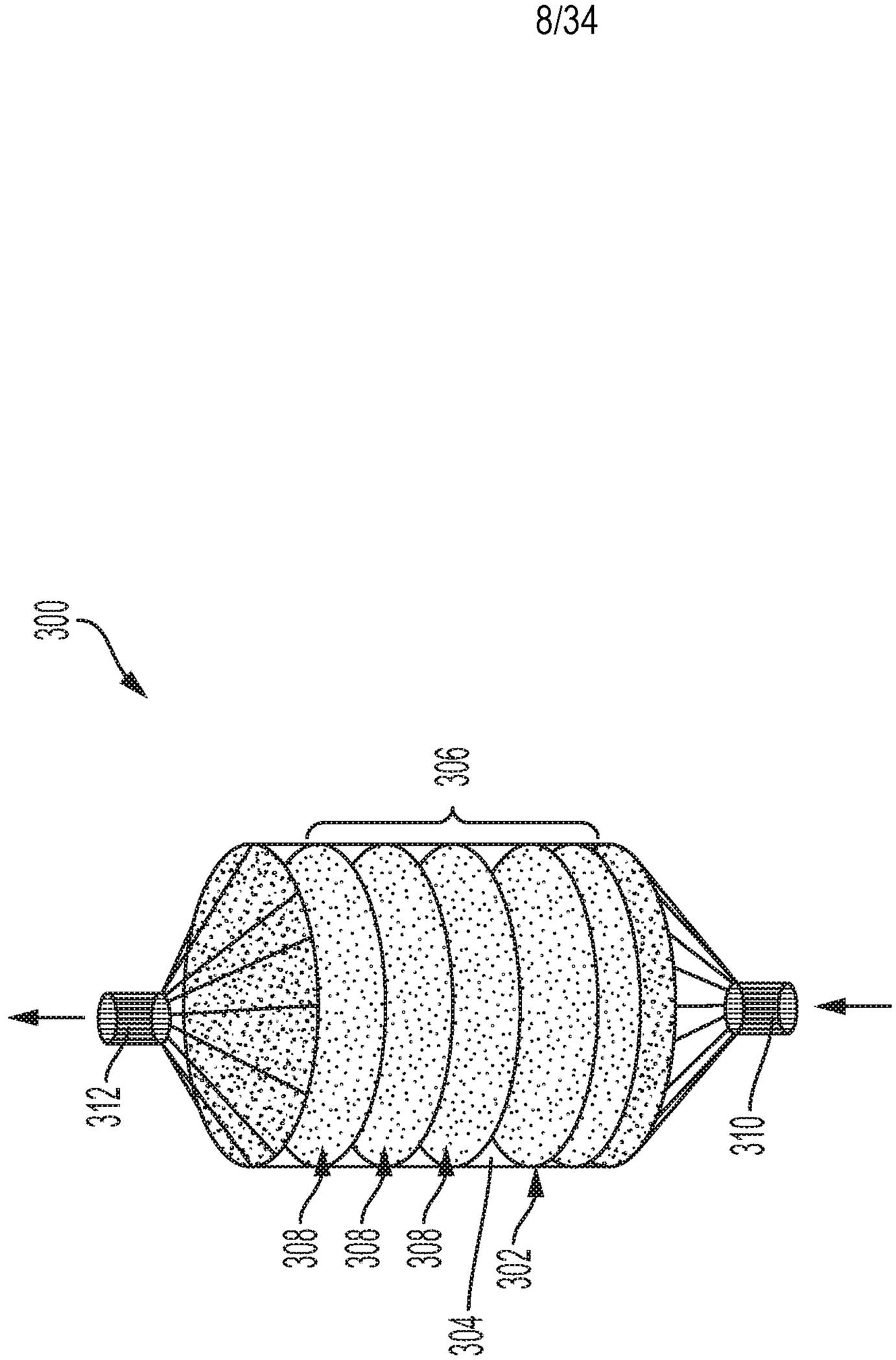


FIGURE 6

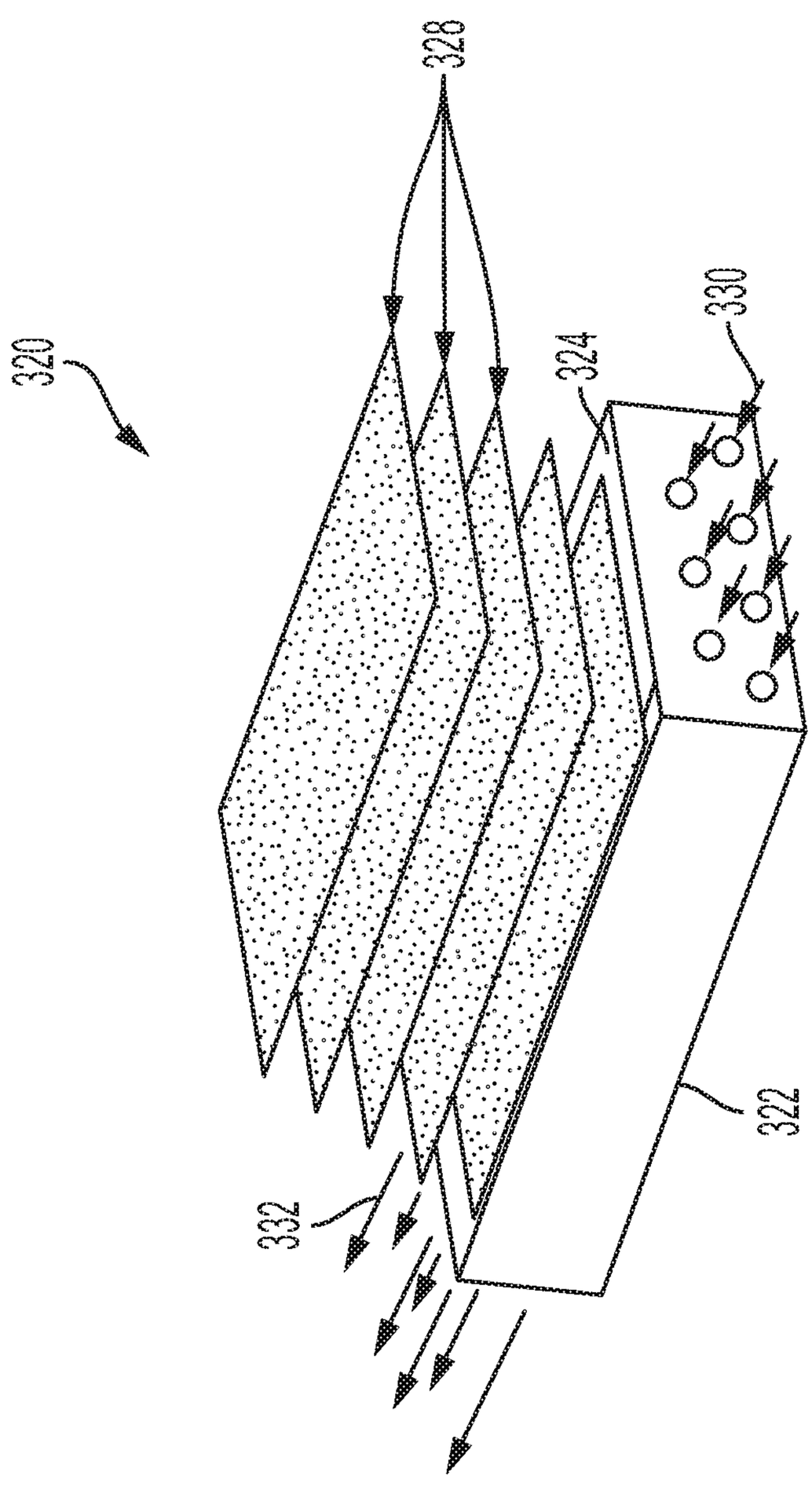


FIGURE 7

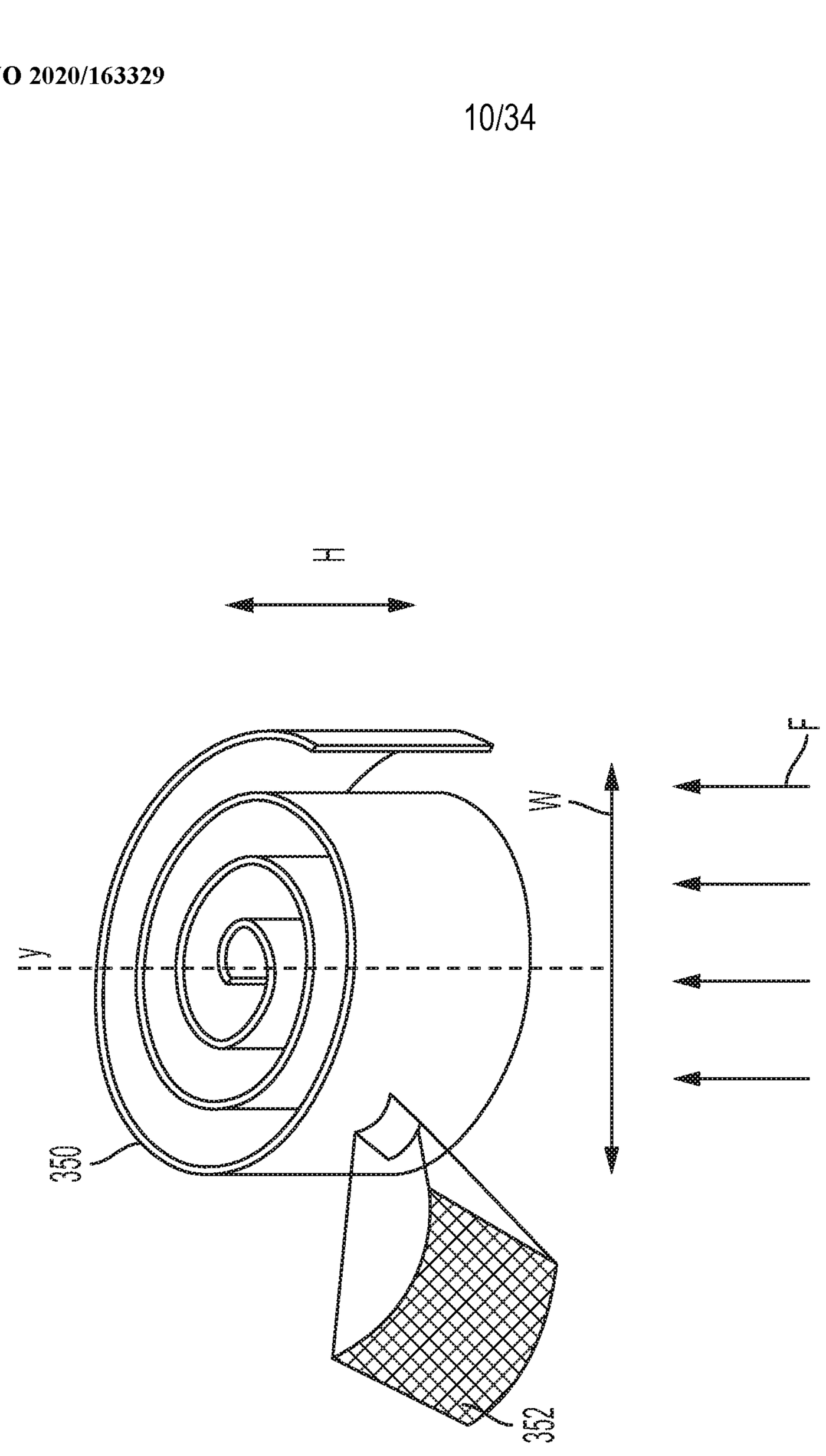


FIGURE 8

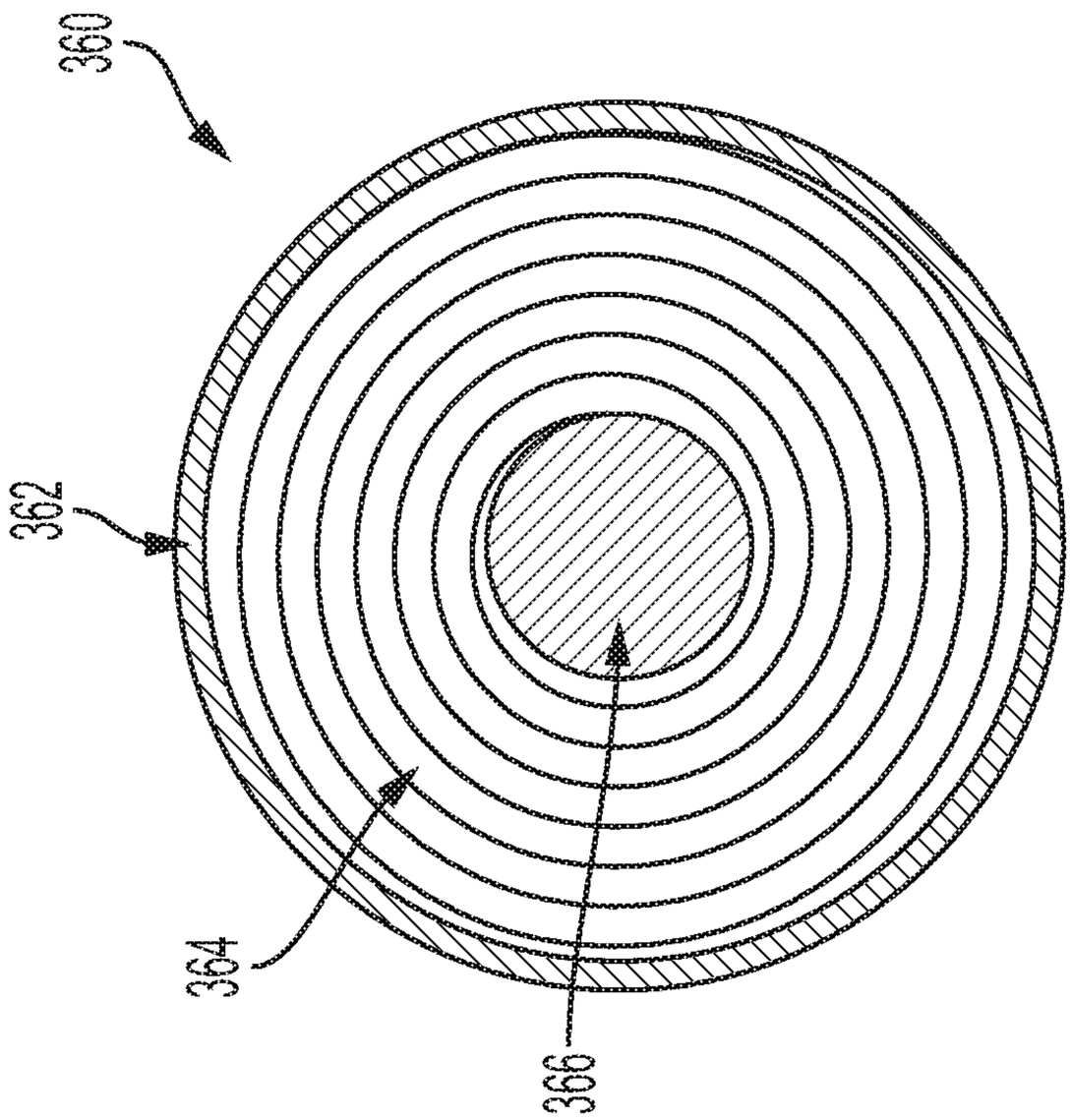


FIGURE 9

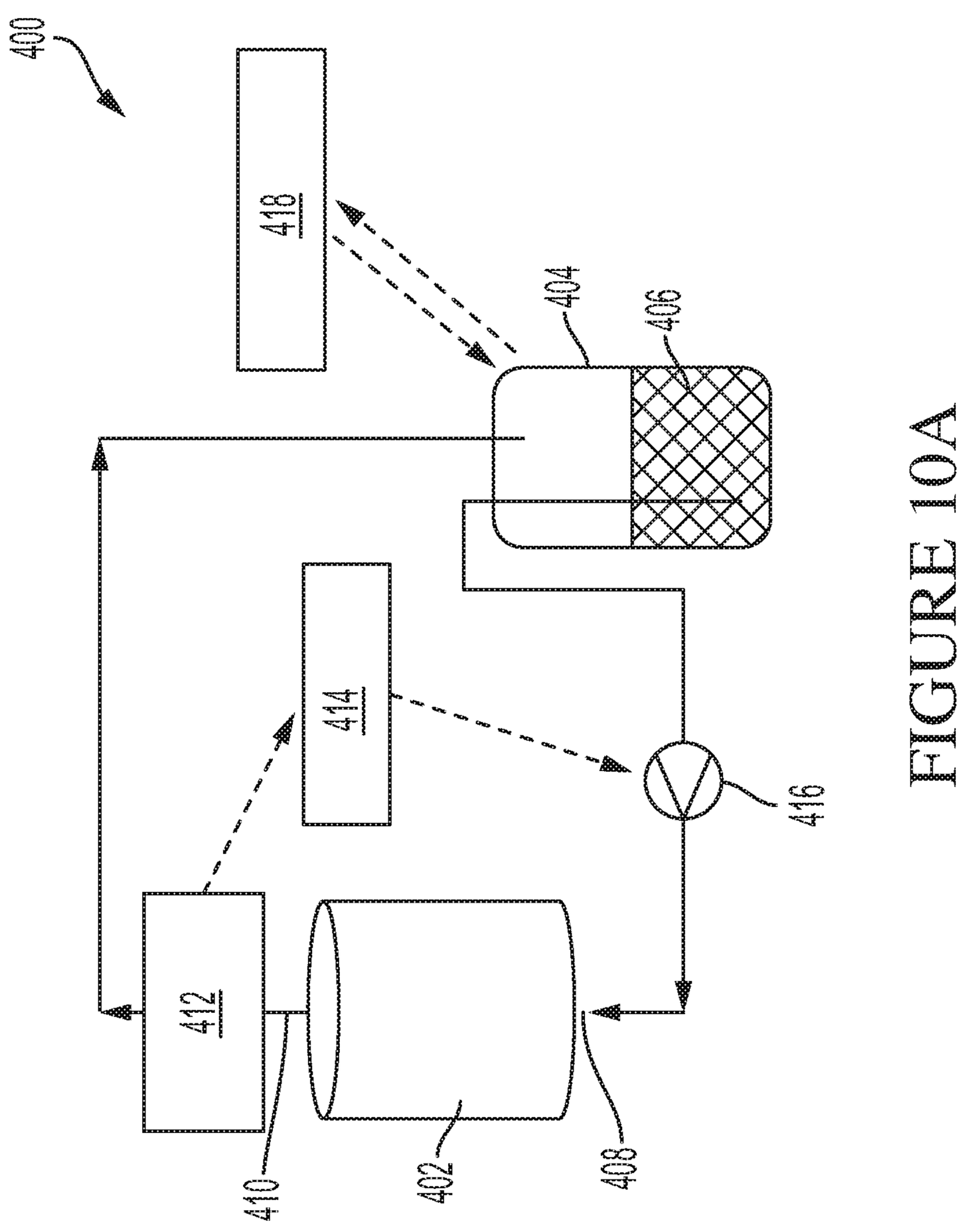


FIGURE 10A

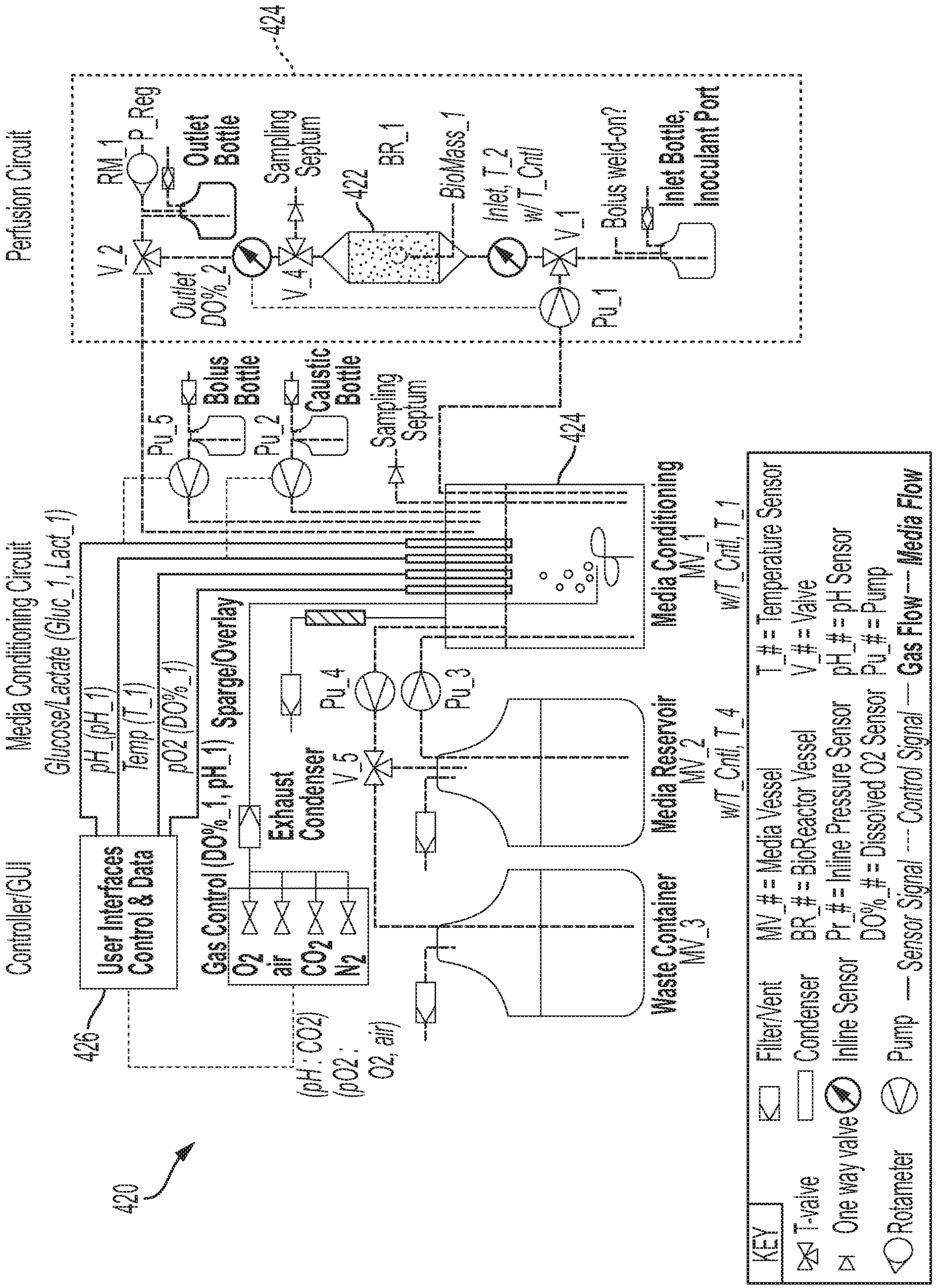

Perfusion Circuit
424
RM_1
P_Reg
Outlet Bottle
Sampling Septum
422
BR_1
BioMass_1
Inlet, T_2 w/ T_Cntl
V_1
Bolus weld-on?
Inlet Bottle, Inoculant Port
V_2
V_4
Pu_1
Pu_5
Bolus Bottle
Pu_2
Caustic Bottle
Sampling Septum
424
Media Conditioning MV_1
Media Conditioning Circuit
Glucose/Lactate (Gluc_1, Lact_1)
pH (pH_1)
Temp (T_1)
pO2 (DO%_1)
Sparge/Overlay
Gas Control (DO%_1, pH_1)
Exhaust Condenser
V_5
Pu_4
Pu_3
Media Reservoir MV_2
Waste Container MV_3
w/T_Cntl, T_4
w/T_Cntl, T_1
User Interfaces Control & Data
Controller/GUI
426
O2
air
CO2
N2
(pH; CO2)
(pO2; O2, air)
420
KEY
Filter/Vent
Condenser
Inline Sensor
Pump
T-valve
One way valve
Rotameter
MV_# = Media Vessel
BR_# = BioReactor Vessel
Pr_# = Inline Pressure Sensor
DO%_# = Dissolved O2 Sensor
Sensor Signal
Control Signal
T_# = Temperature Sensor
V_# = Valve
pH_# = pH Sensor
Pu_# = Pump
Gas Flow
Media Flow

FIGURE 10B

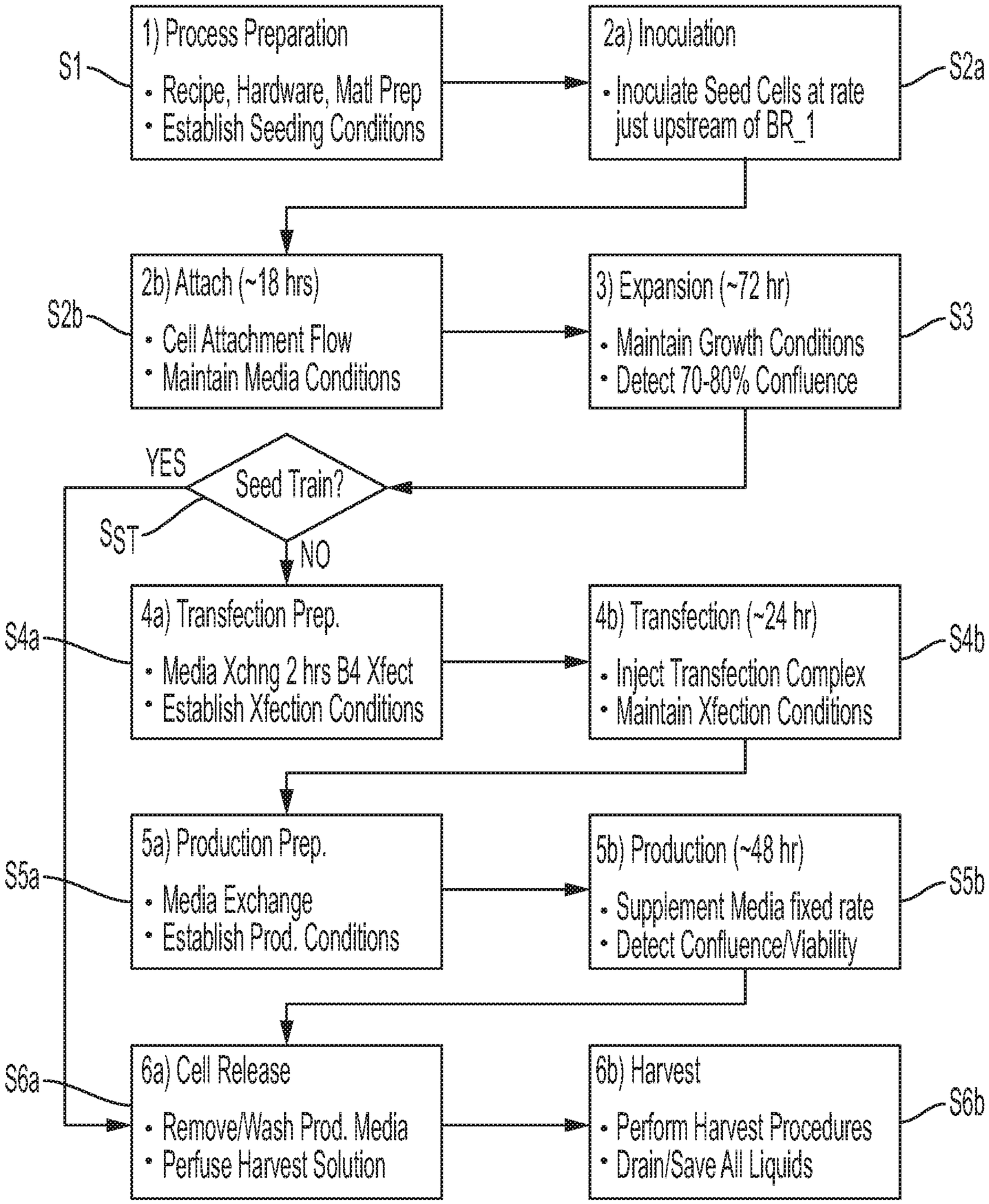

S1
1) Process Preparation
• Recipe, Hardware, Matl Prep
• Establish Seeding Conditions
2a) Inoculation
• Inoculate Seed Cells at rate just upstream of BR_1
S2a
S2b
2b) Attach (~18 hrs)
• Cell Attachment Flow
• Maintain Media Conditions
3) Expansion (~72 hr)
• Maintain Growth Conditions
• Detect 70-80% Confluence
S3
YES
Seed Train?
SST
NO
S4a
4a) Transfection Prep.
• Media Xchng 2 hrs B4 Xfect
• Establish Xfection Conditions
4b) Transfection (~24 hr)
• Inject Transfection Complex
• Maintain Xfection Conditions
S4b
S5a
5a) Production Prep.
• Media Exchange
• Establish Prod. Conditions
5b) Production (~48 hr)
• Supplement Media fixed rate
• Detect Confluence/Viability
S5b
S6a
6a) Cell Release
• Remove/Wash Prod. Media
• Perfuse Harvest Solution
6b) Harvest
• Perform Harvest Procedures
• Drain/Save All Liquids
S6b

FIGURE 11A

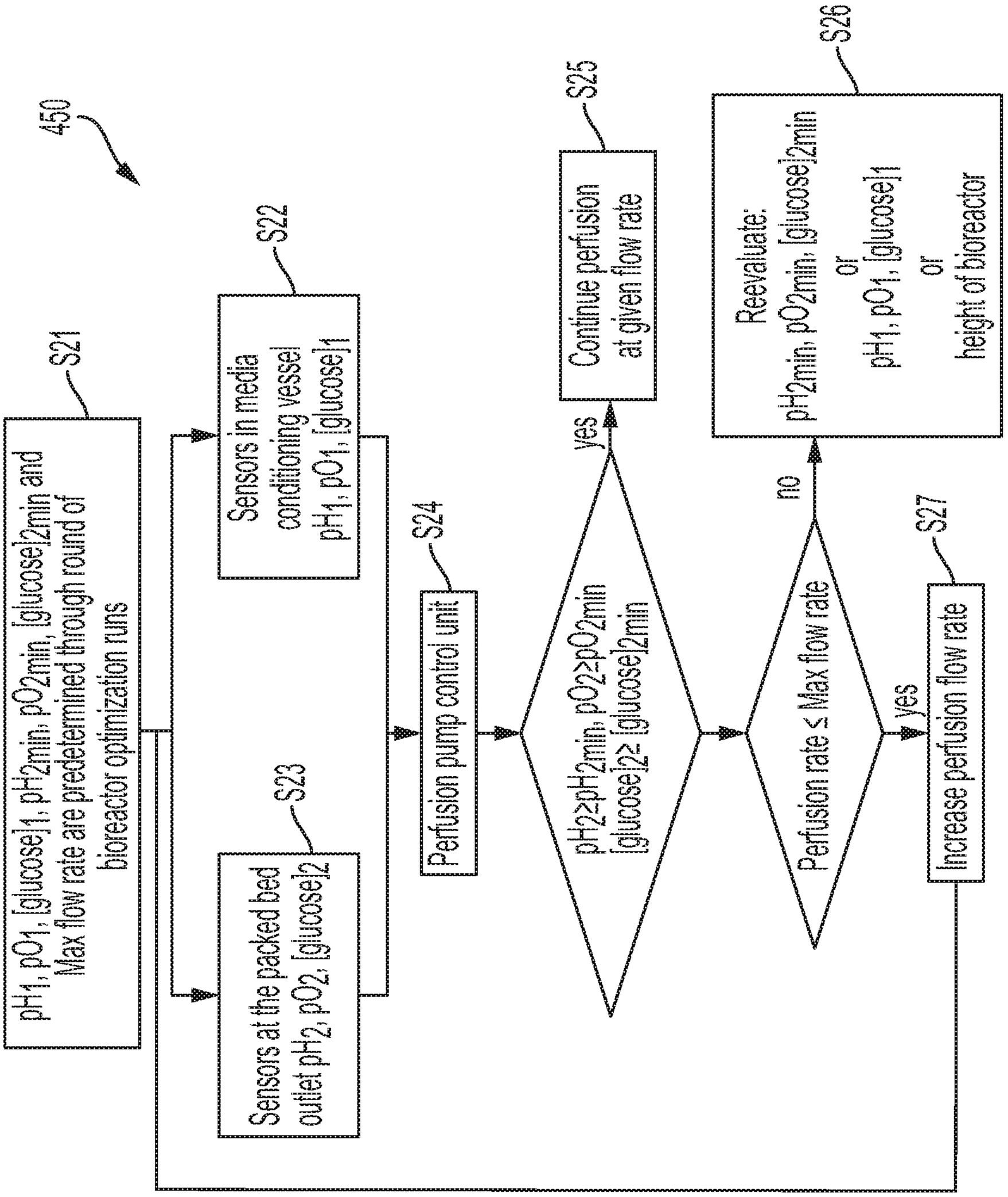

450
S21
pH1, pO1, [glucose]1, pH2min, pO2min, [glucose]2min and
Max flow rate are predetermined through round of
bioreactor optimization runs
S22
Sensors in media
conditioning vessel
pH1, pO1, [glucose]1
S23
Sensors at the packed bed
outlet pH2, pO2, [glucose]2
S24
Perfusion pump control unit
pH2≥pH2min, pO2≥pO2min
[glucose]2≥ [glucose]2min
yes
S25
Continue perfusion
at given flow rate
no
S26
Reevaluate:
pH2min, pO2min, [glucose]2min
or
pH1, pO1, [glucose]1
or
height of bioreactor
S27
Perfusion rate ≤ Max flow rate
yes
Increase perfusion flow rate

FIGURE 11B

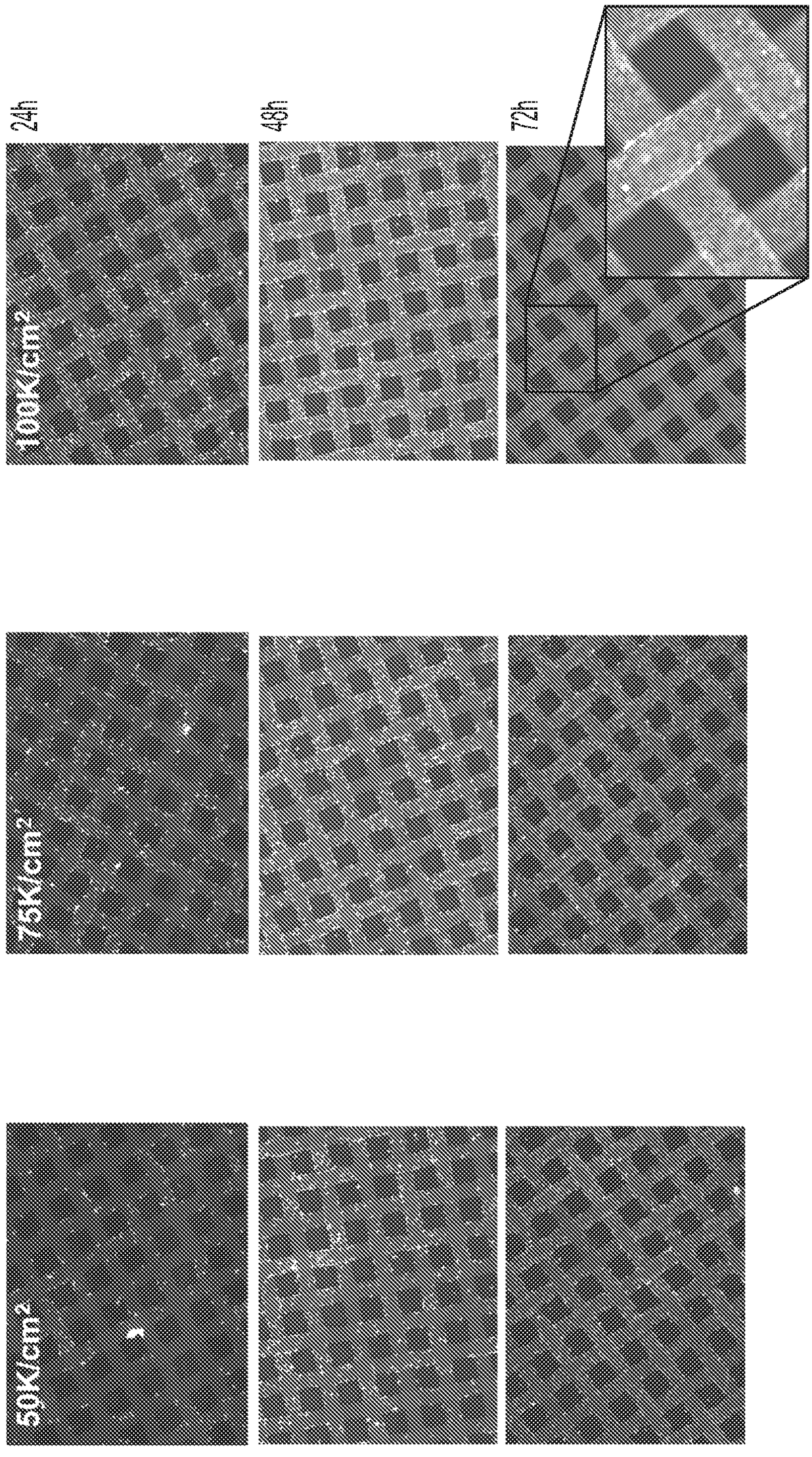


FIGURE 12C

FIGURE 12B

FIGURE 12A

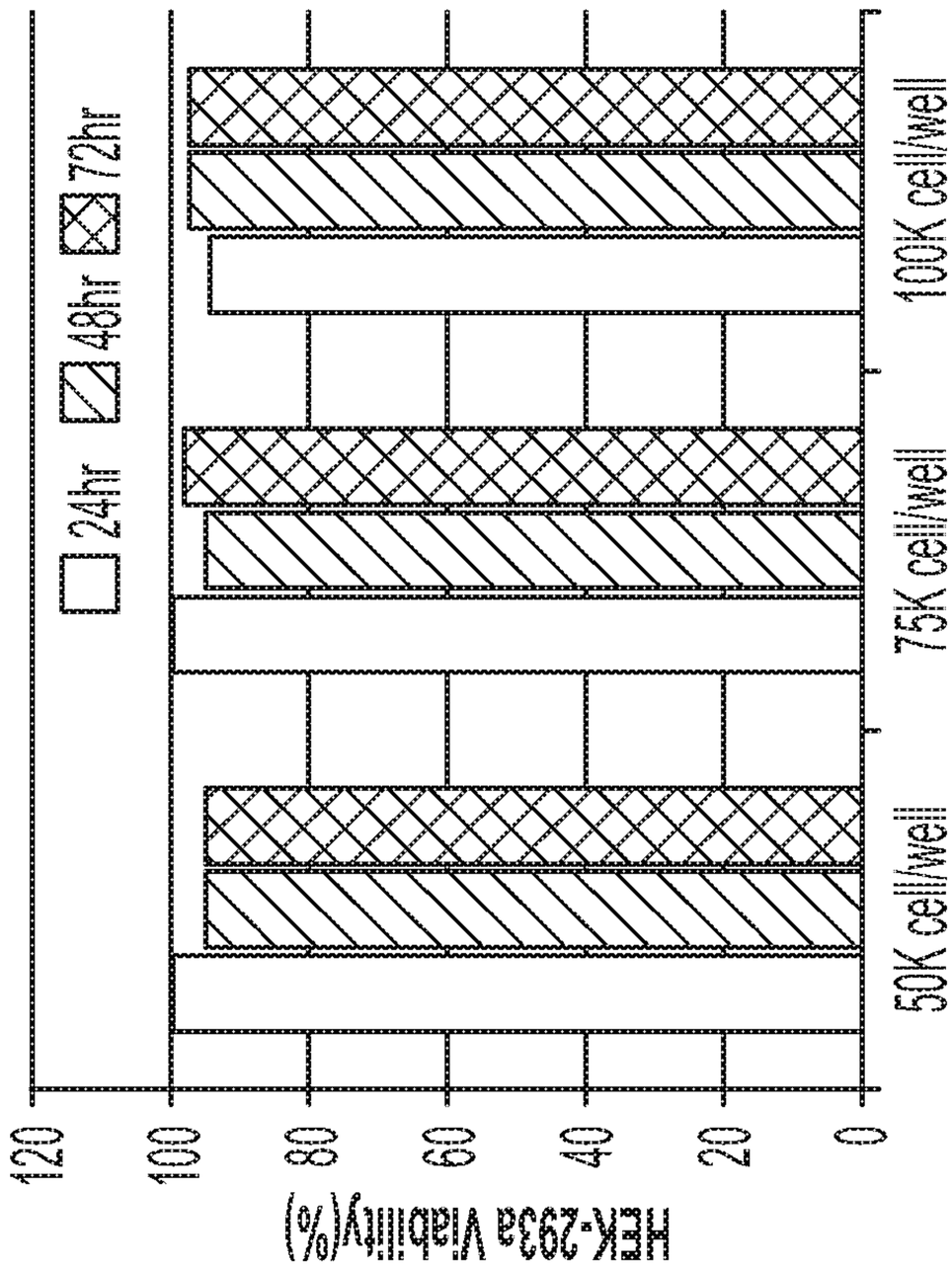


FIGURE 13B

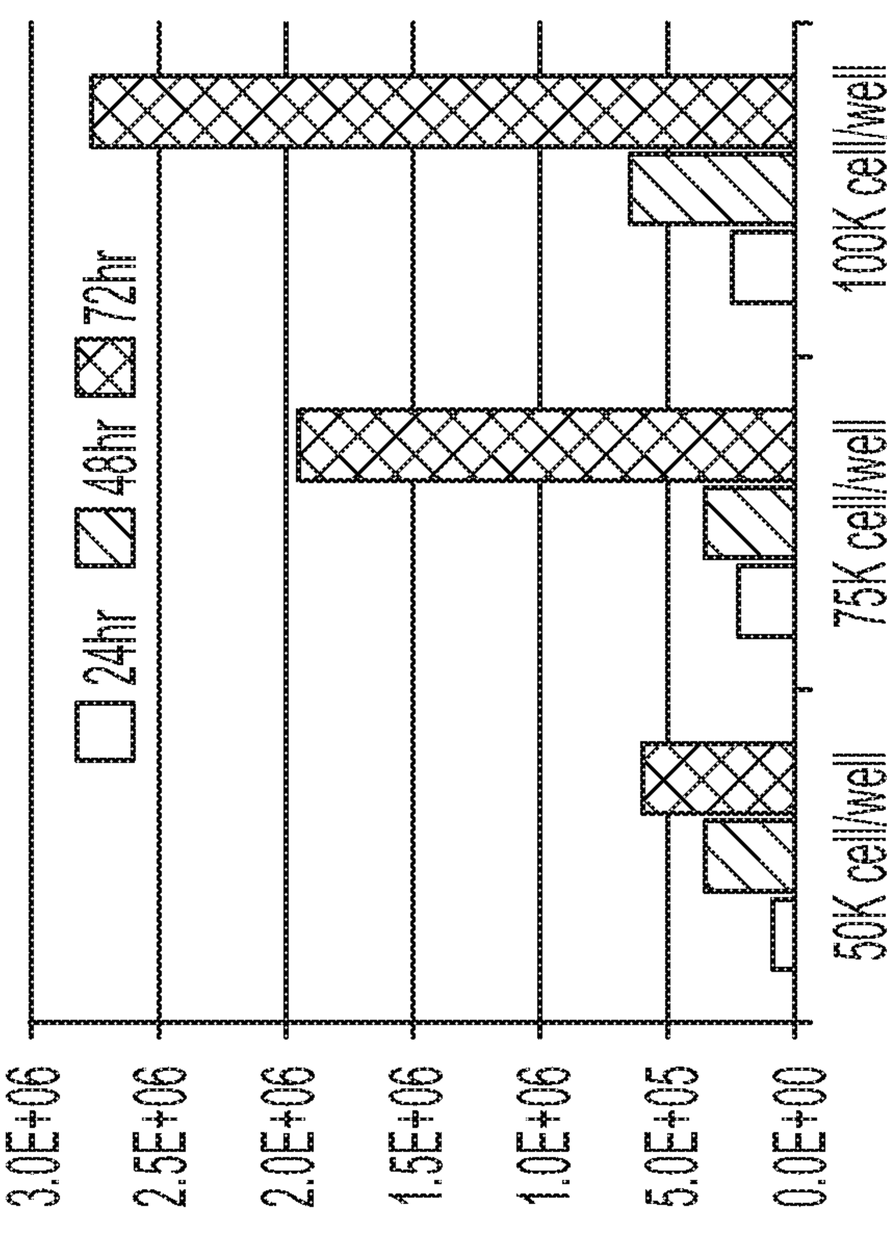


FIGURE 13A

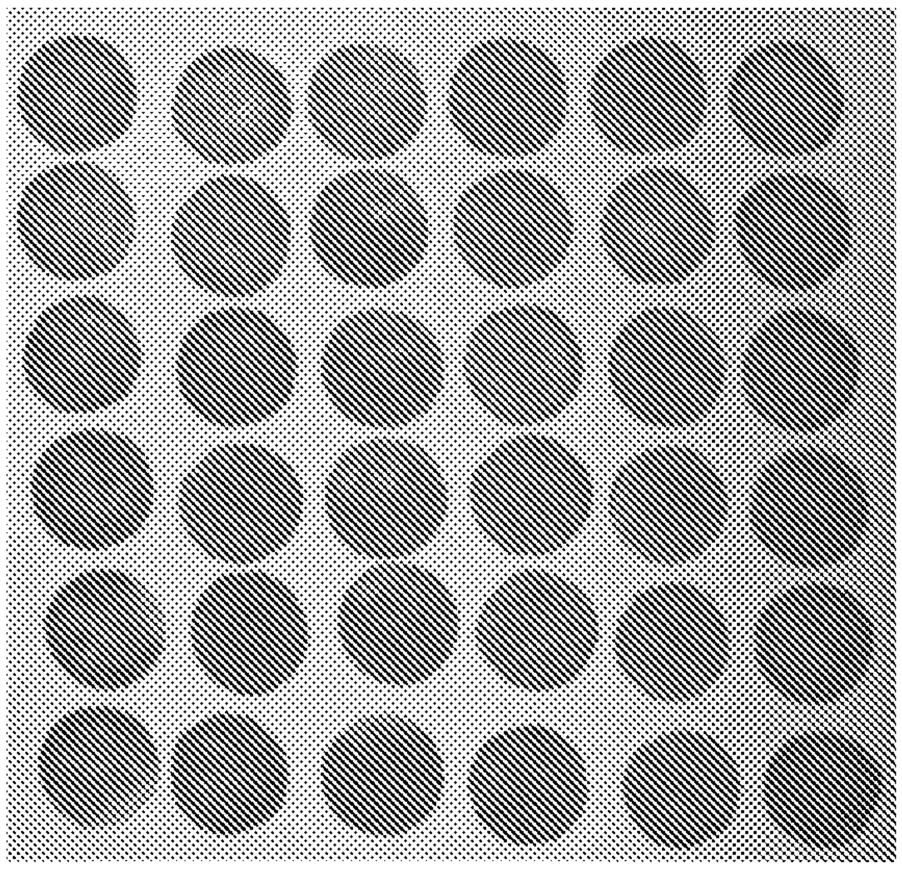


FIGURE 14B

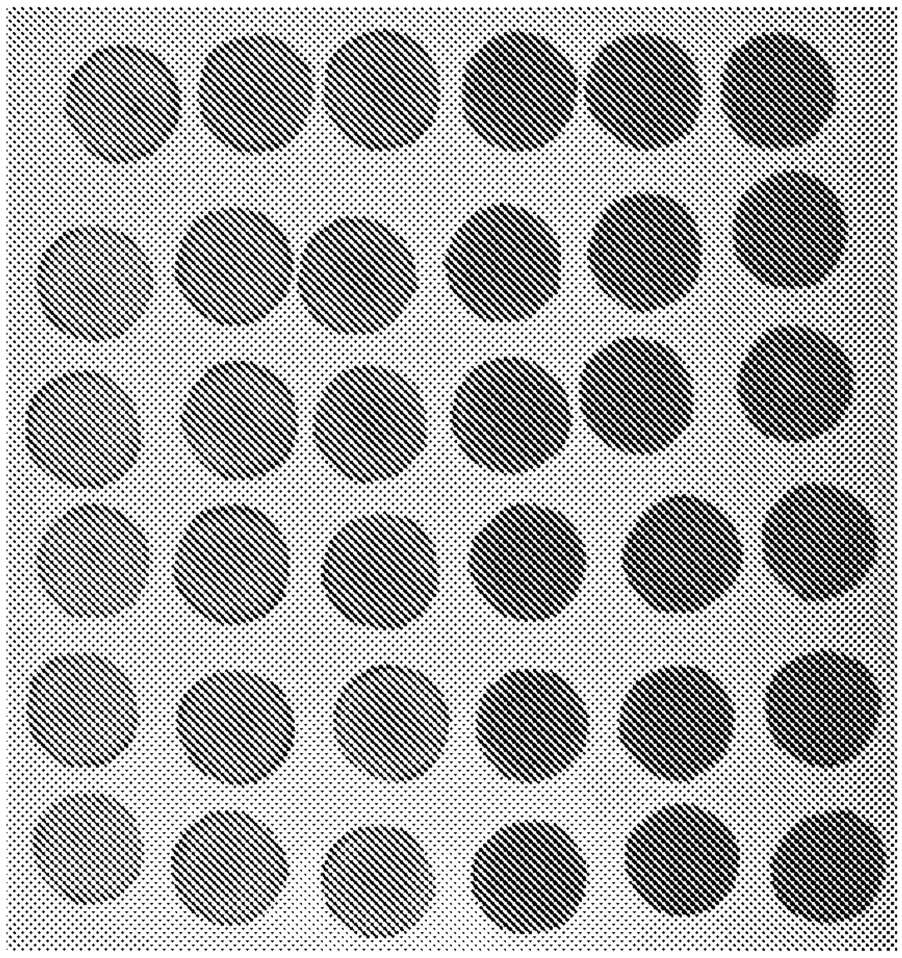


FIGURE 14A

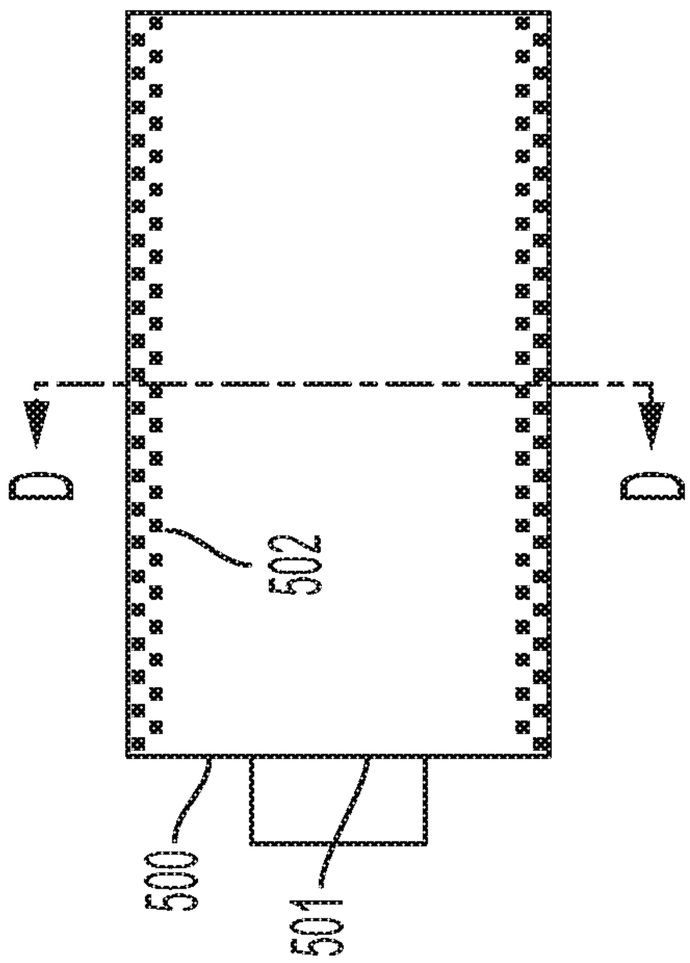
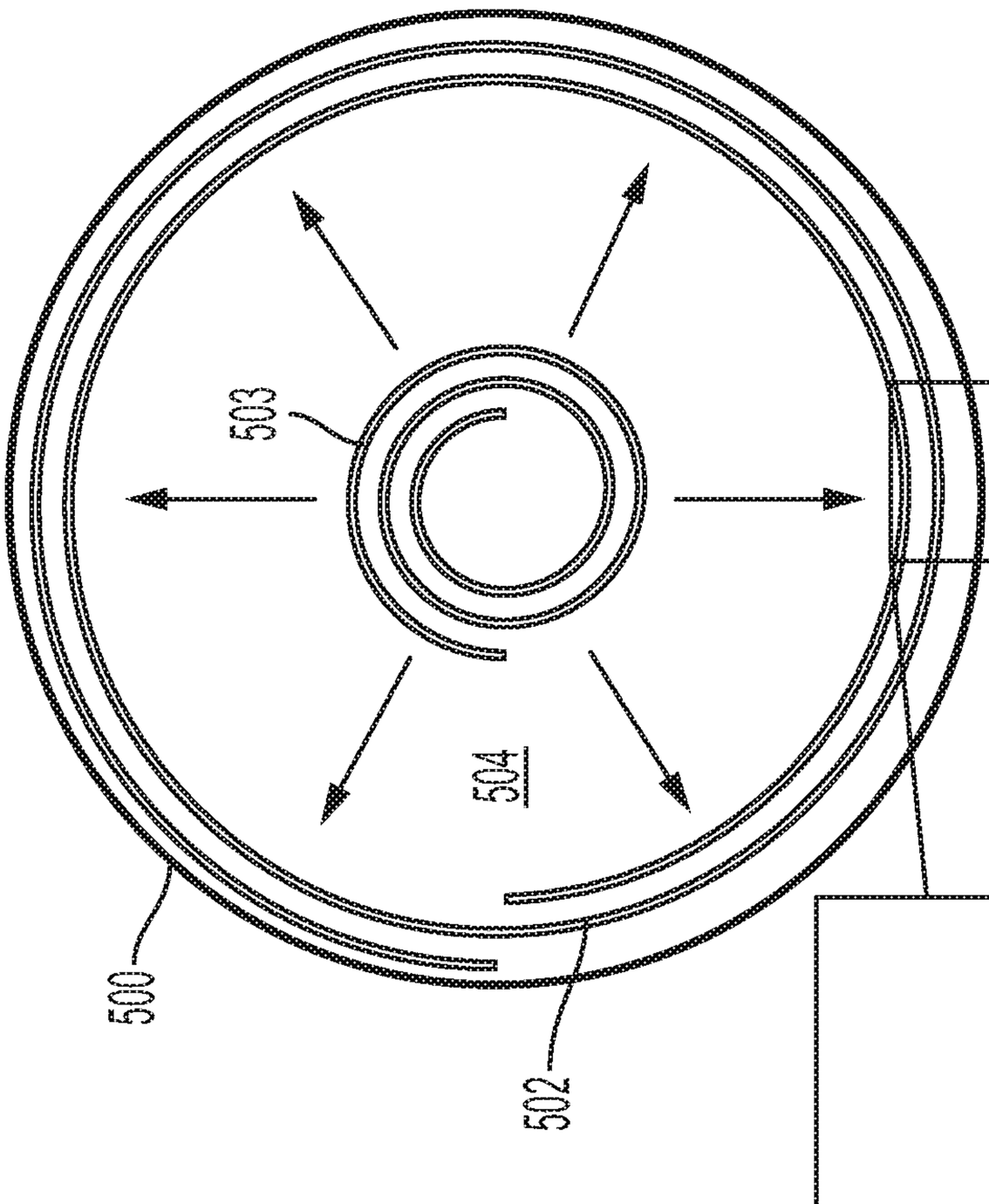


FIGURE 16



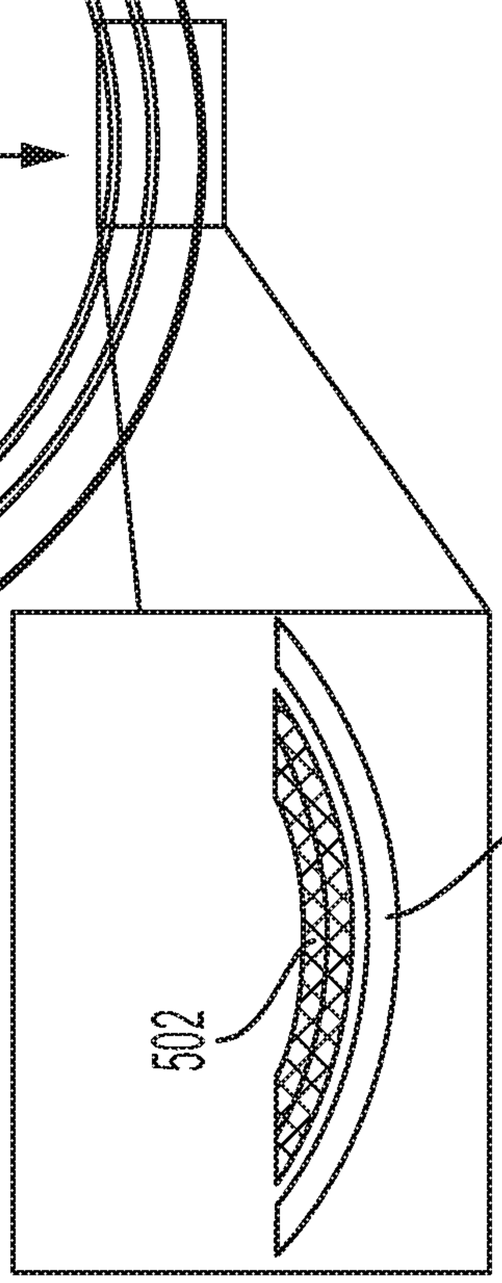


FIGURE 15

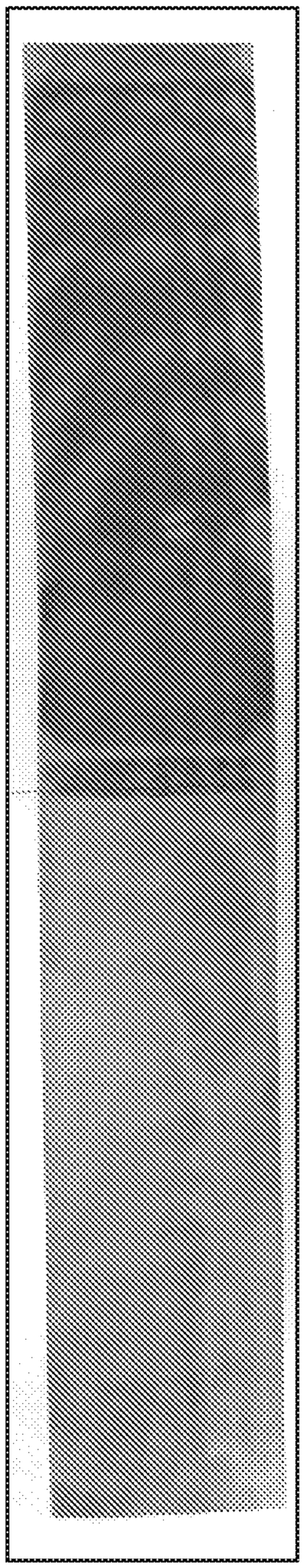


FIGURE 17A

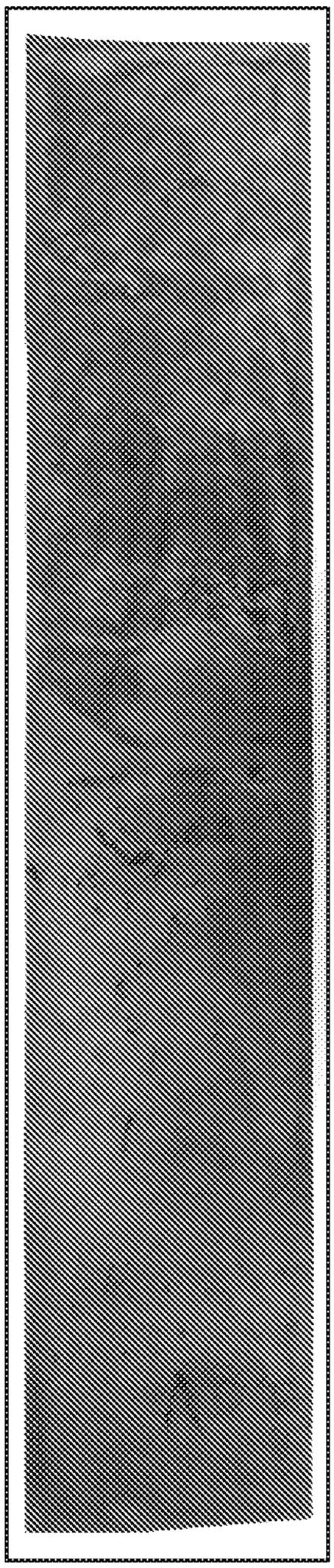


FIGURE 17B

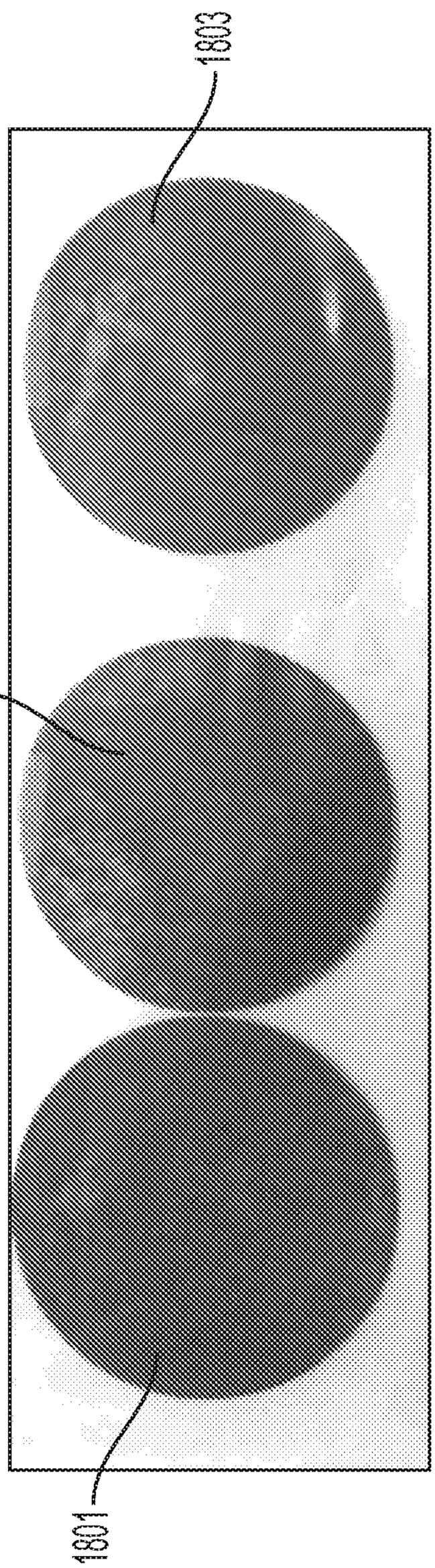


FIGURE 18A

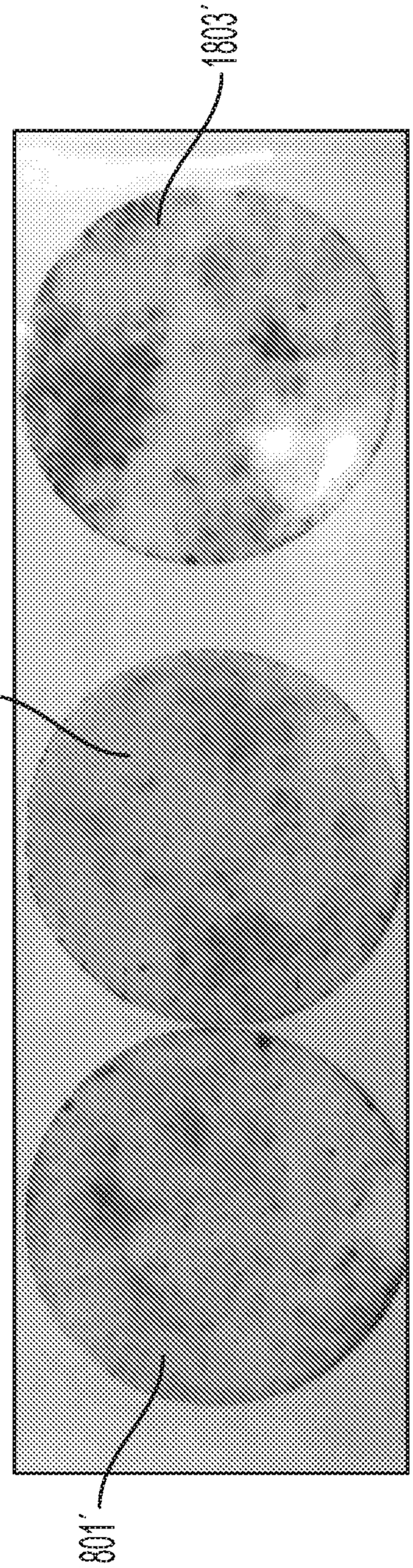


FIGURE 18B

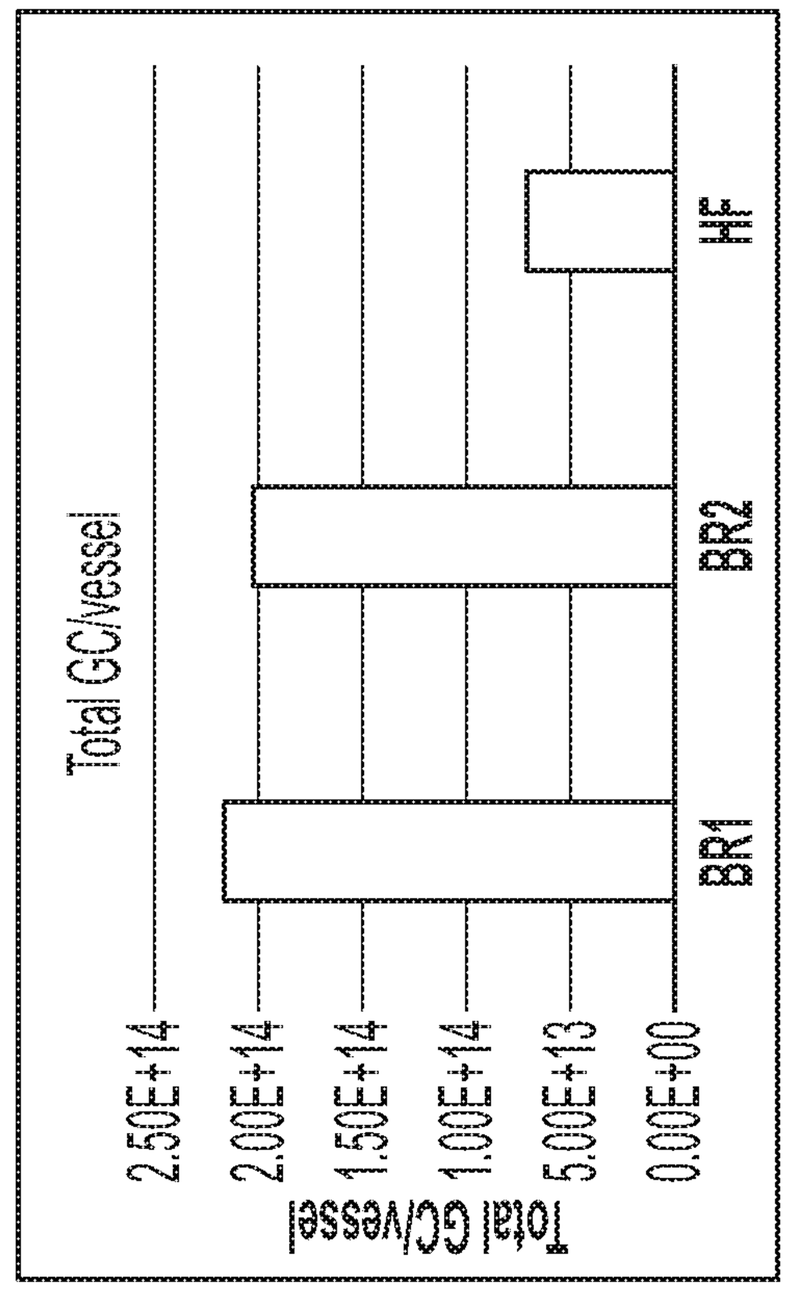


FIGURE 19B

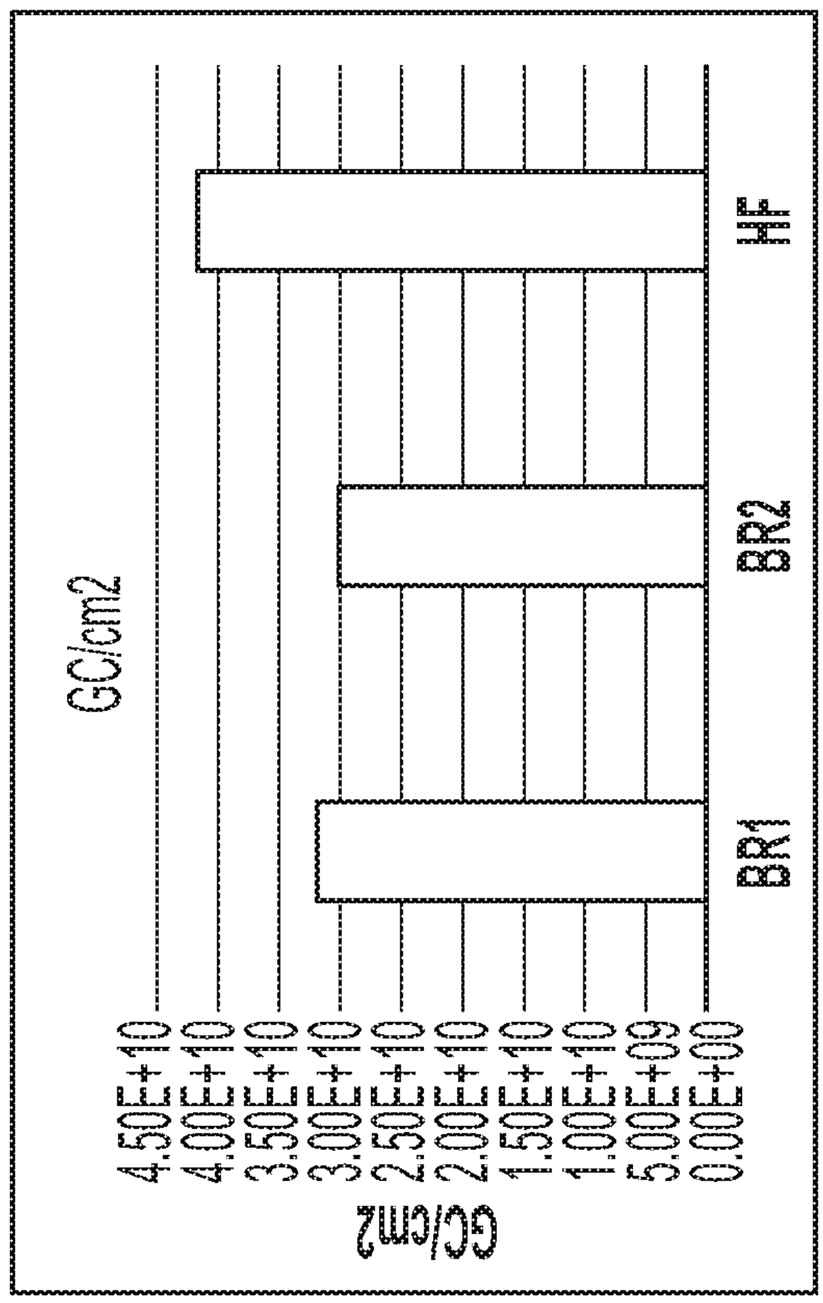


FIGURE 19C

FIGURE 19A

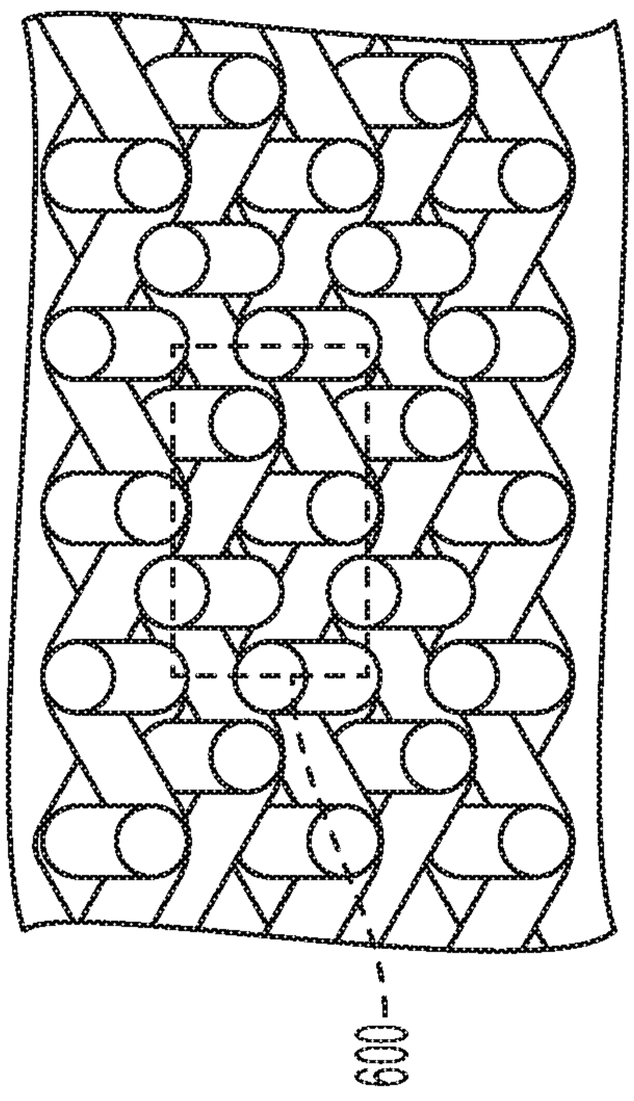


FIGURE 20B

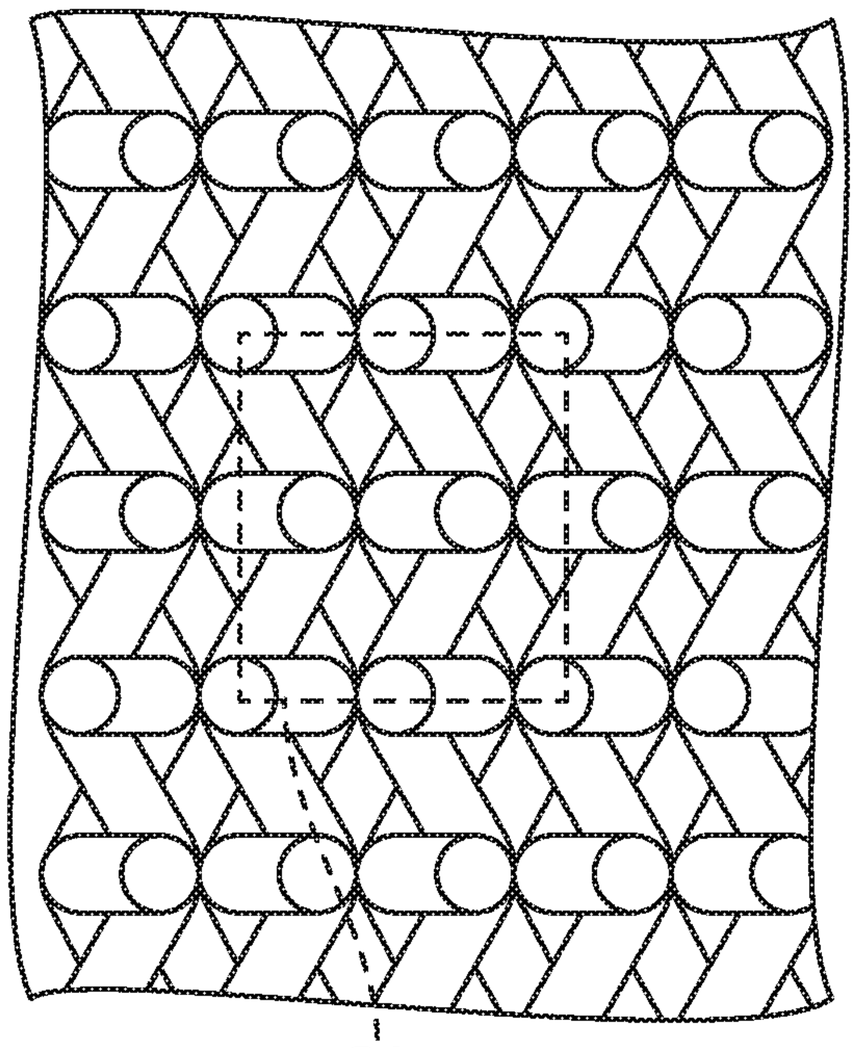


FIGURE 21B

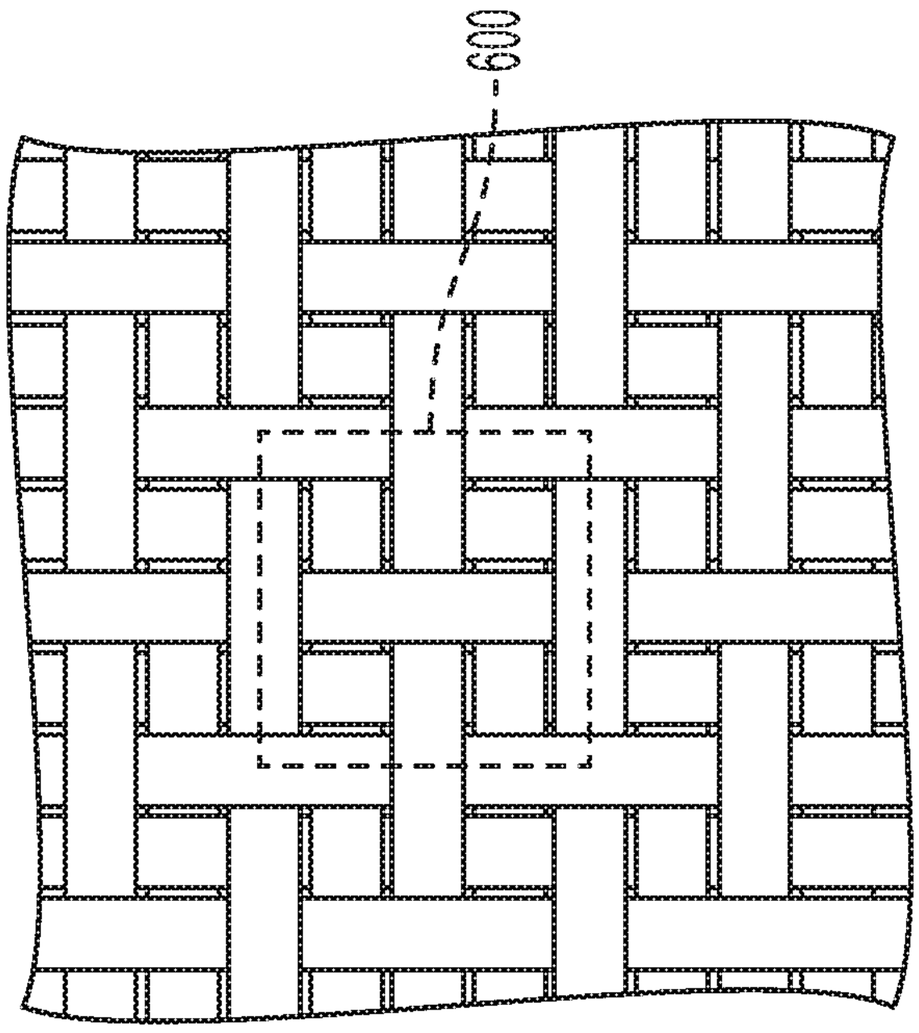


FIGURE 20A

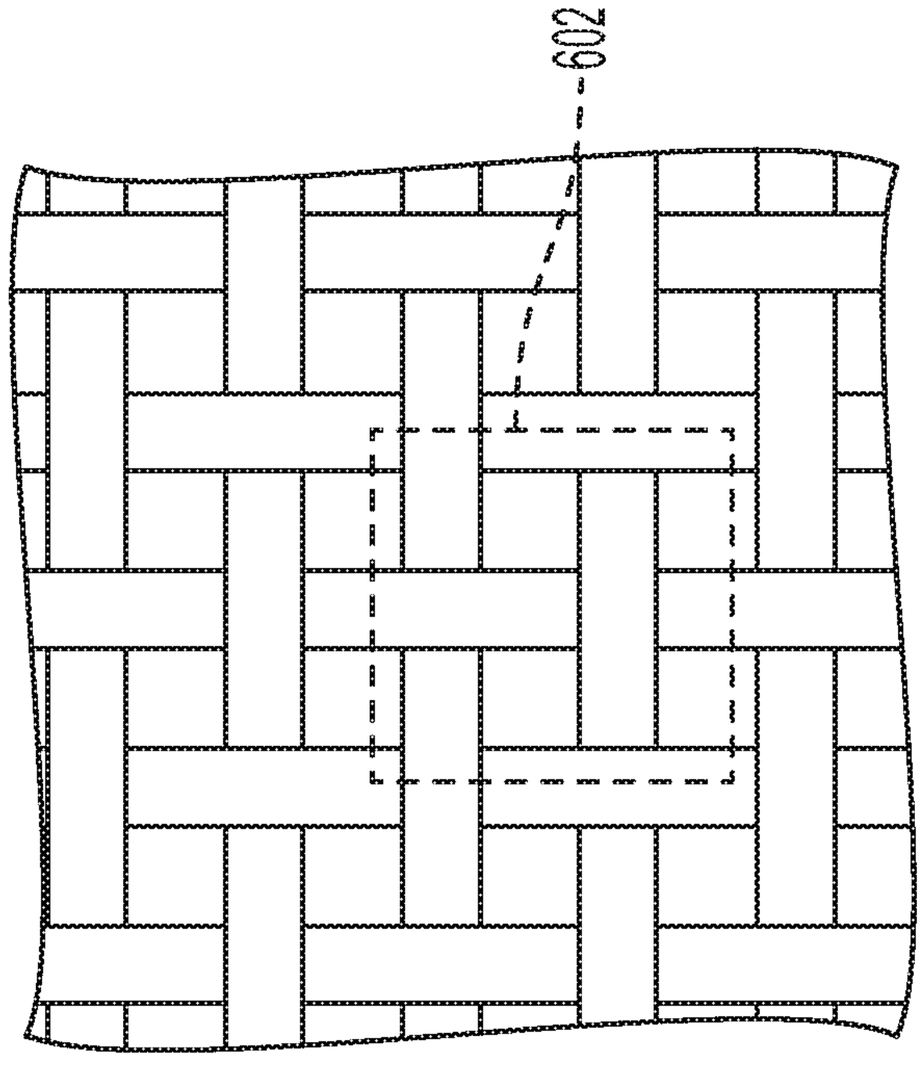


FIGURE 21A

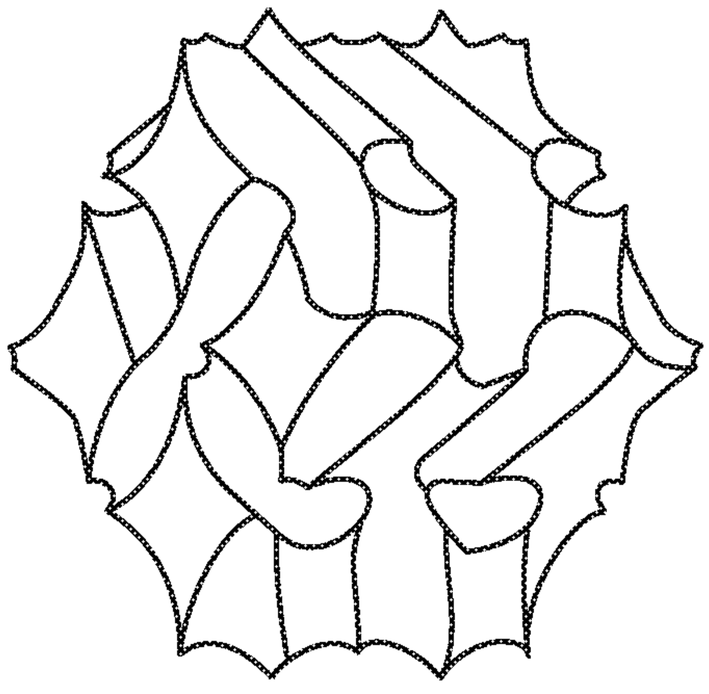


FIGURE 22 B

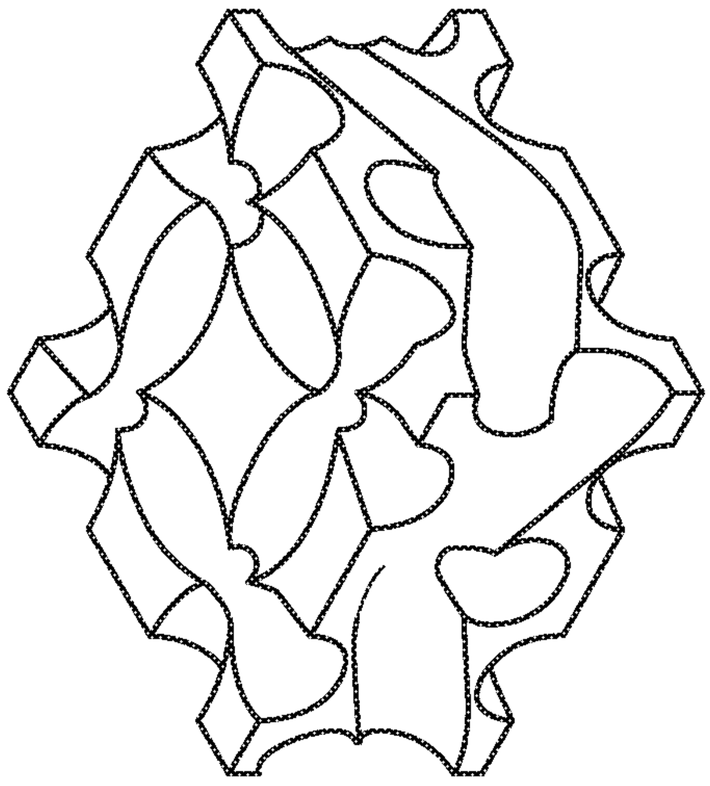


FIGURE 22 A

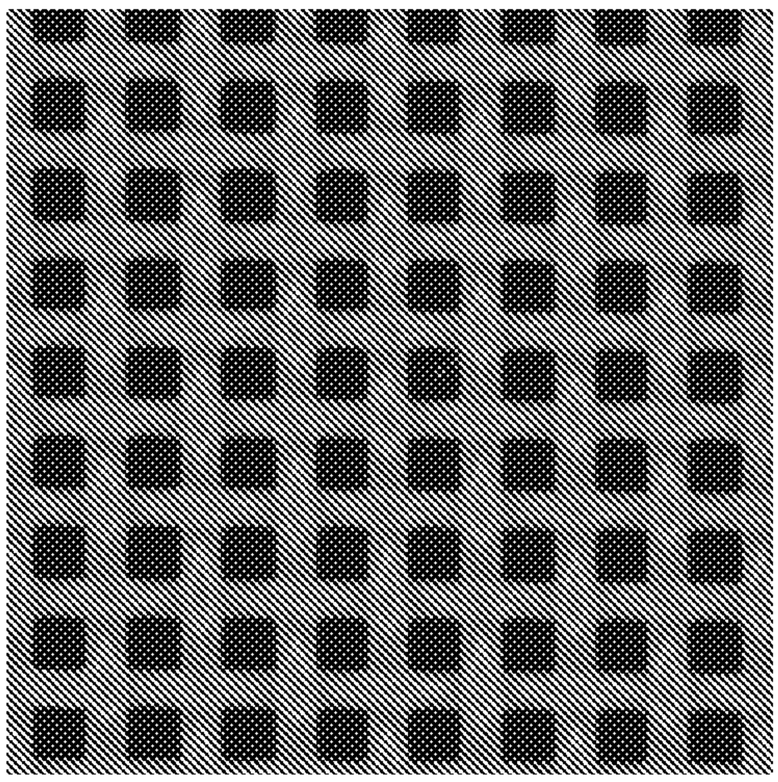


FIGURE 23A

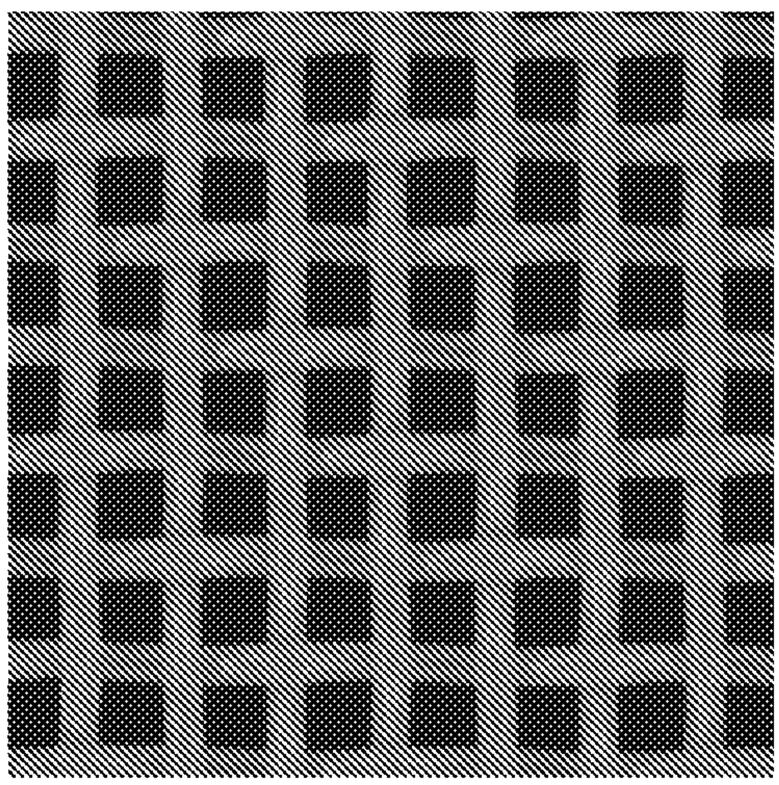


FIGURE 23B

FIGURE 23C

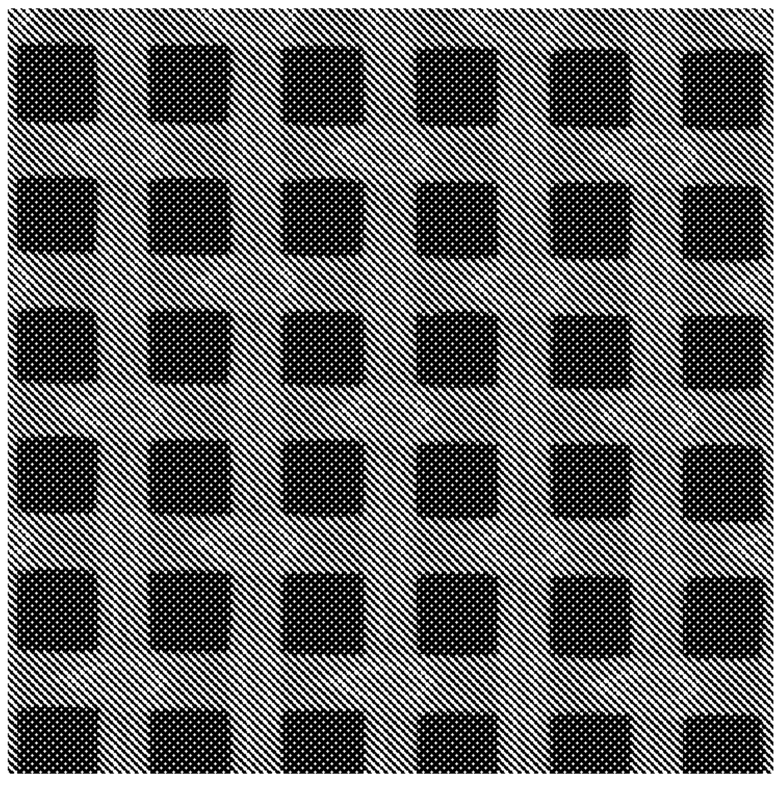


FIGURE 23D

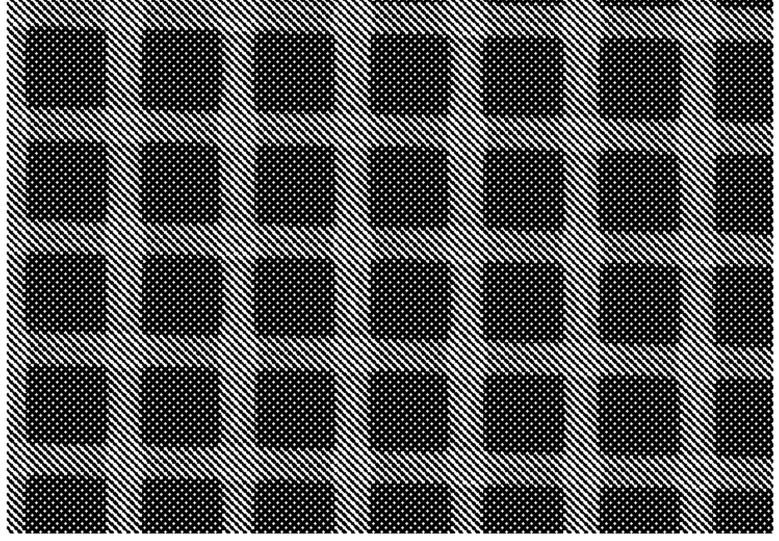


FIGURE 23E

FIGURE 23F

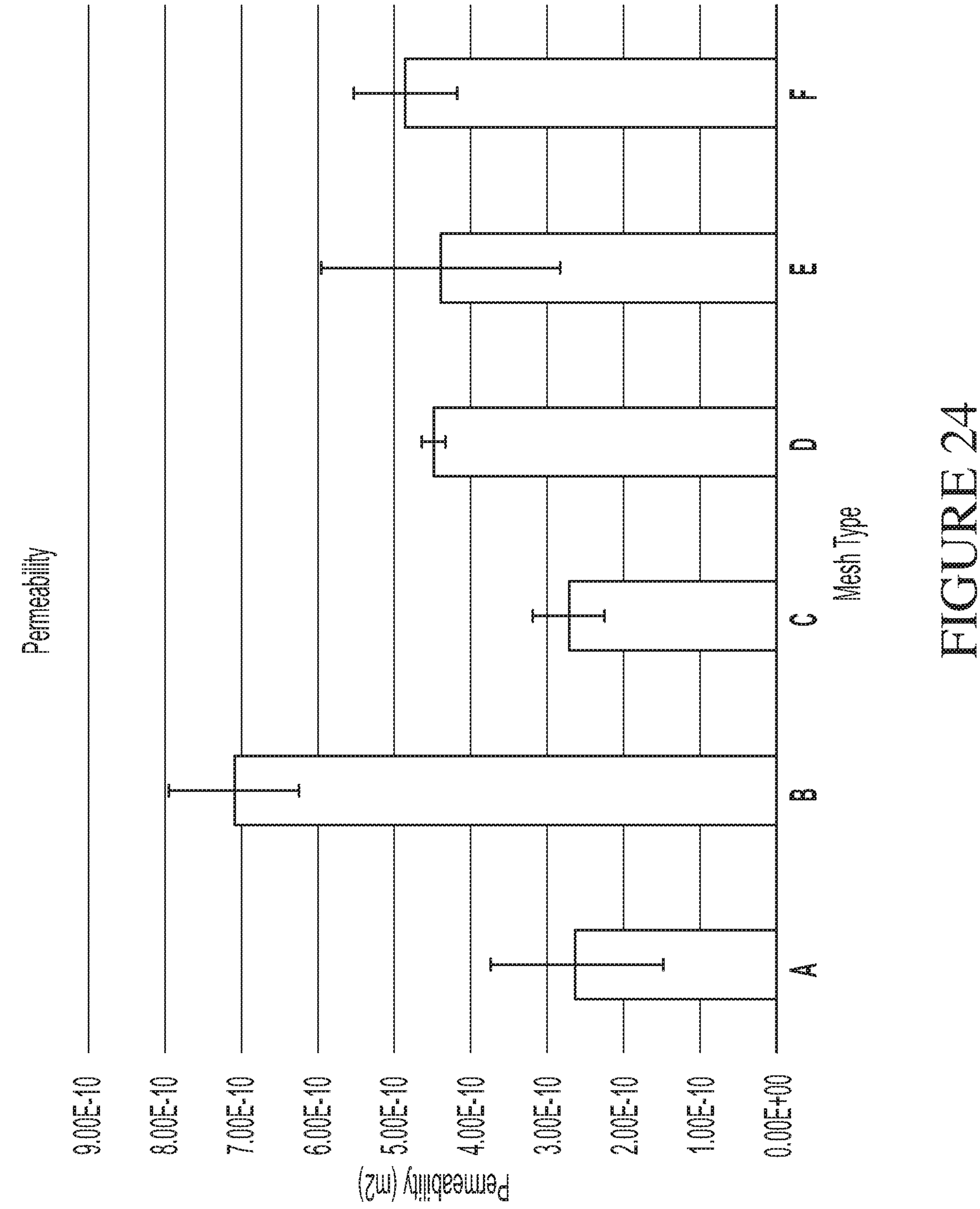

Permeability
9.00E-10
8.00E-10
7.00E-10
6.00E-10
5.00E-10
4.00E-10
3.00E-10
2.00E-10
1.00E-10
0.00E+00
Permeability (m2)
A
B
C
D
E
Mesh Type

FIGURE 24

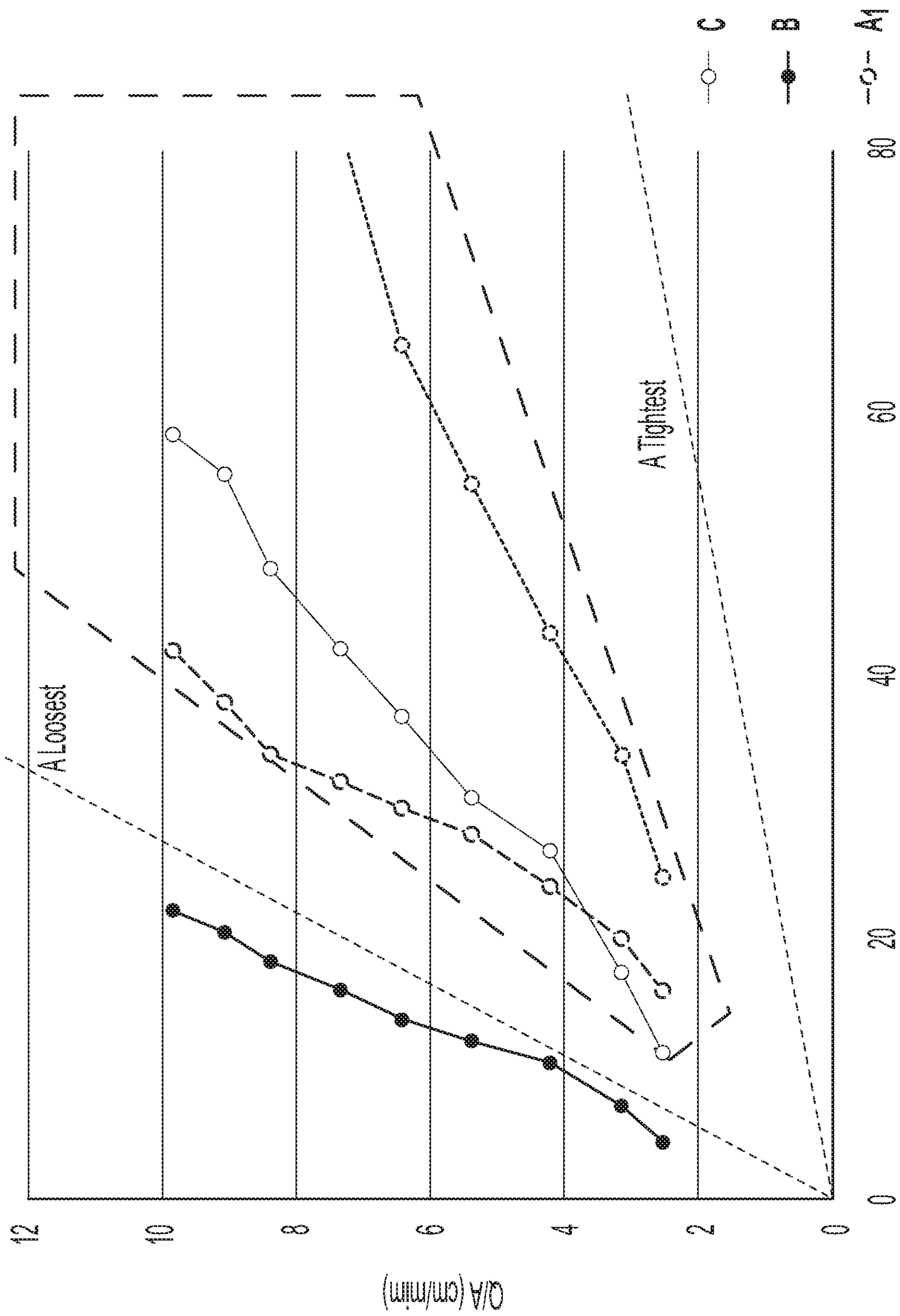

C
B
A1
A2
A Tightest
A Loosest
ΔP/l (Pa/cm)
Q/A (cm/min)
0
20
40
60
80
0
2
4
6
8
10
12

FIGURE 25

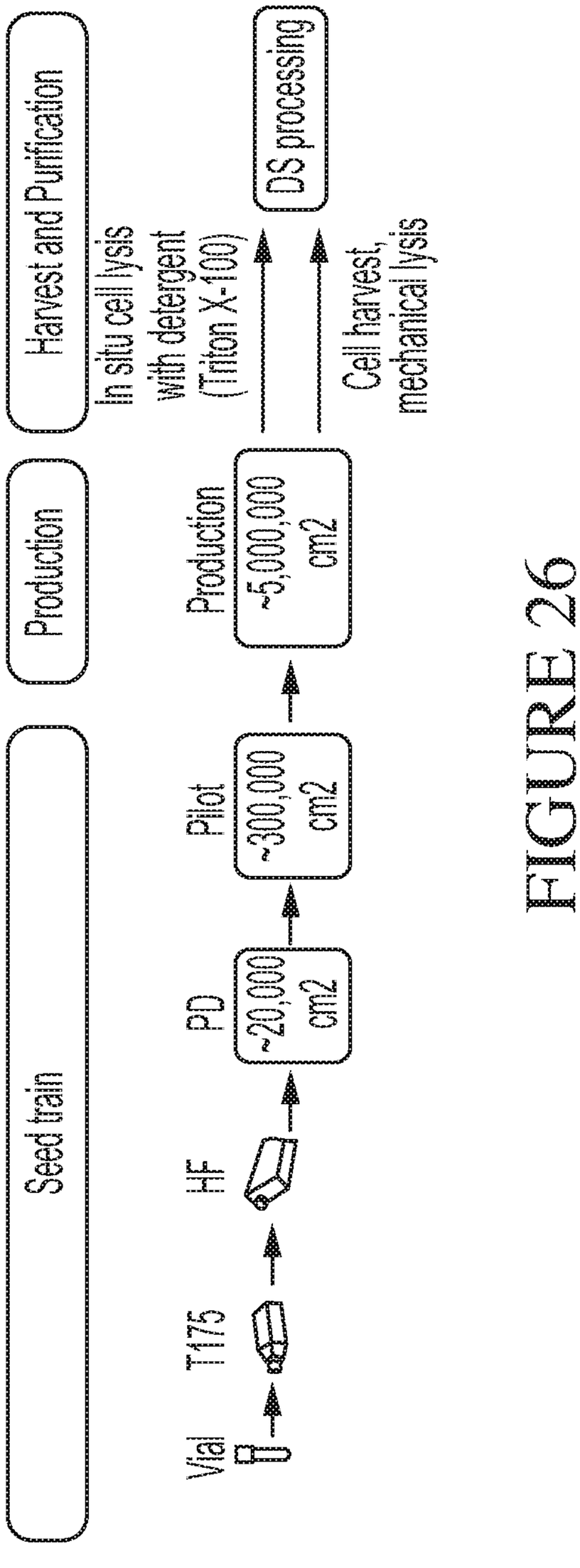

Seed train
Vial
T175
HF
PD
Pilot
Production
~5,000,000 cm2
Production
~20,000 cm2
~300,000 cm2
Cell harvest, mechanical lysis
In situ cell lysis with detergent (Triton X-100)
Harvest and Purification
DS processing

FIGURE 26

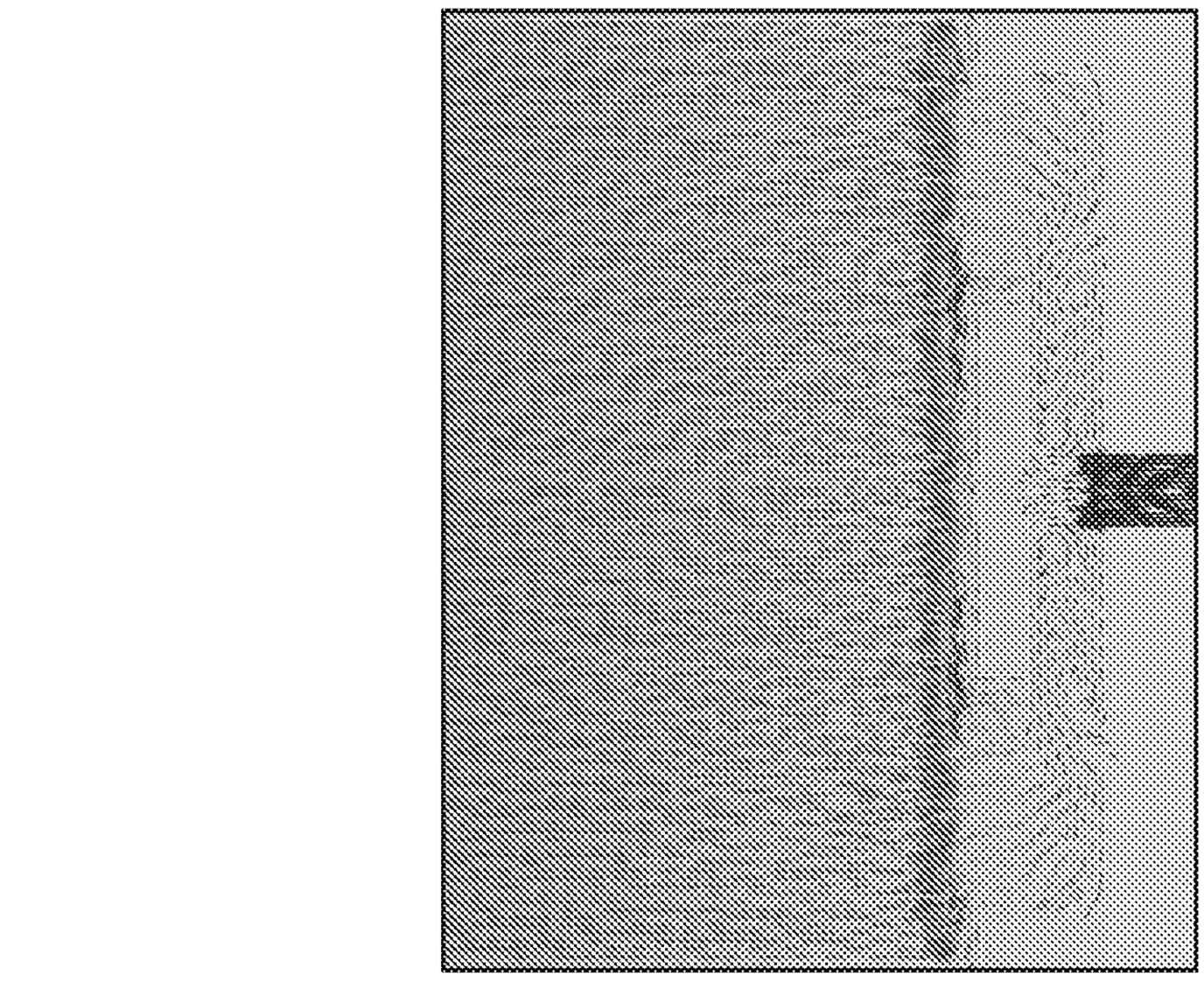


FIGURE 27B

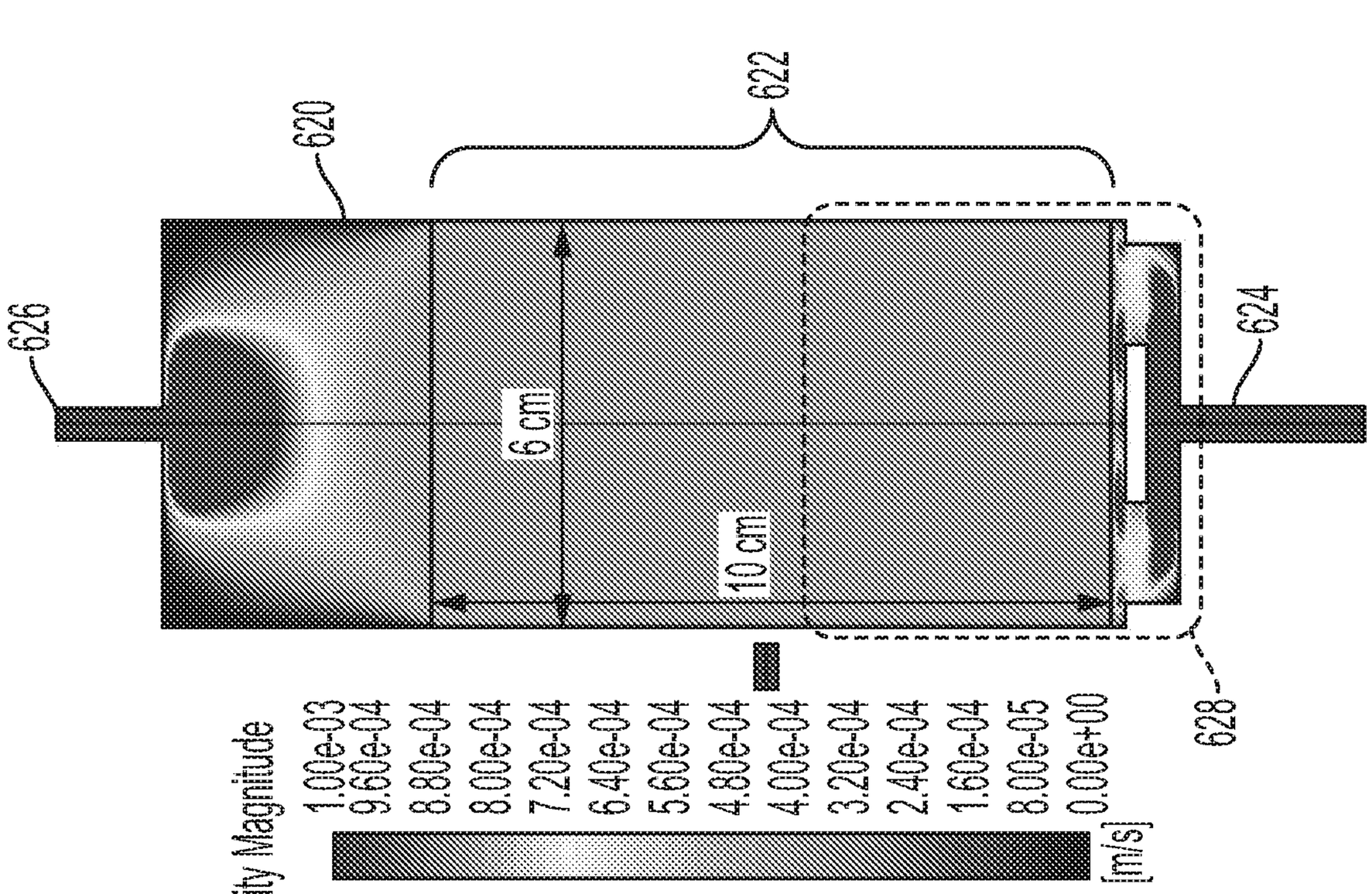


FIGURE 27A

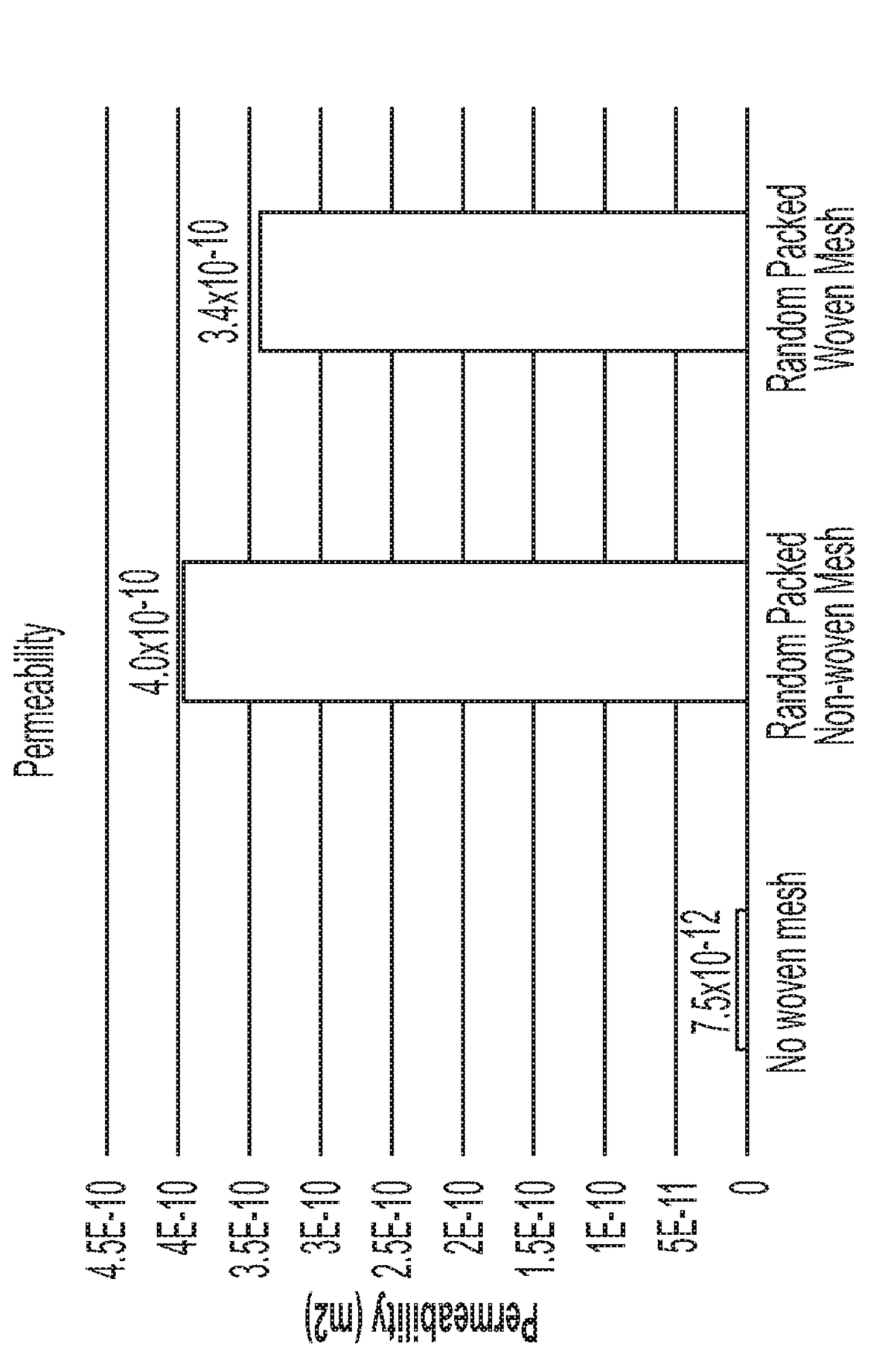

Permeability
4.0x10-10
3.4x10-10
7.5x10-12
4,5E-10
4E-10
3,5E-10
3E-10
2,5E-10
2E-10
1,5E-10
1E-10
5E-11
0
Permeability (m2)
No woven mesh
Random Packed Non-woven Mesh
Random Packed Woven Mesh
Materials Type

FIGURE 28

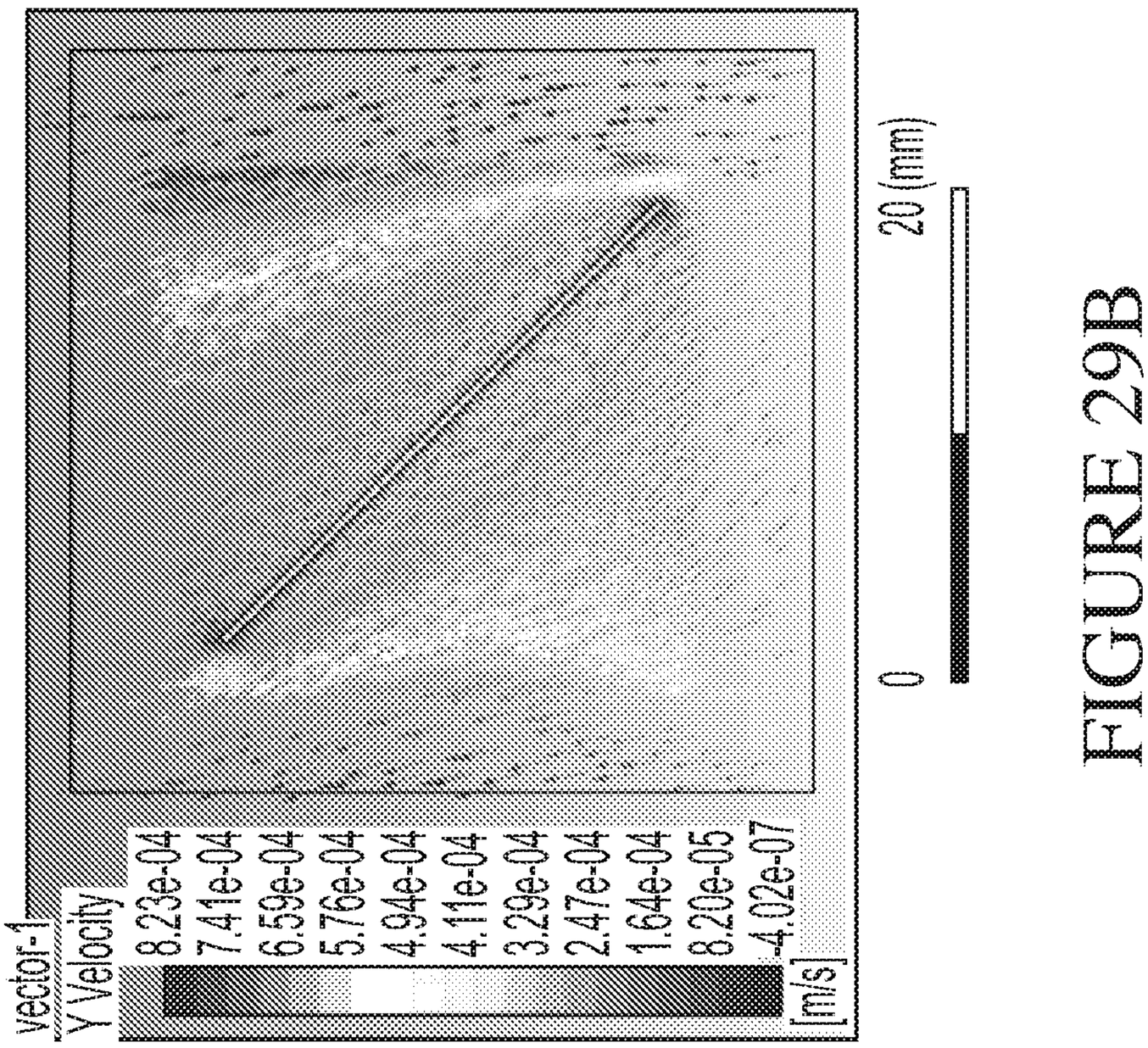


FIGURE 29B

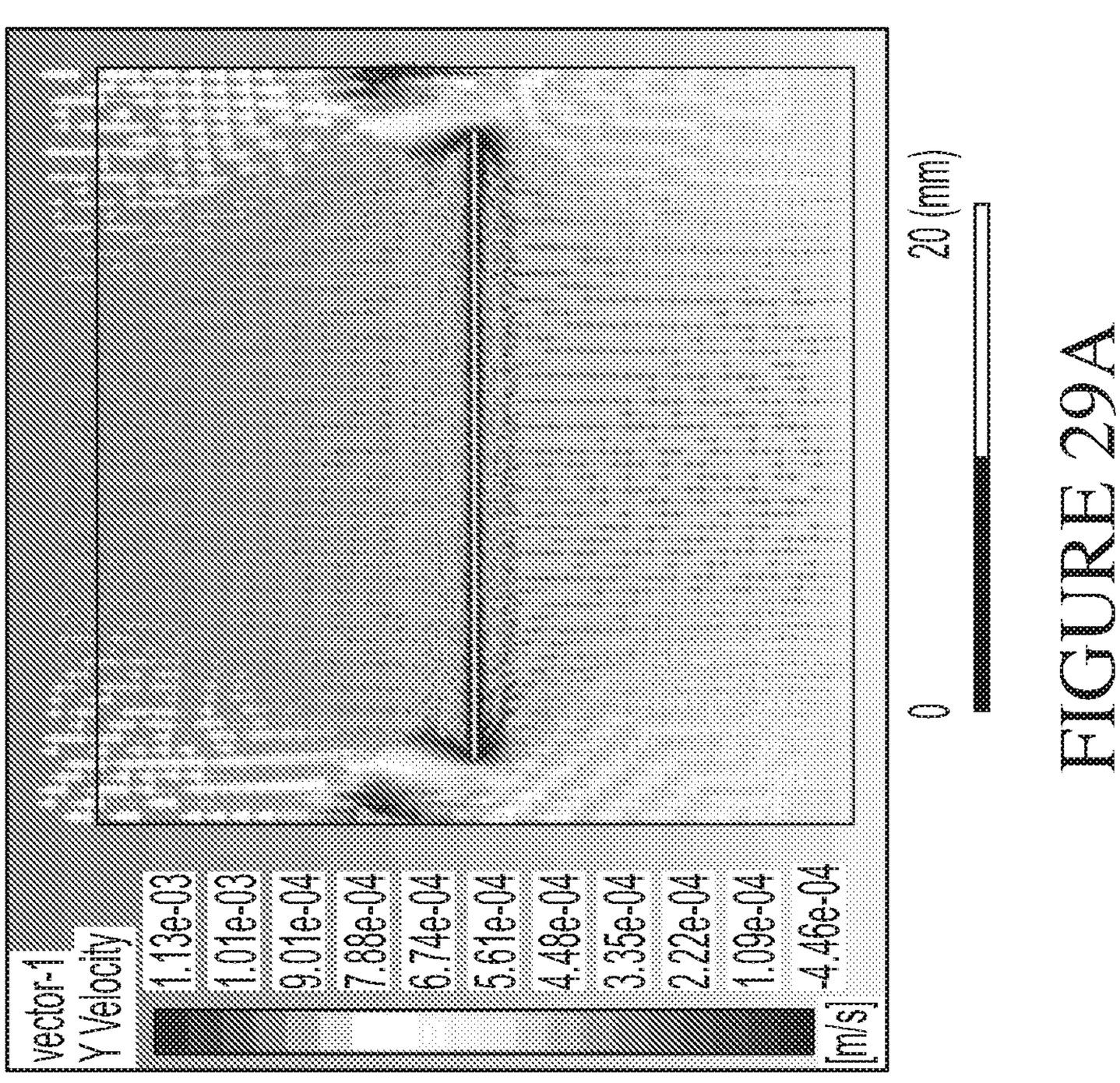


FIGURE 29A

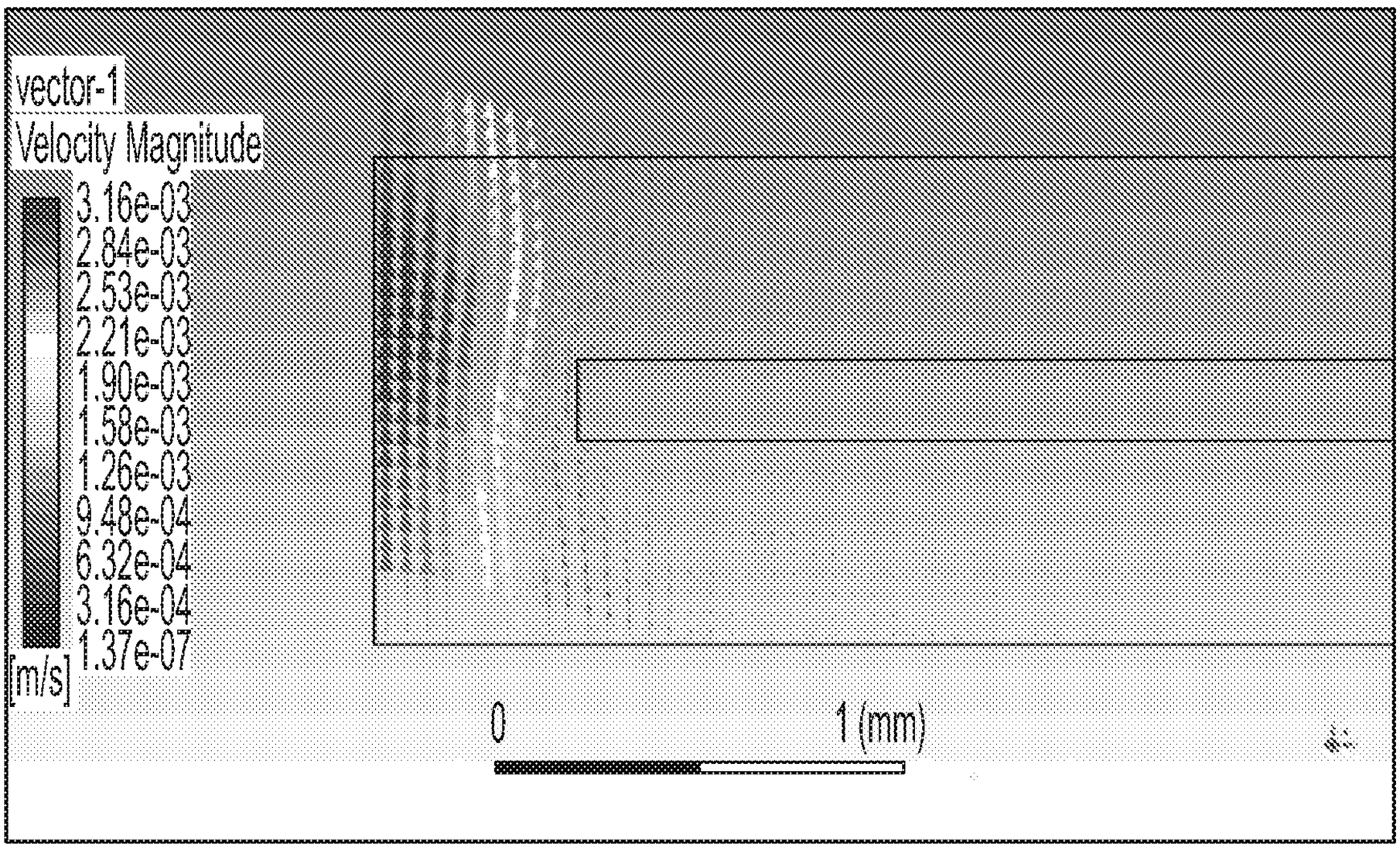


FIGURE 30A

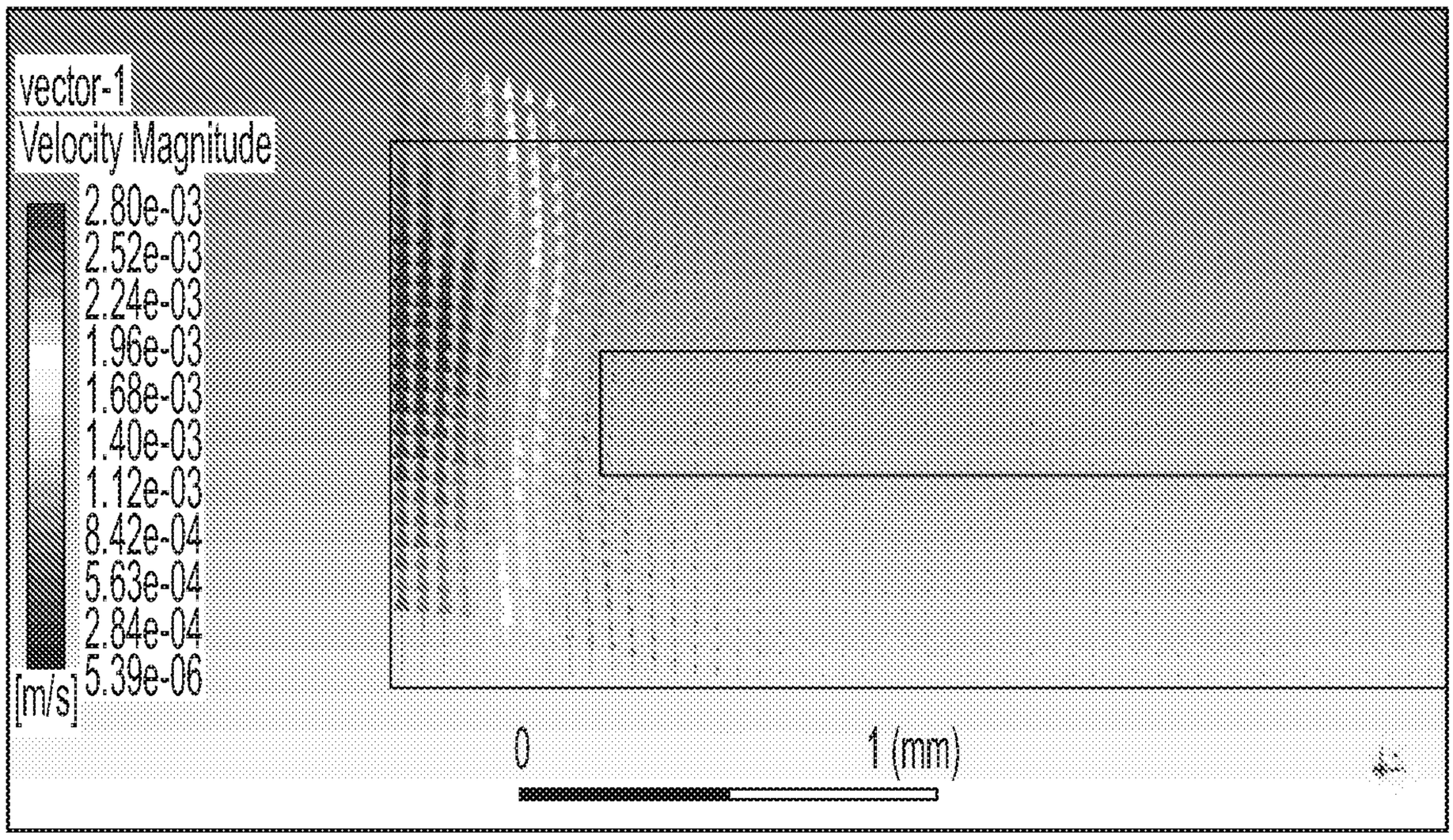


FIGURE 30B

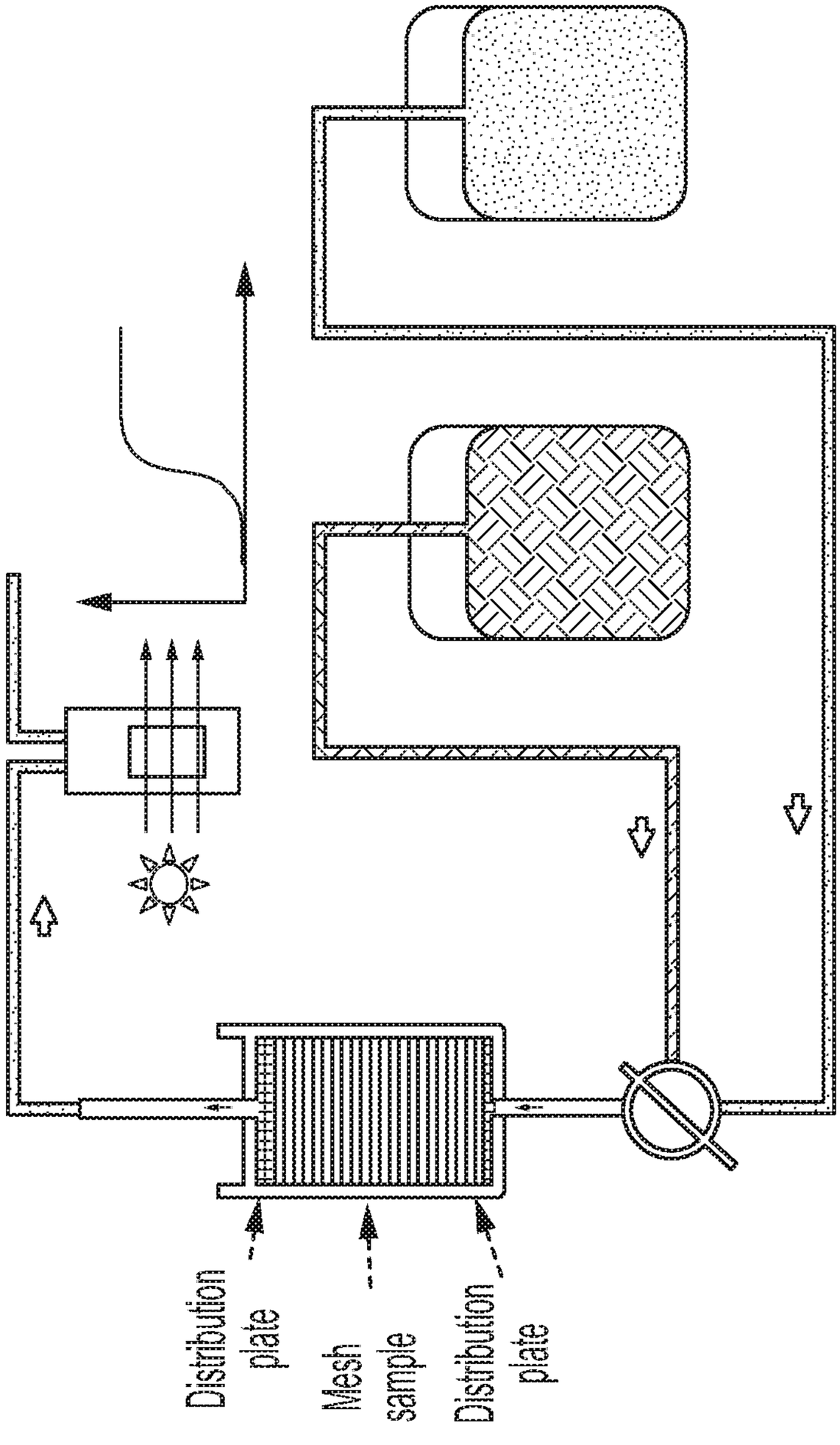


FIGURE 31

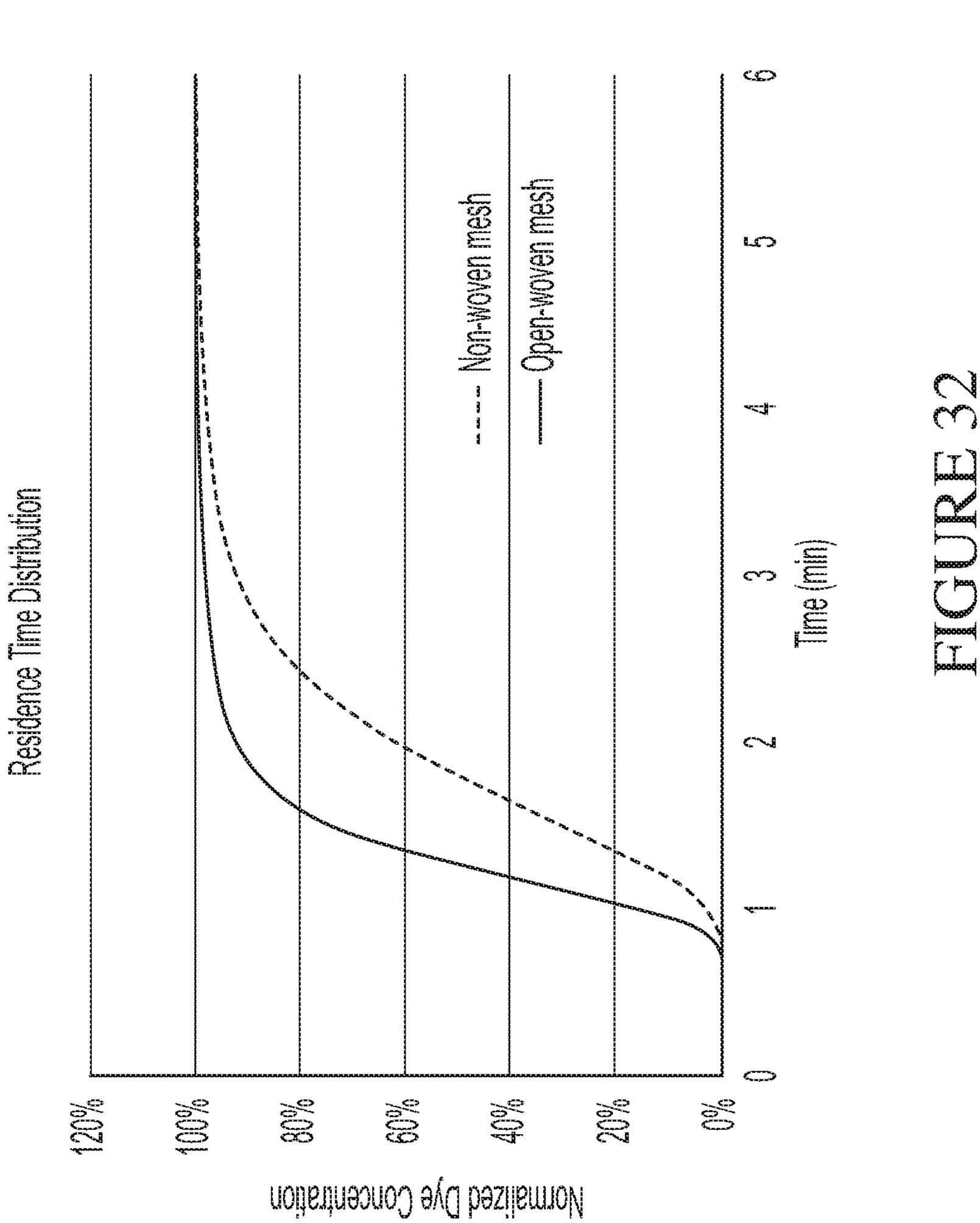

Residence Time Distribution
Non-woven mesh
Open-woven mesh
Normalized Dye Concentration
120%
100%
80%
60%
40%
20%
0
1
2
3
4
5
6
Time (min)

FIGURE 32