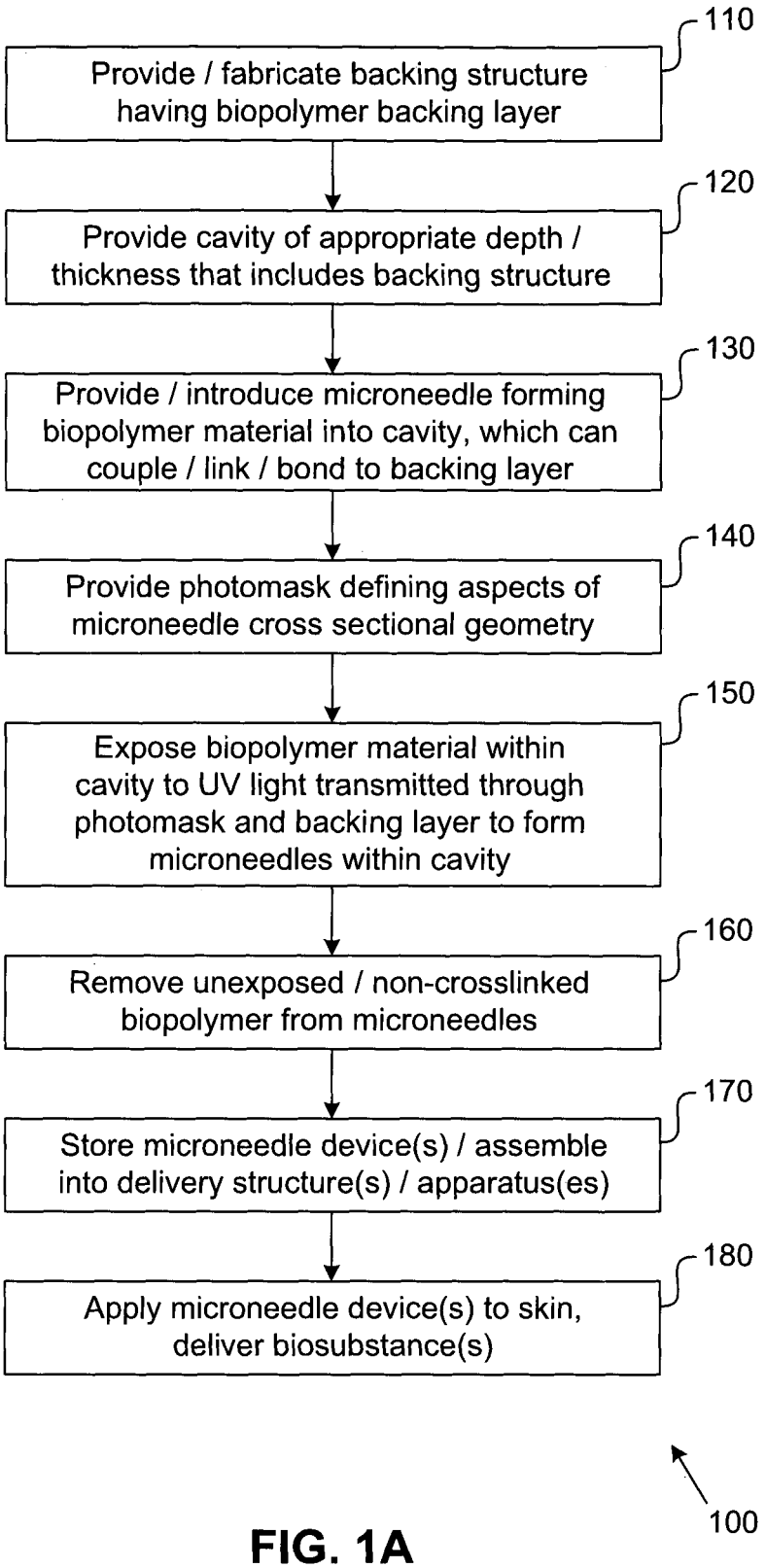

110
Provide / fabricate backing structure having biopolymer backing layer
120
Provide cavity of appropriate depth / thickness that includes backing structure
130
Provide / introduce microneedle forming biopolymer material into cavity, which can couple / link / bond to backing layer
140
Provide photomask defining aspects of microneedle cross sectional geometry
150
Expose biopolymer material within cavity to UV light transmitted through photomask and backing layer to form microneedles within cavity
160
Remove unexposed / non-crosslinked biopolymer from microneedles
170
Store microneedle device(s) / assemble into delivery structure(s) / apparatus(es)
180
Apply microneedle device(s) to skin, deliver biosubstance(s)
100

FIG. 1A

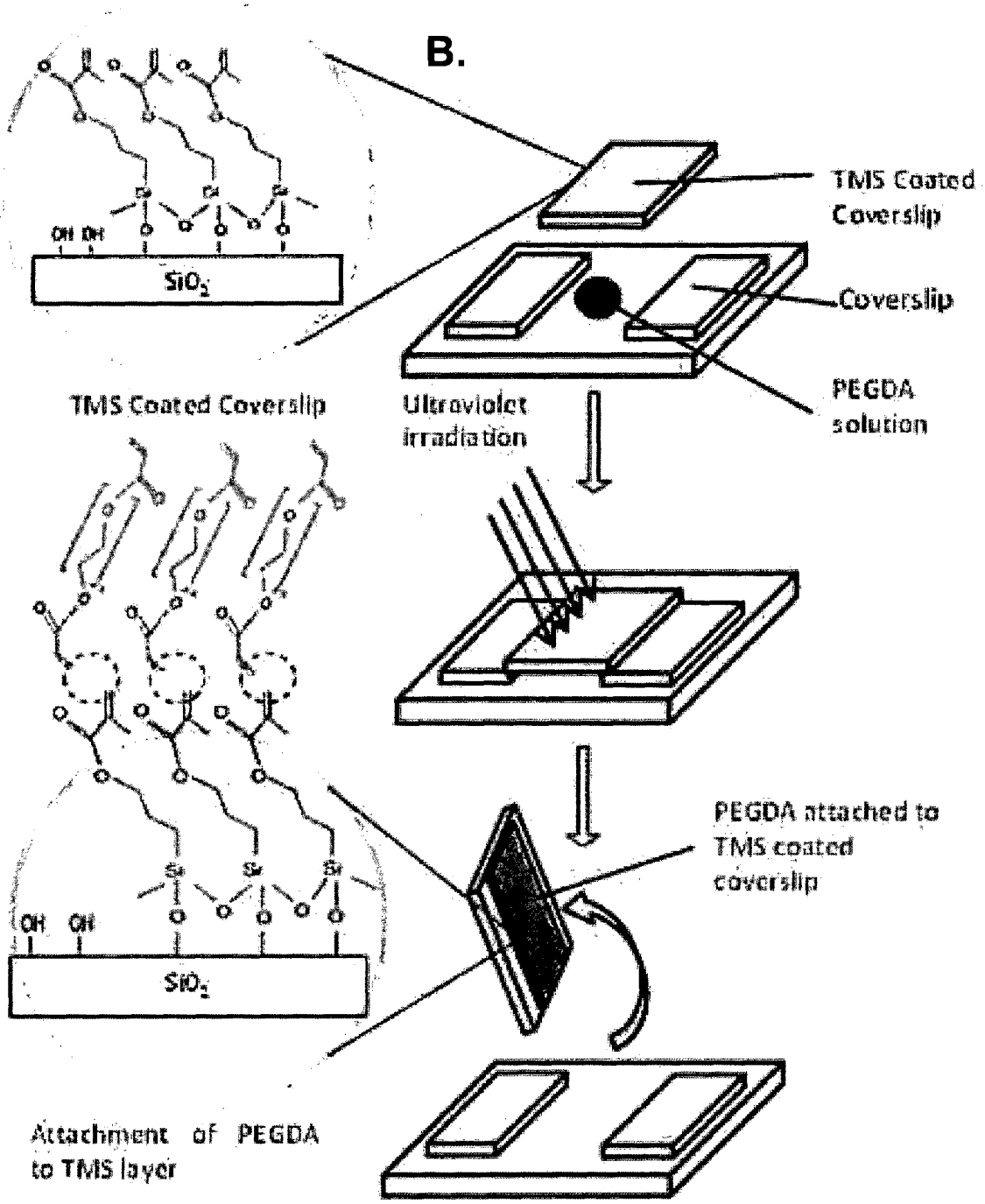

B.
TMS Coated Coverslip
Coverslip
PEGDA solution
Ultraviolet irradiation
PEGDA attached to TMS coated coverslip
Attachment of PEGDA to TMS layer
TMS Coated Coverslip
OH OH
SiO2

FIG. 1B

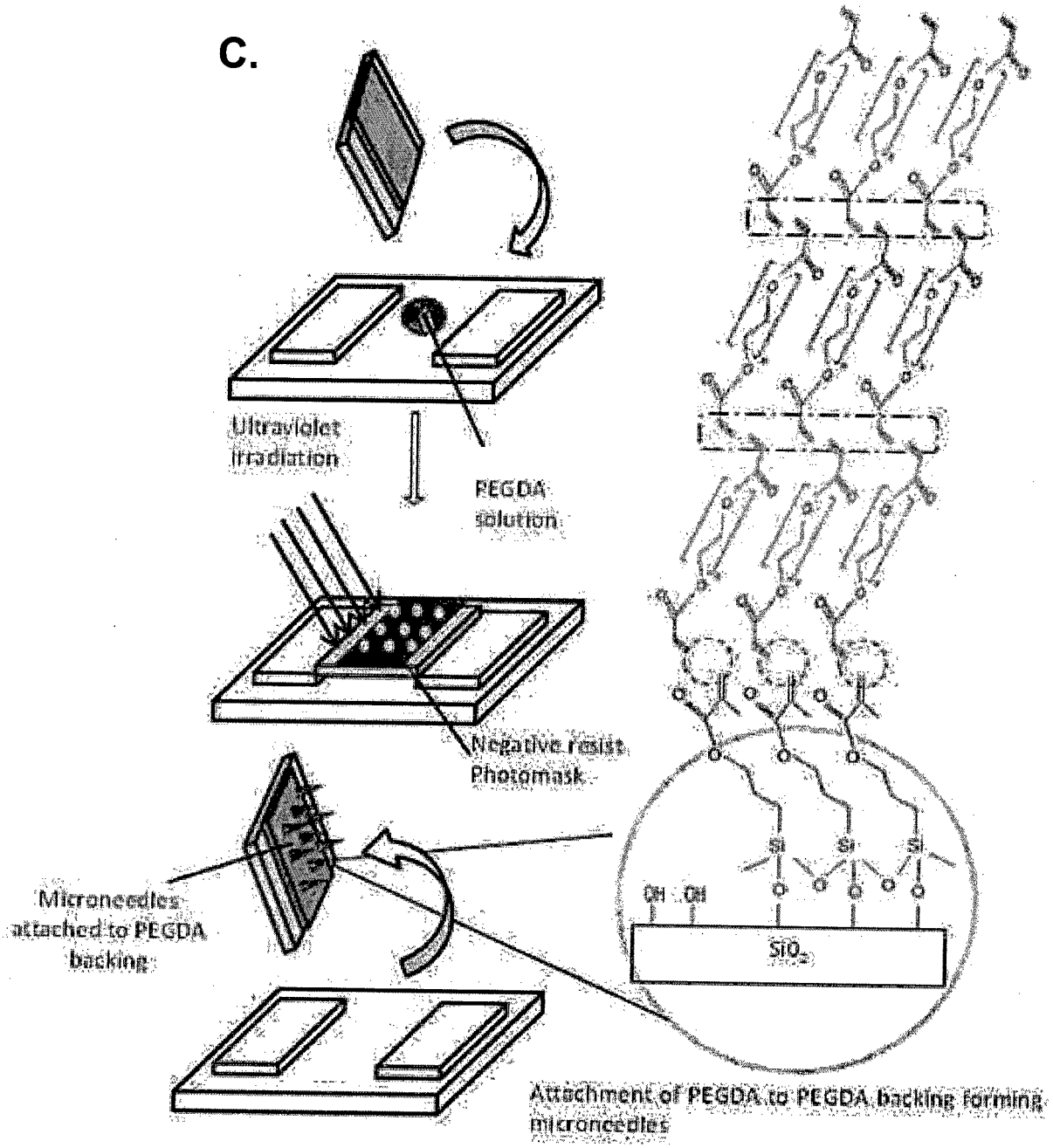

C.
Ultraviolet Irradiation
PEGDA solution
Negative resist Photomask
Microneedles attached to PEGDA backing
Attachment of PEGDA to PEGDA backing forming microneedles
Si
OH
SiO_2

FIG. 1C

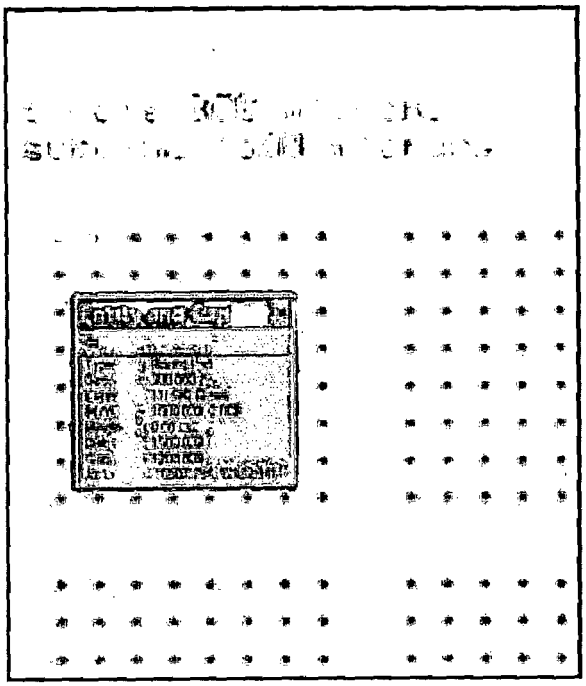


FIG. 2

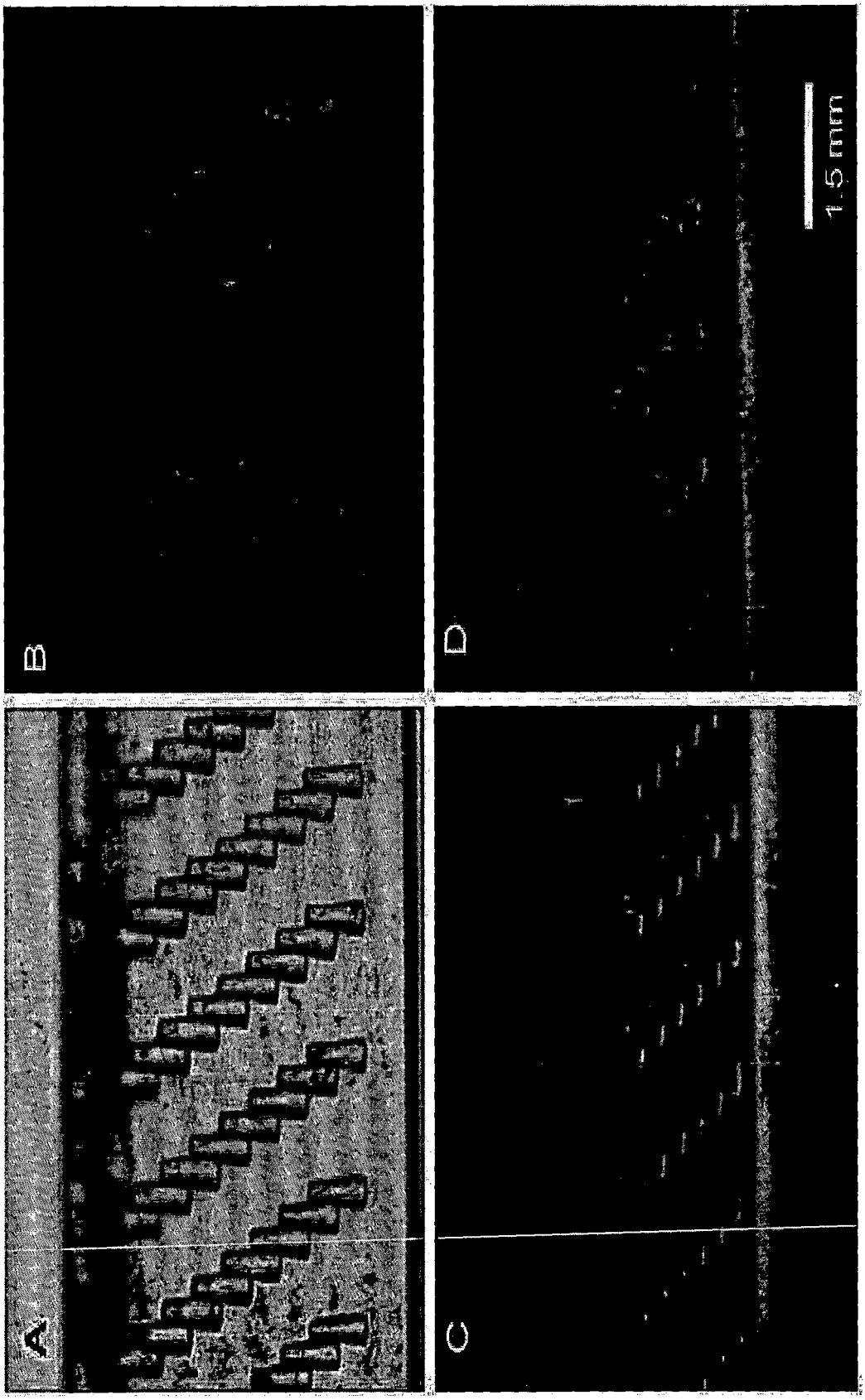


FIG. 3A-D

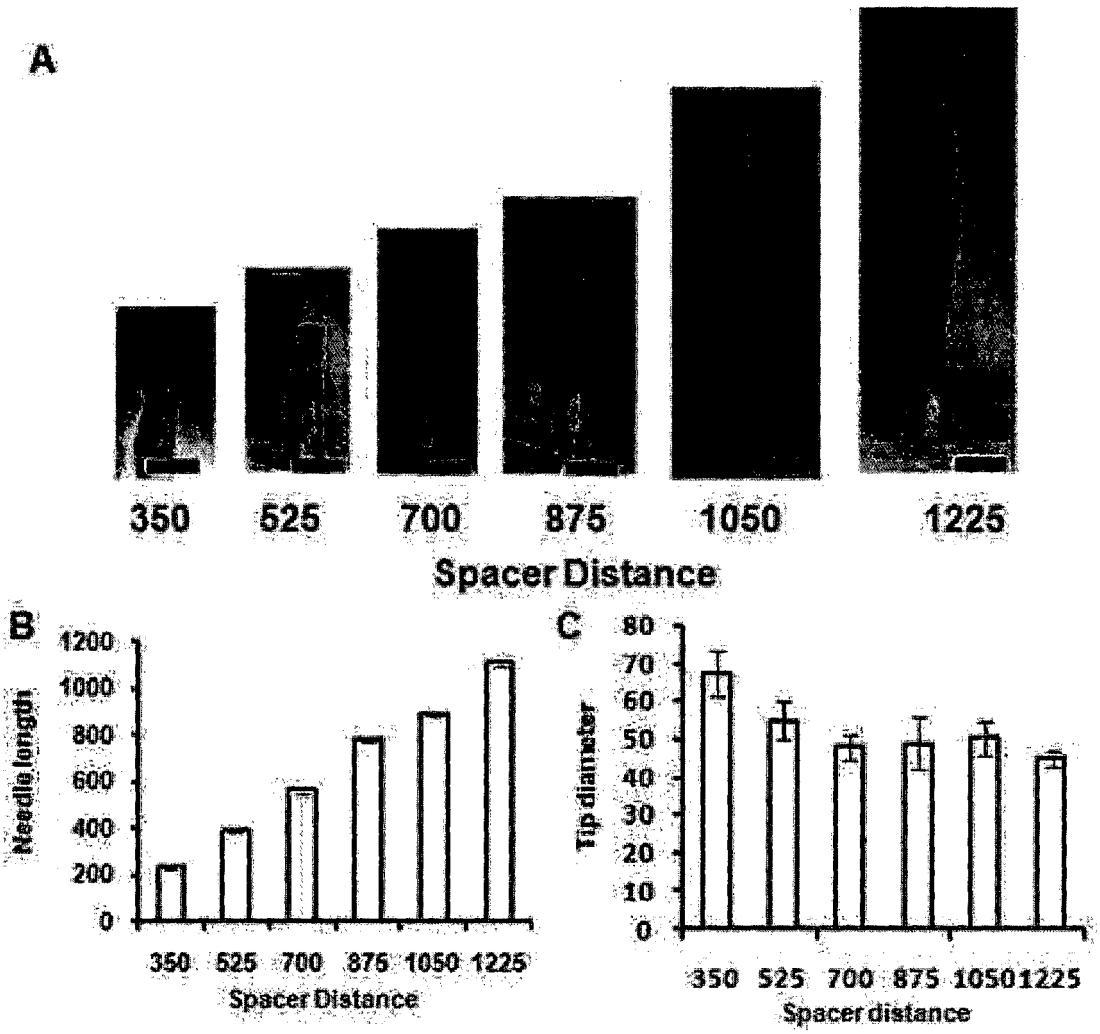

A
350
525
700
875
1050
1225
Spacer Distance
B
Needle length
1200
1000
800
600
400
200
0
350 525 700 875 1050 1225
Spacer Distance
C
Tip diameter
80
70
60
50
40
30
20
10
0
350 525 700 875 10501225
Spacer distance

FIG 4A - 4C

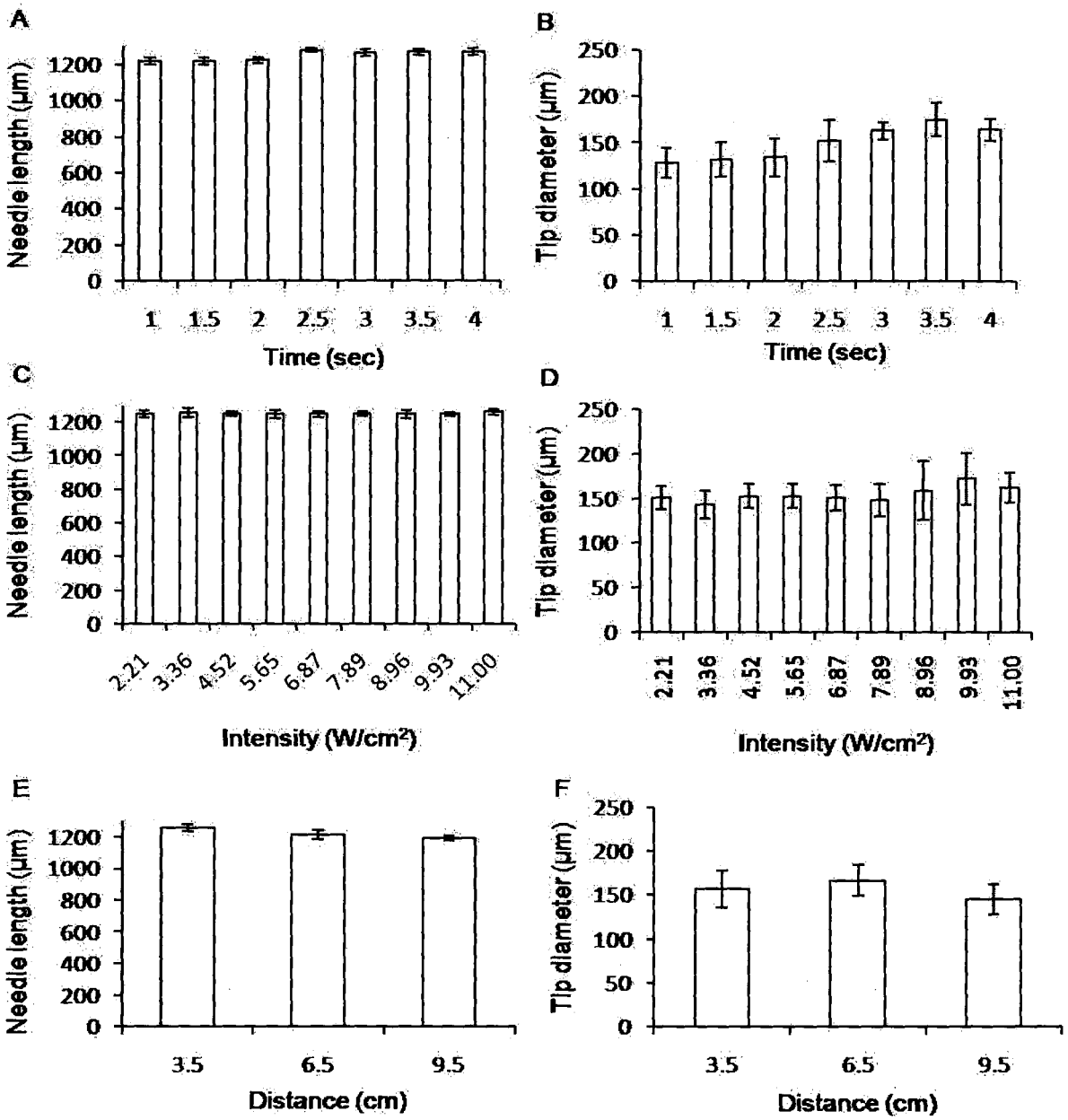

A
Needle length (µm)
1200
1000
800
600
400
200
0
1 1.5 2 2.5 3 3.5 4
Time (sec)
B
Tip diameter (µm)
250
200
150
100
50
0
1 1.5 2 2.5 3 3.5 4
Time (sec)
C
Needle length (µm)
1200
1000
800
600
400
200
0
2.21 3.36 4.52 5.65 6.87 7.89 8.96 9.93 11.00
Intensity (W/cm²)
D
Tip diameter (µm)
250
200
150
100
50
0
2.21 3.36 4.52 5.65 6.87 7.89 8.96 9.93 11.00
Intensity (W/cm²)
E
Needle length (µm)
1200
1000
800
600
400
200
0
3.5 6.5 9.5
Distance (cm)
F
Tip diameter (µm)
250
200
150
100
50
0
3.5 6.5 9.5
Distance (cm)

FIG. 5A - F

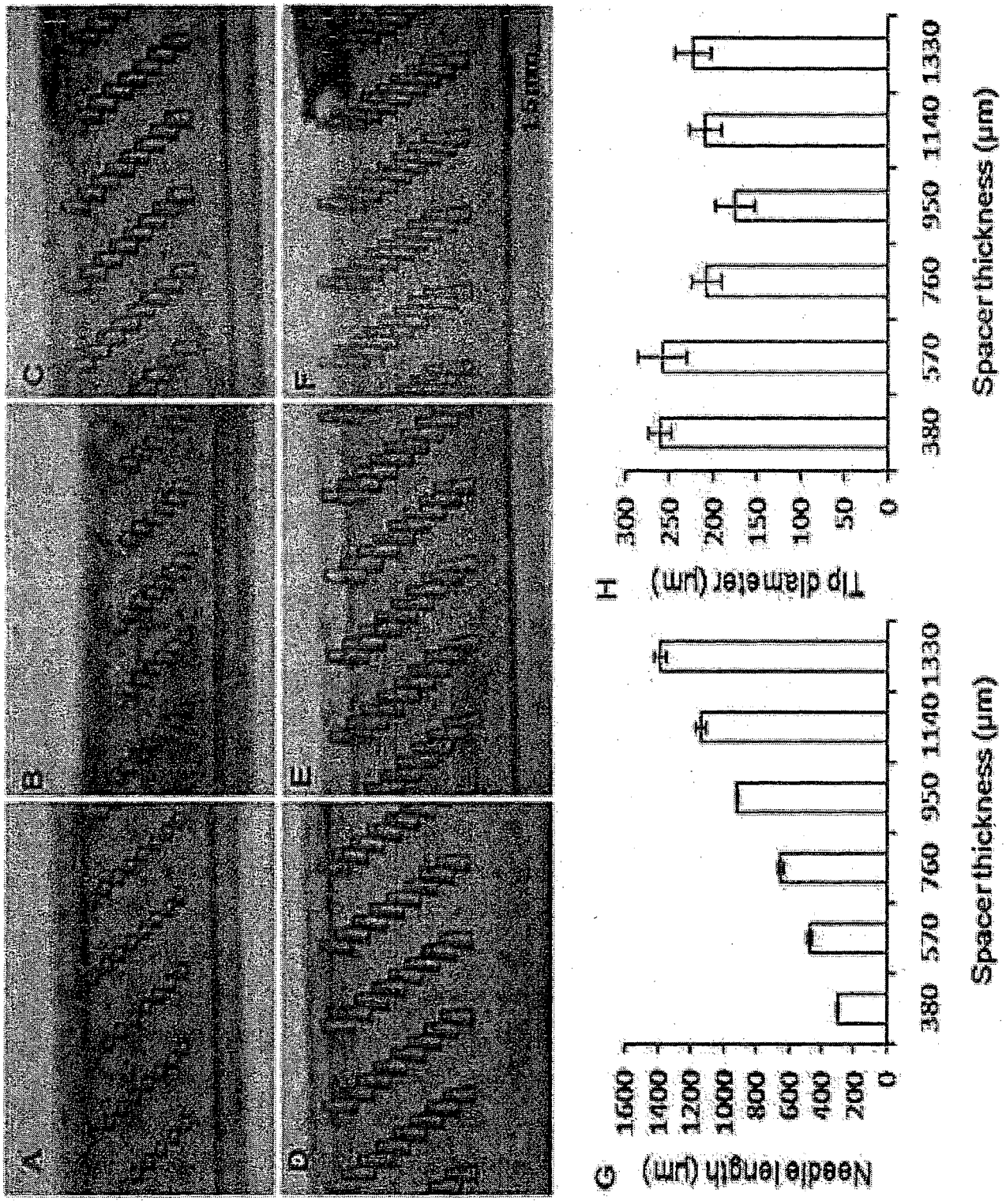

A
B
C
D
E
F
G
Needle length (μm)
1600
1400
1200
1000
800
600
400
200
0
380 570 760 950 1140 1330
Spacer thickness (μm)
H
Tip diameter (μm)
300
250
200
150
100
50
0
380 570 760 950 1140 1330
Spacer thickness (μm)

FIG. 6A - H

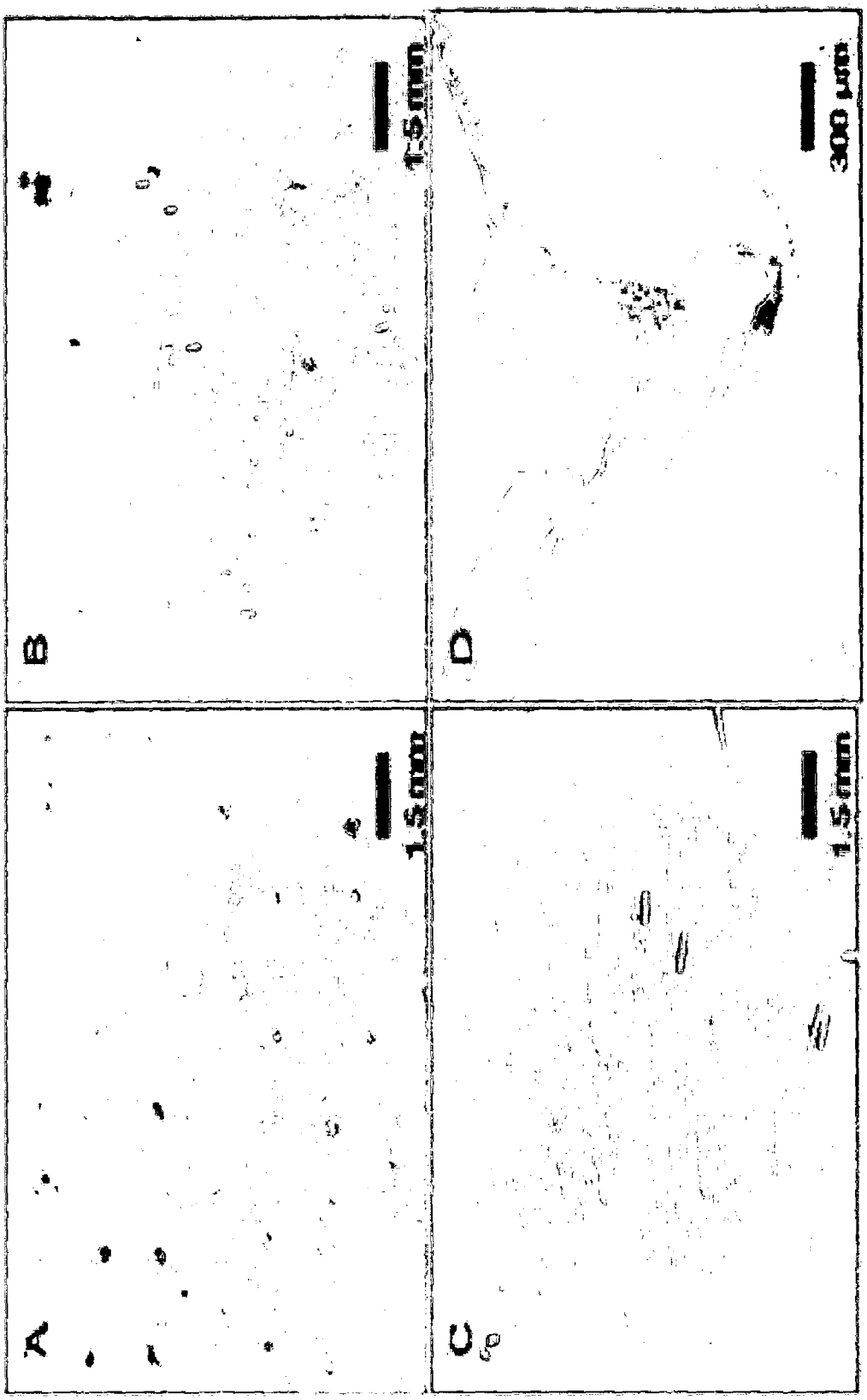
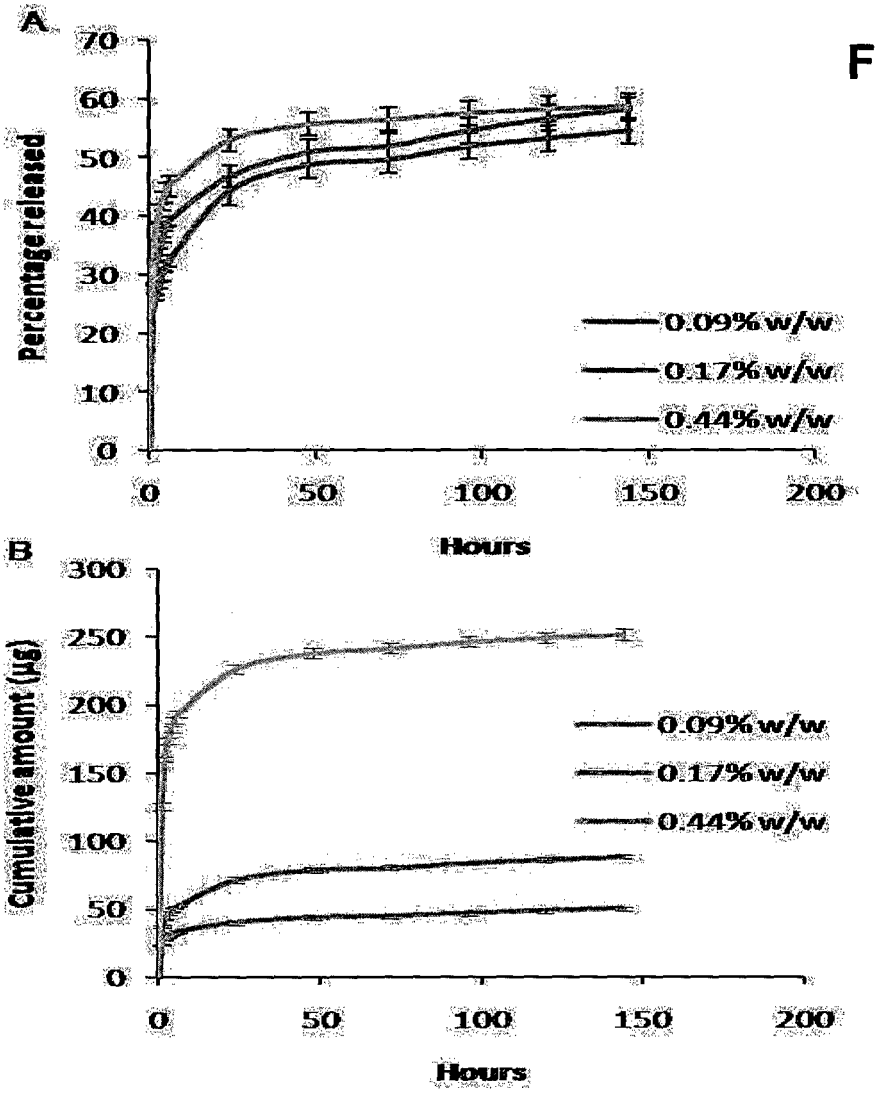


FIG. 7A-D

FIG. 8A-B


A
Percentage released
70
60
50
40
30
20
10
0
0
50
100
150
200
Hours
0.09% w/w
0.17% w/w
0.44% w/w
B
Cumulative amount (µg)
300
250
200
150
100
50
0
0
50
100
150
200
Hours
0.09% w/w
0.17% w/w
0.44% w/w

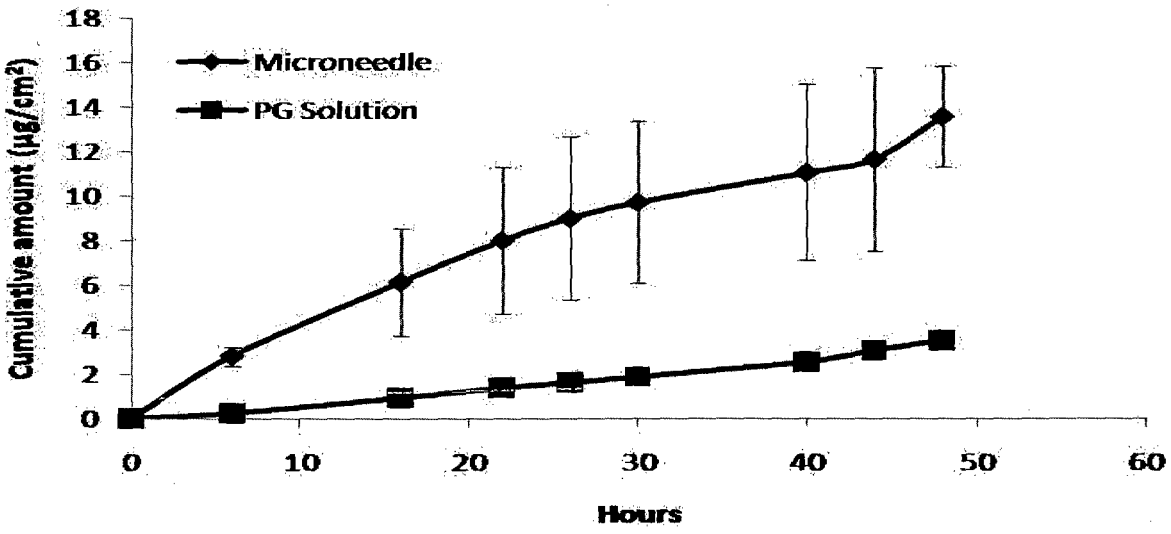

Cumulative amount (µg/cm²)
18
16
14
12
10
8
6
4
2
0
0
10
20
30
40
50
60
Hours
Microneedle
PG Solution

FIG. 9

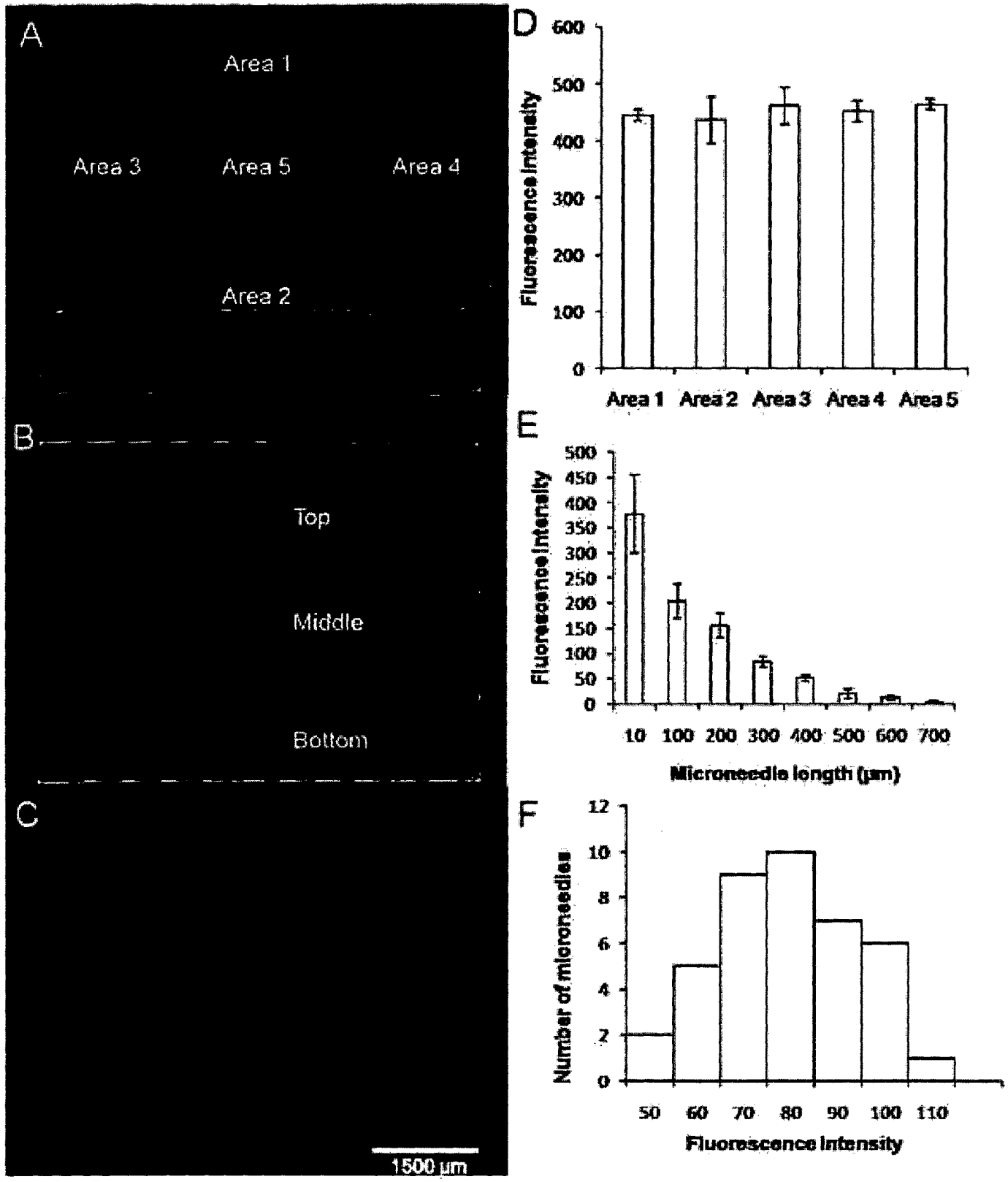

A
Area 1
Area 3
Area 5
Area 4
Area 2
B
Top
Middle
Bottom
C
1500 µm
D
Fluorescence Intensity
600
500
400
300
200
100
0
Area 1
Area 2
Area 3
Area 4
Area 5
E
Fluorescence Intensity
500
450
400
350
300
250
200
150
100
50
0
10 100 200 300 400 500 600 700
Microneedle length (µm)
F
Number of microneedles
12
10
8
6
4
2
0
50 60 70 80 90 100 110
Fluorescence Intensity

FIG. 10A-F

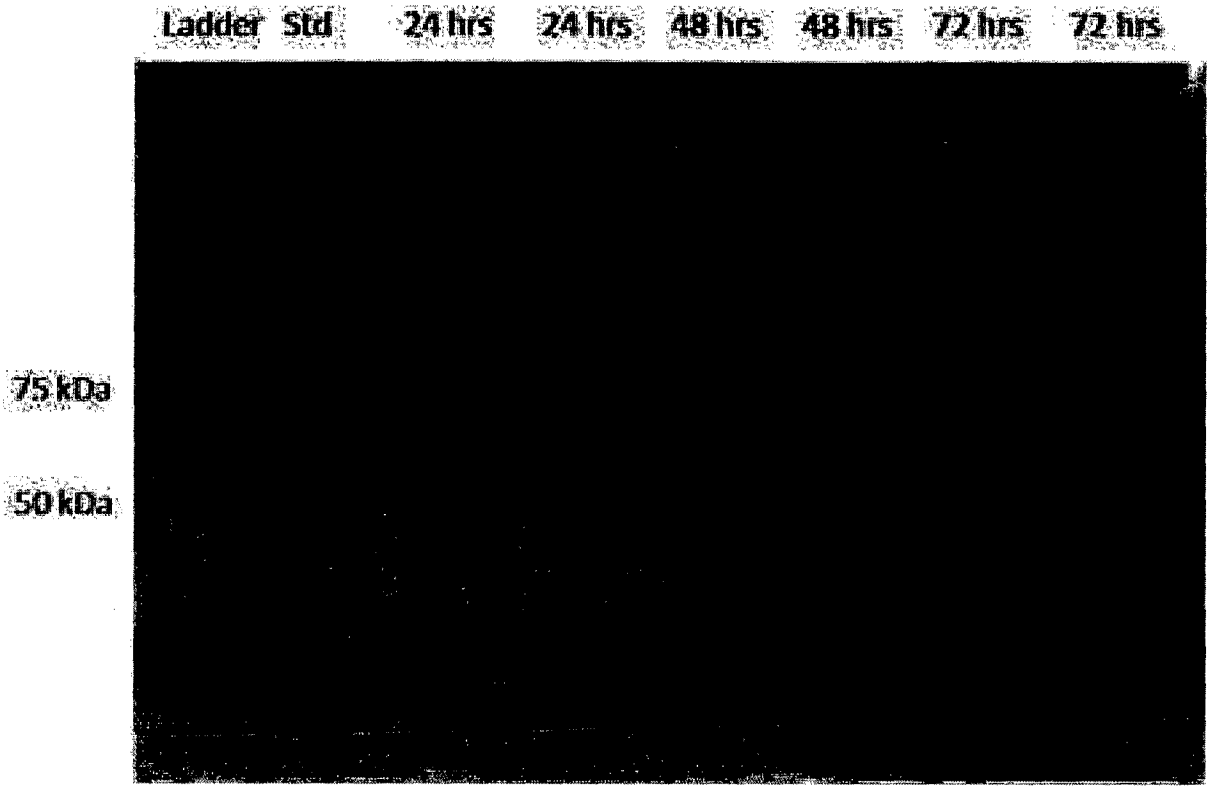


FIG. 11

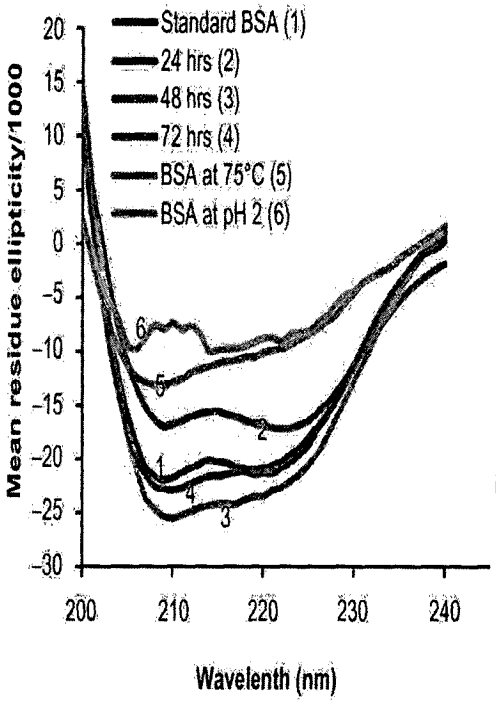


FIG. 12A

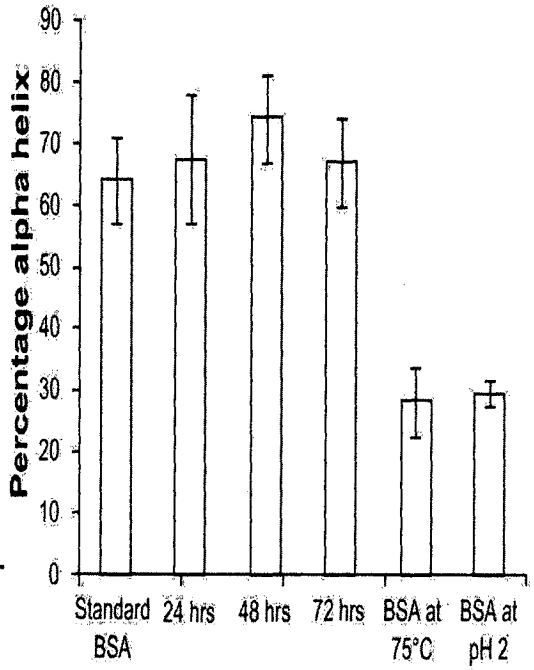


FIG. 12B

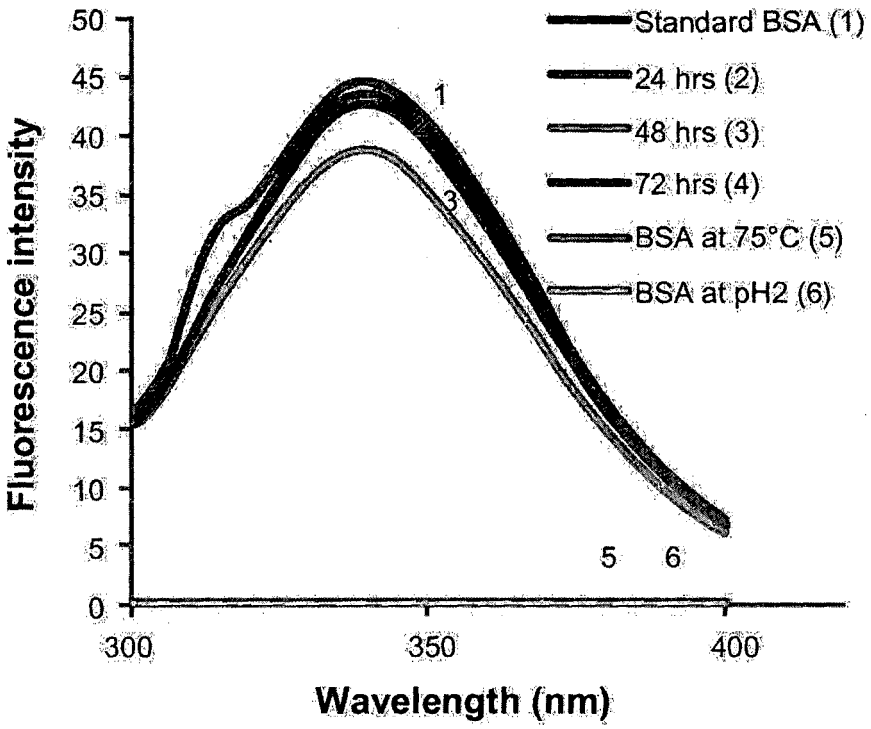

Fluorescence intensity
50
45
40
35
30
25
20
15
10
5
0
300
350
400
Wavelength (nm)
Standard BSA (1)
24 hrs (2)
48 hrs (3)
72 hrs (4)
BSA at 75°C (5)
BSA at pH2 (6)
1
3
5
6

FIG. 13

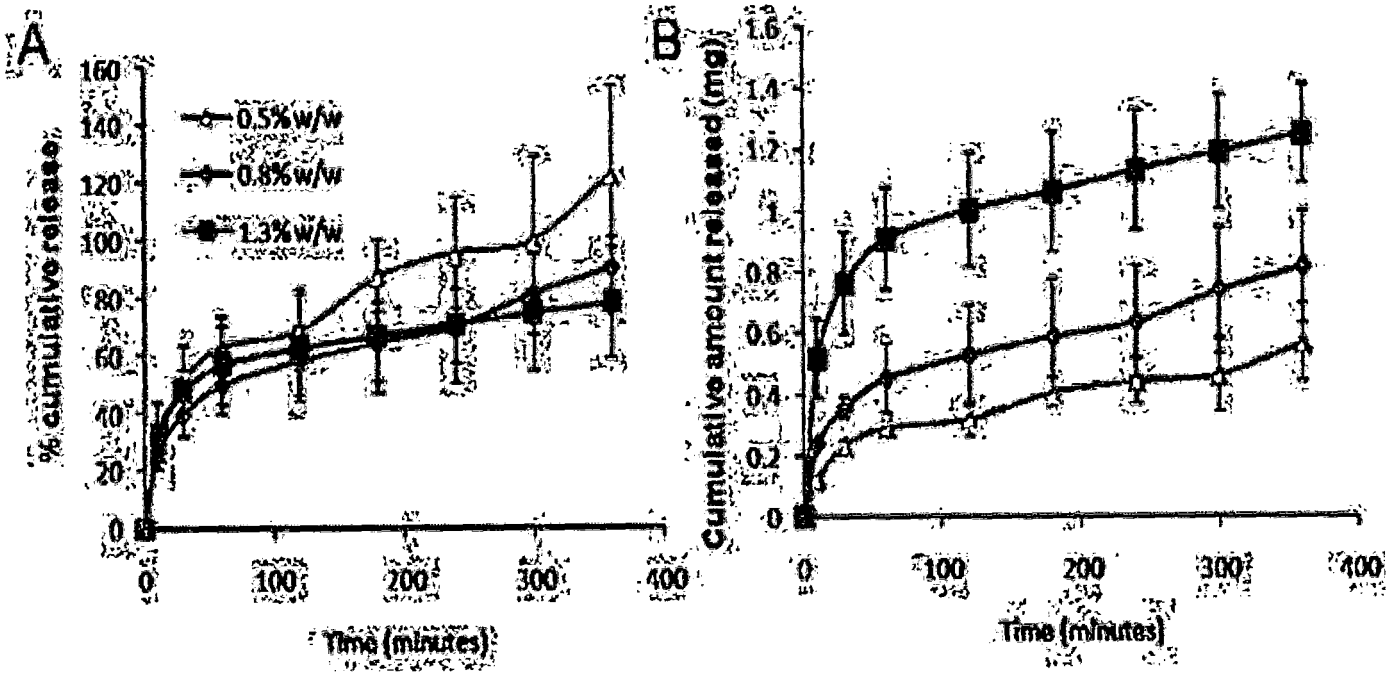

A
% cumulative release
0.5%w/w
0.8%w/w
1.3%w/w
Time (minutes)
B
Cumulative amount released (mg)
Time (minutes)

FIG. 14A-B

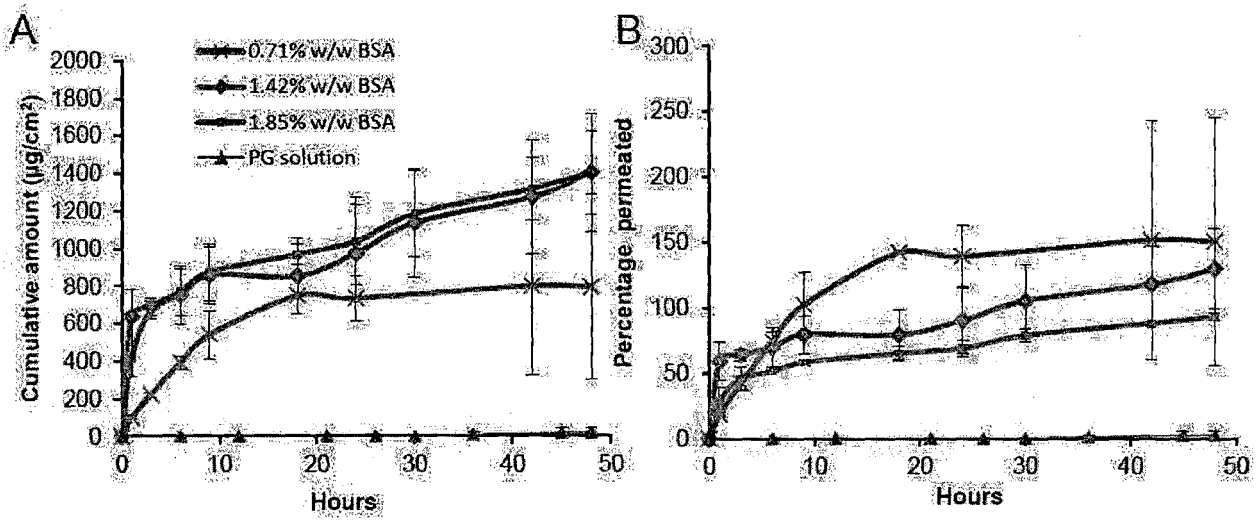

A
0.71% w/w BSA
1.42% w/w BSA
1.85% w/w BSA
PG solution
Cumulative amount (µg/cm²)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
Hours
B
Percentage permeated
300
250
200
150
100
50
0
0
10
20
30
40
50
Hours

FIG. 15A-B

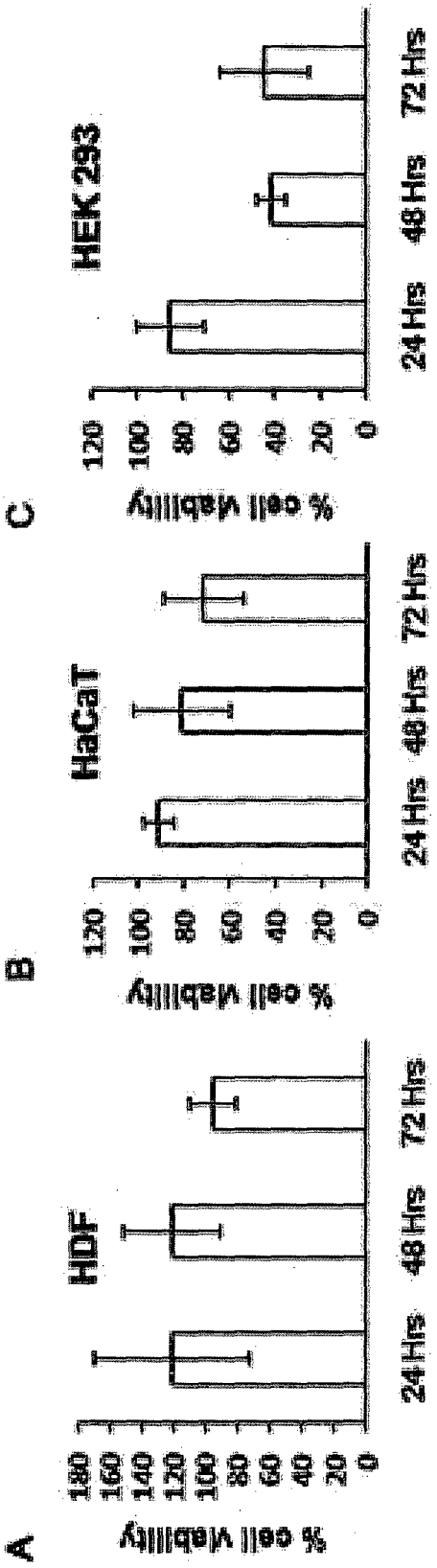

A
% cell viability
180
160
140
120
100
80
60
40
20
0
HDF
24 Hrs
48 Hrs
72 Hrs
B
% cell viability
120
100
80
60
40
20
0
HaCaT
24 Hrs
48 Hrs
72 Hrs
C
% cell viability
120
100
80
60
40
20
0
HEK 293
24 Hrs
48 Hrs
72 Hrs

FIG. 16A-C

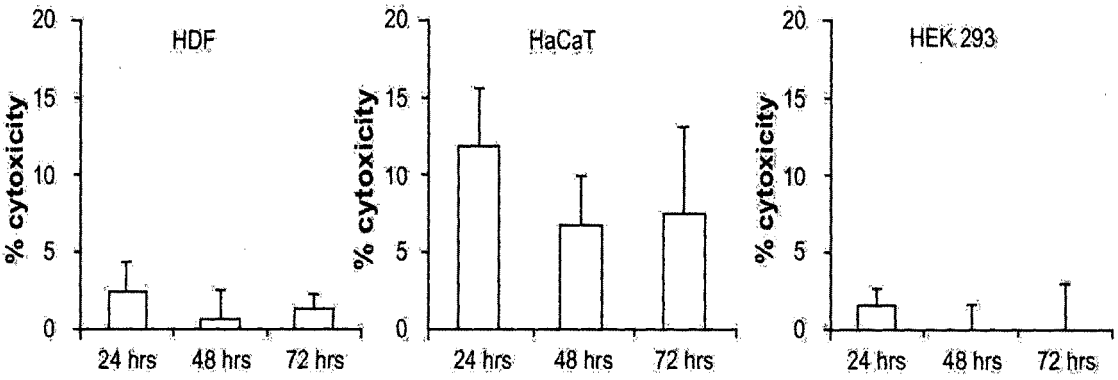


FIG. 16D

FIG. 16E

FIG. 16F

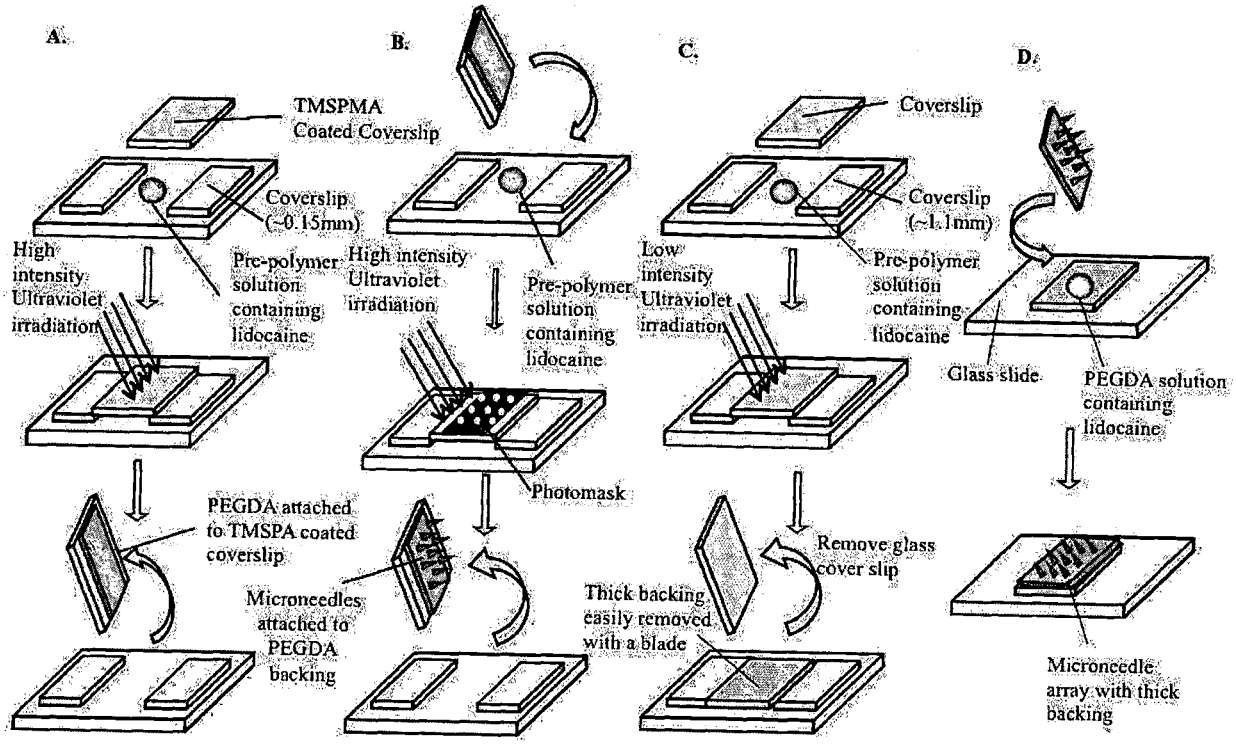
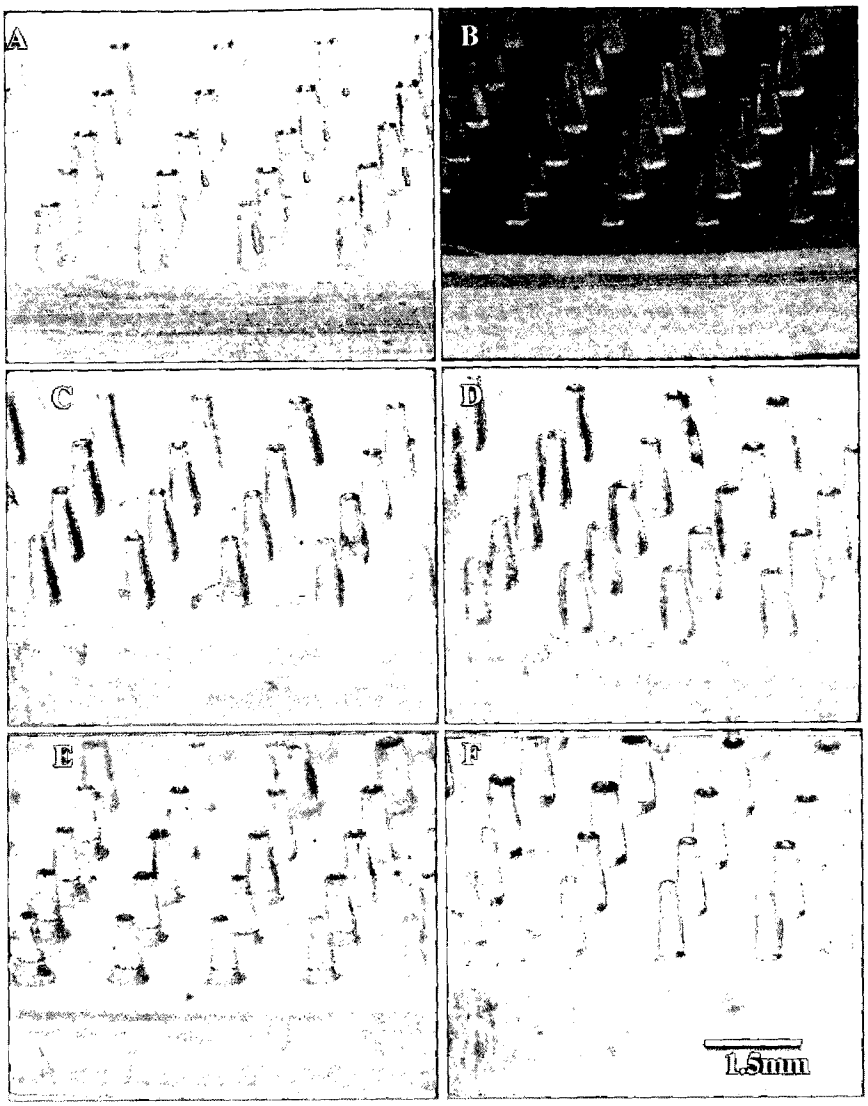

A.
B.
C.
D.
TMSPMA Coated Coverslip
Coverslip (~0.15mm)
High intensity Ultraviolet irradiation
Pre-polymer solution containing lidocaine
PEGDA attached to TMSPA coated coverslip
Microneedles attached to PEGDA backing
High intensity Ultraviolet irradiation
Pre-polymer solution containing lidocaine
Photomask
Coverslip
Coverslip (~1.1mm)
Low intensity Ultraviolet irradiation
Pre-polymer solution containing lidocaine
Remove glass cover slip
Thick backing easily removed with a blade
Glass slide
PEGDA solution containing lidocaine
Microneedle array with thick backing

FIG. 17A-D


A
B
C
D
E
F
1.5mm

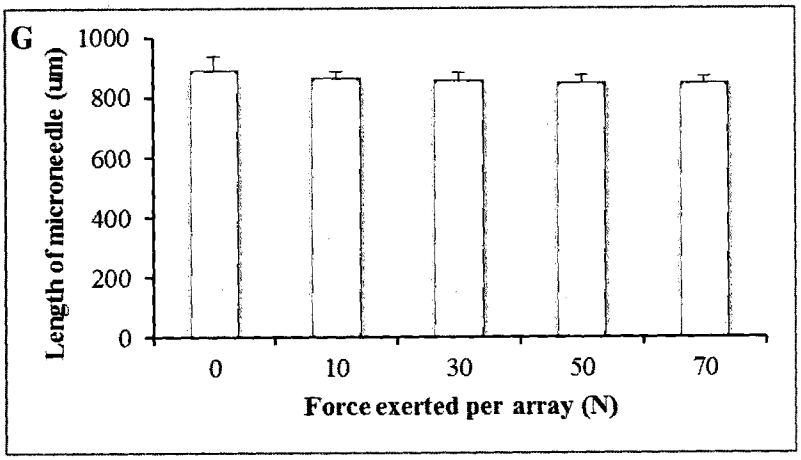
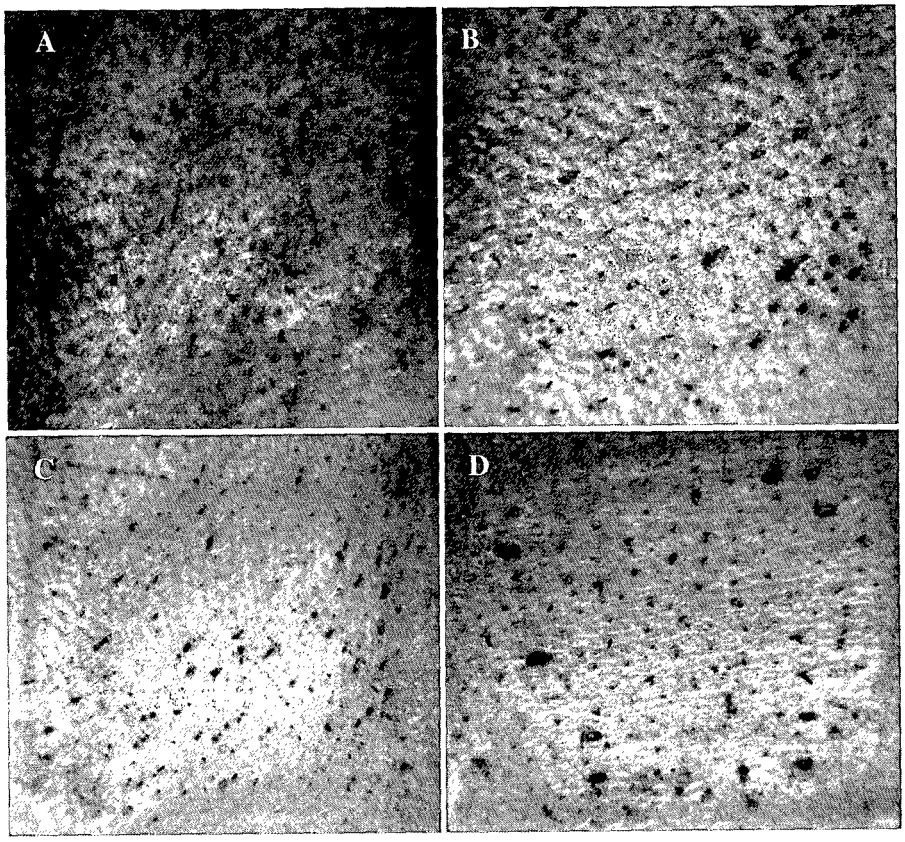

G
Length of microneedle (um)
1000
800
600
400
200
0
0
10
30
50
70
Force exerted per array (N)

FIG. 18A-G


A
B
C
D

E

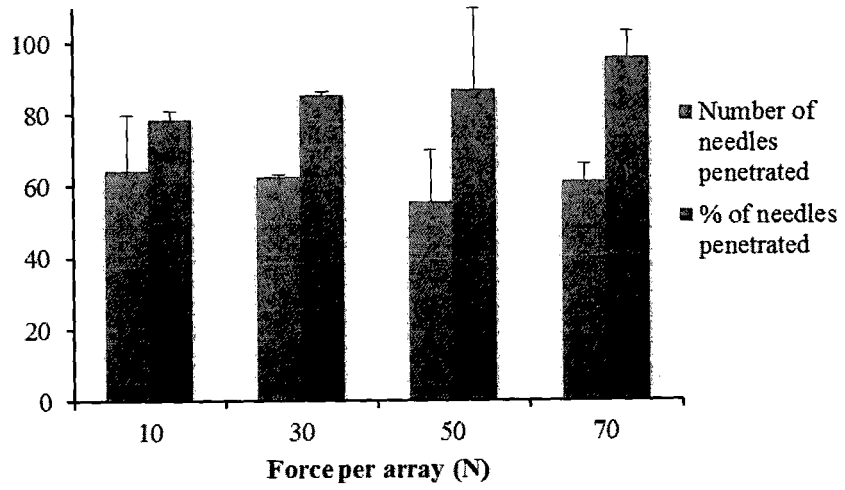

100
80
60
40
20
0
10
30
50
70
Force per array (N)
Number of needles penetrated
% of needles penetrated

FIG. 19A-E

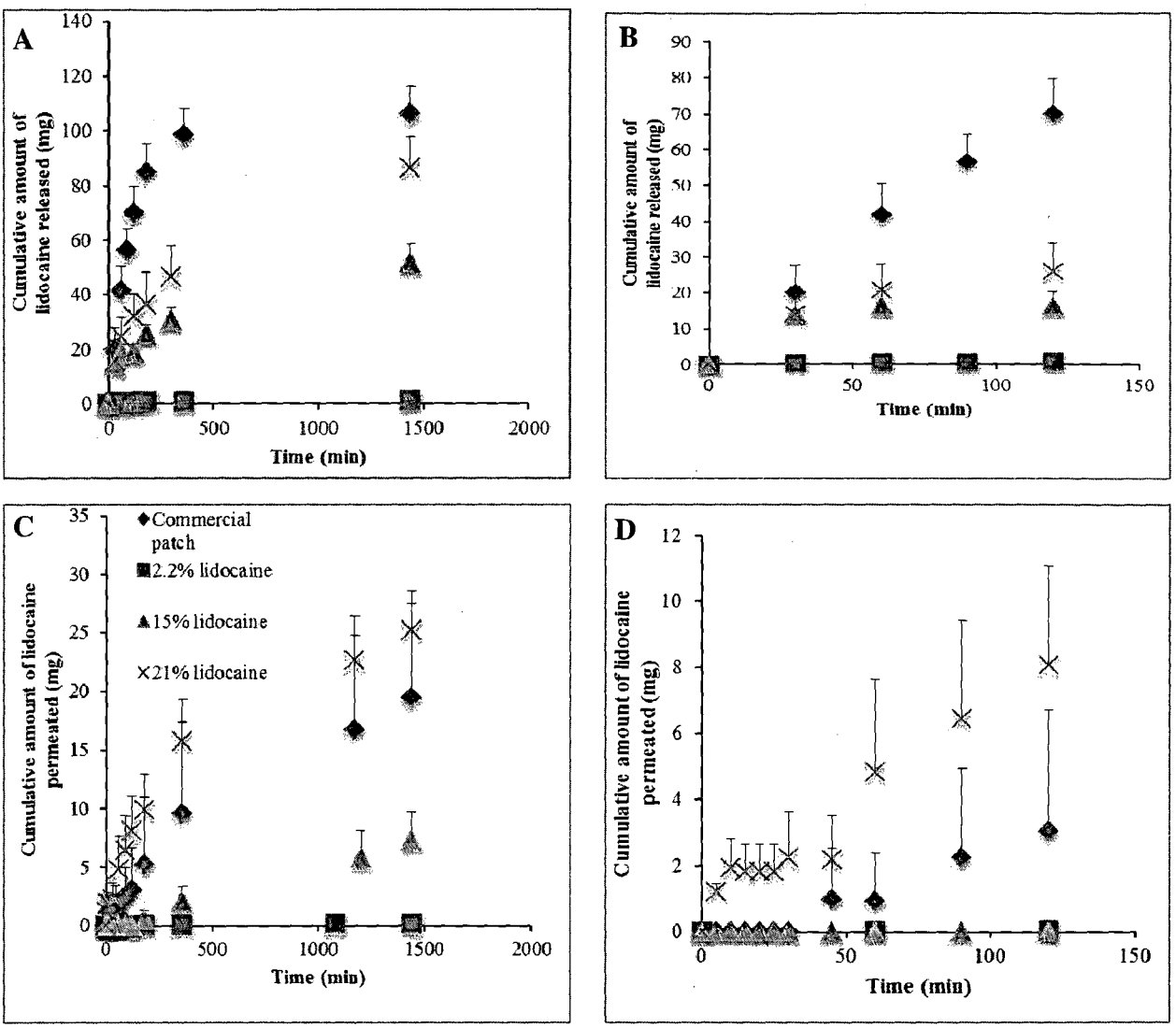

A
Cumulative amount of lidocaine released (mg)
Time (min)
B
Cumulative amount of lidocaine released (mg)
Time (min)
C
Cumulative amount of lidocaine permeated (mg)
Time (min)
Commercial patch
2.2% lidocaine
15% lidocaine
21% lidocaine
D
Cumulative amount of lidocaine permeated (mg)
Time (min)

FIG. 20A-D

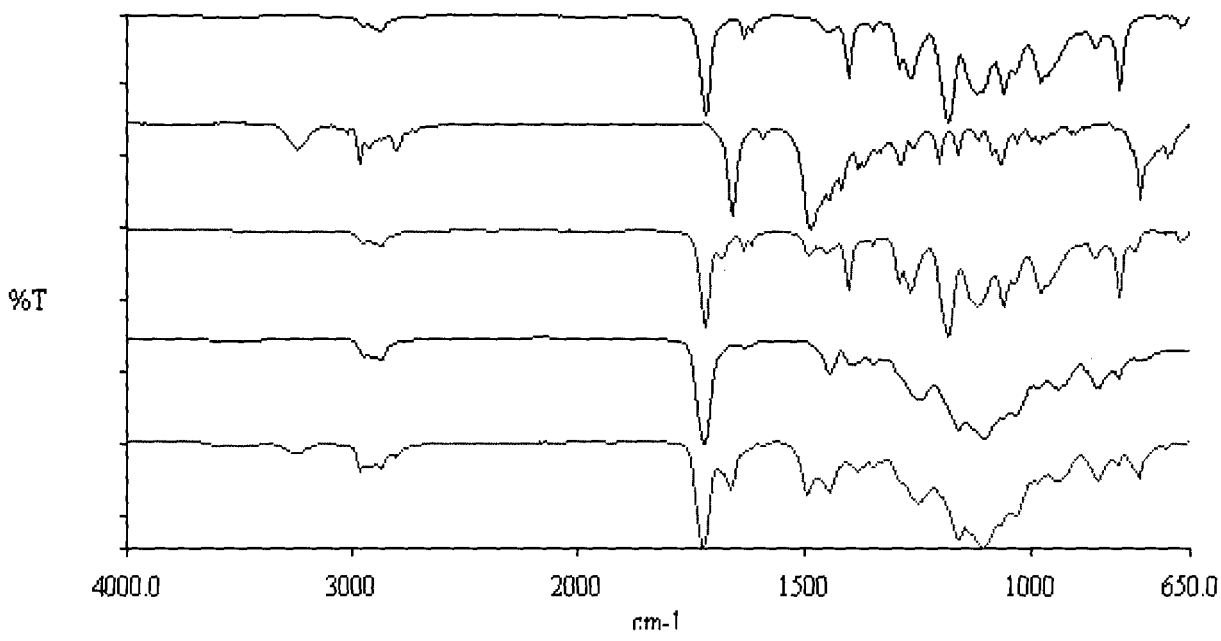


FIG. 21

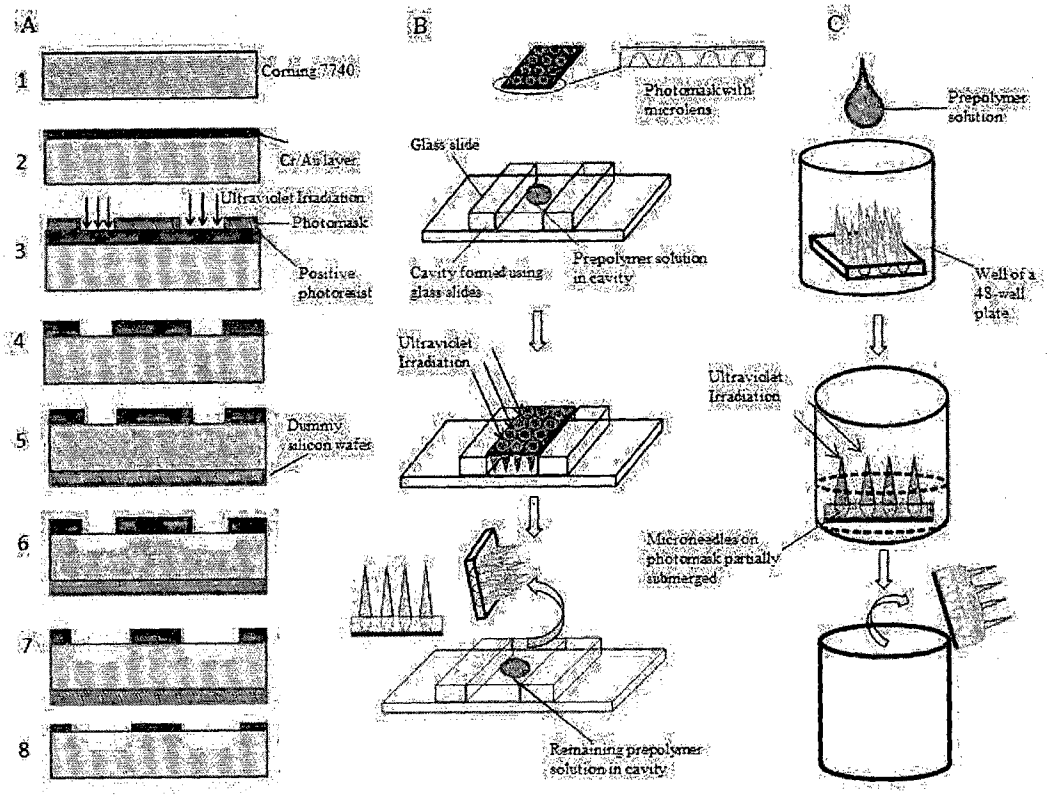

A
1
Corning 7740
2
Cr/Au layer
Ultraviolet Irradiation
Photomask
3
Positive photoresist
4
5
Dummy silicon wafer
6
7
8
B
Photomask with microlens
Glass slide
Cavity formed using glass slides
Prepolymer solution in cavity
Ultraviolet Irradiation
Microneedles on photomask partially submerged
Remaining prepolymer solution in cavity
C
Prepolymer solution
Well of a 48-well plate
Ultraviolet Irradiation

FIG. 22A-C

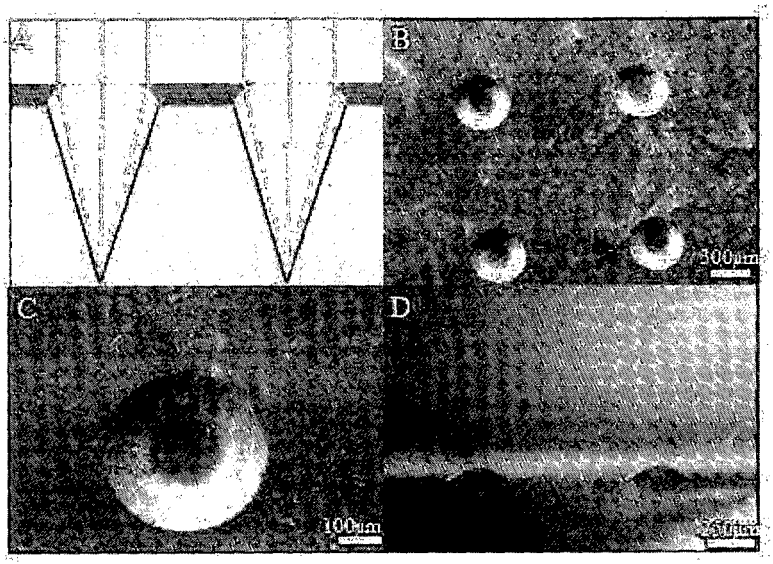


FIG. 23A-D

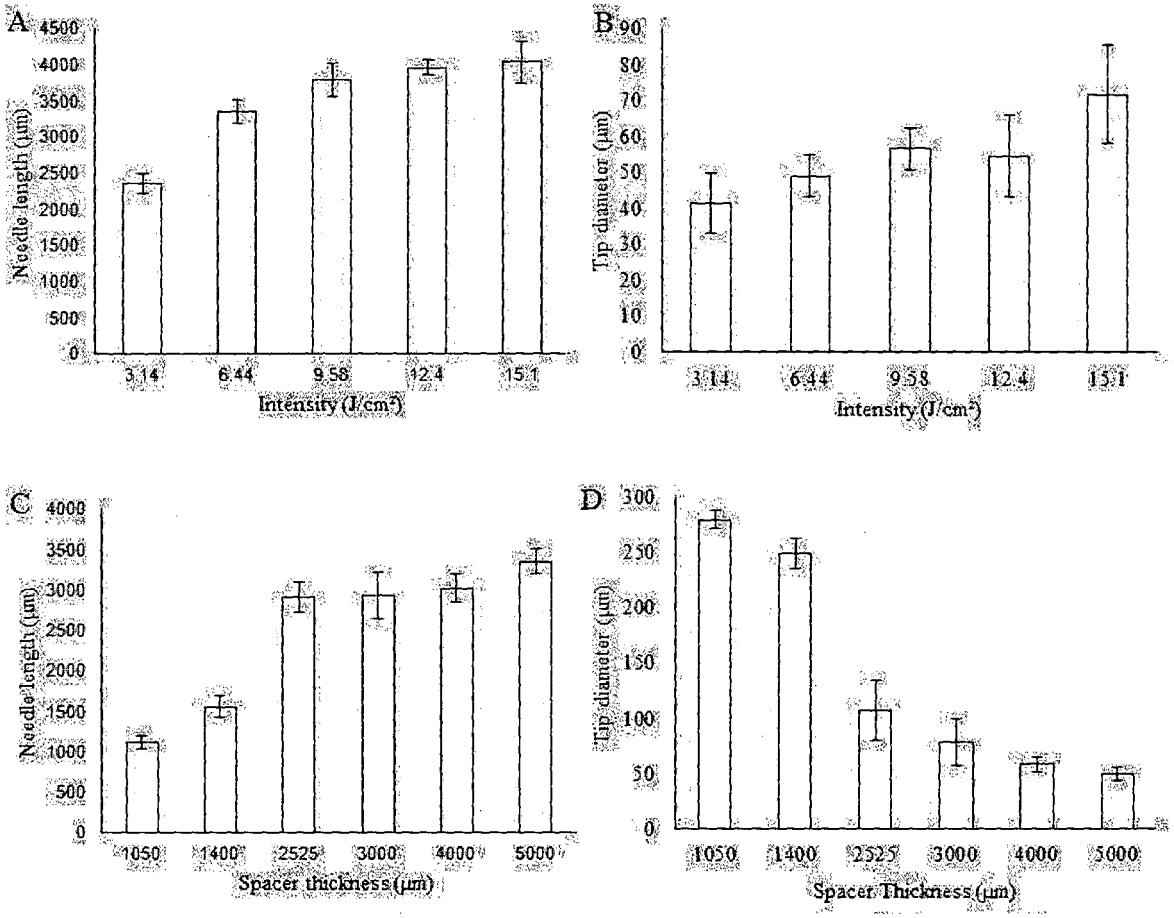

A
Needle length (µm)
4500
4000
3500
3000
2500
2000
1500
1000
500
0
3.14
6.44
9.58
12.4
15.1
Intensity (J/cm²)
B
Tip diameter (µm)
90
80
70
60
50
40
30
20
10
0
3.14
6.44
9.58
12.4
15.1
Intensity (J/cm²)
C
Needle length (µm)
4000
3500
3000
2500
2000
1500
1000
500
0
1050
1400
2525
3000
4000
5000
Spacer thickness (µm)
D
Tip diameter (µm)
300
250
200
150
100
50
0
1050
1400
2525
3000
4000
5000
Spacer Thickness (µm)

FIG. 24A-D

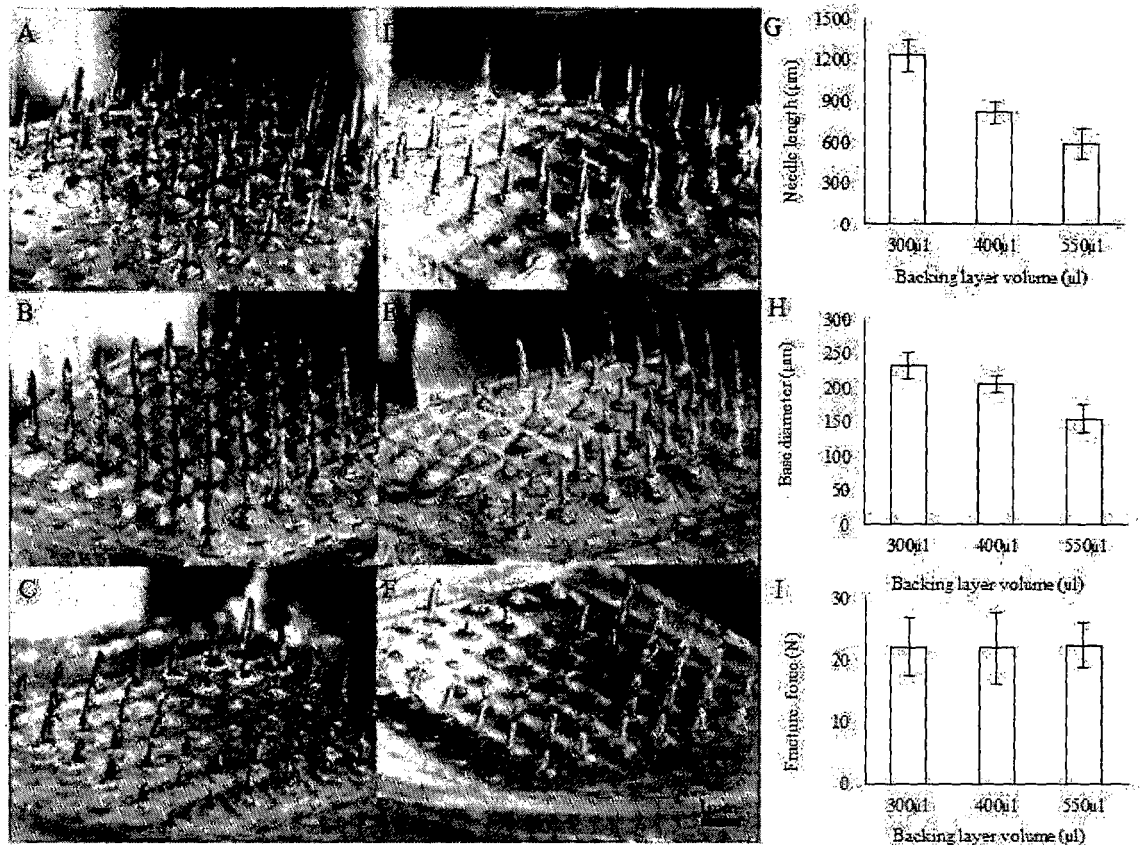

A
D
G
1500
1200
900
600
300
0
Needle length (μm)
300μl
400μl
550μl
Backing layer volume (ul)
B
E
H
300
250
200
150
100
50
0
Base diameter (μm)
300μl
400μl
550μl
Backing layer volume (ul)
C
F
I
30
20
10
0
Fracture force (N)
300μl
400μl
550μl
Backing layer volume (ul)

FIG. 25A-I

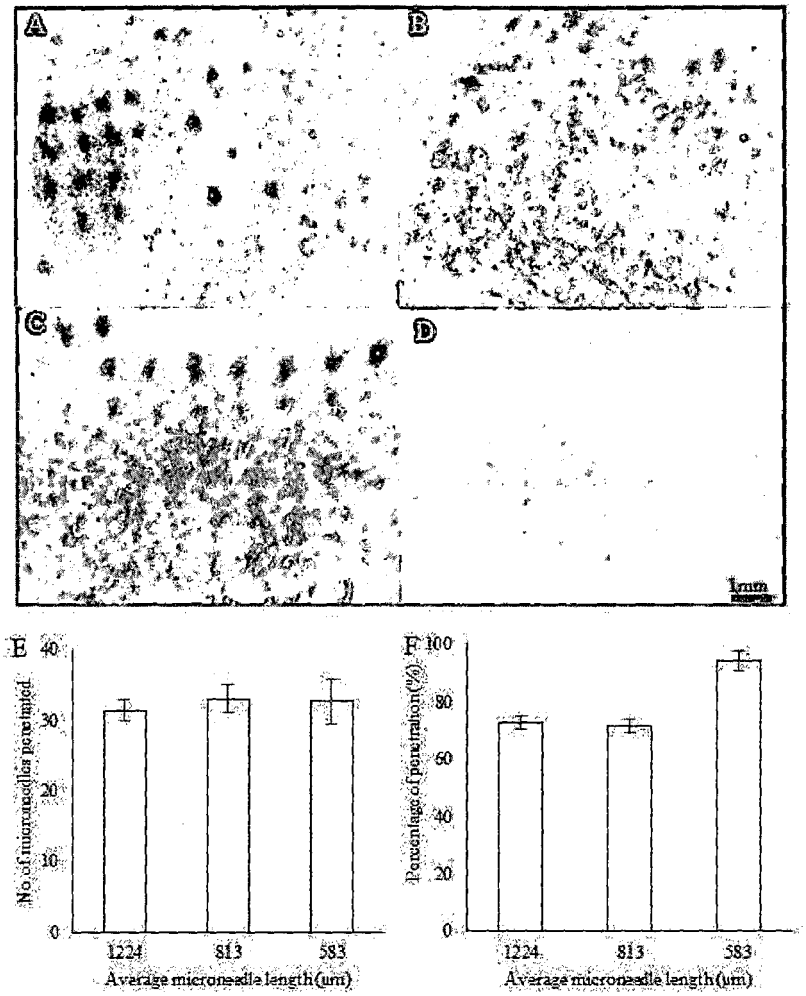

A
B
C
D
1mm
E
No. of microneedles penetrated
0
10
20
30
40
1224
813
583
Average microneedle length (um)
F
Percentage of penetration (%)
0
20
40
60
80
100
1224
813
583
Average microneedle length (um)

FIG. 26A-F

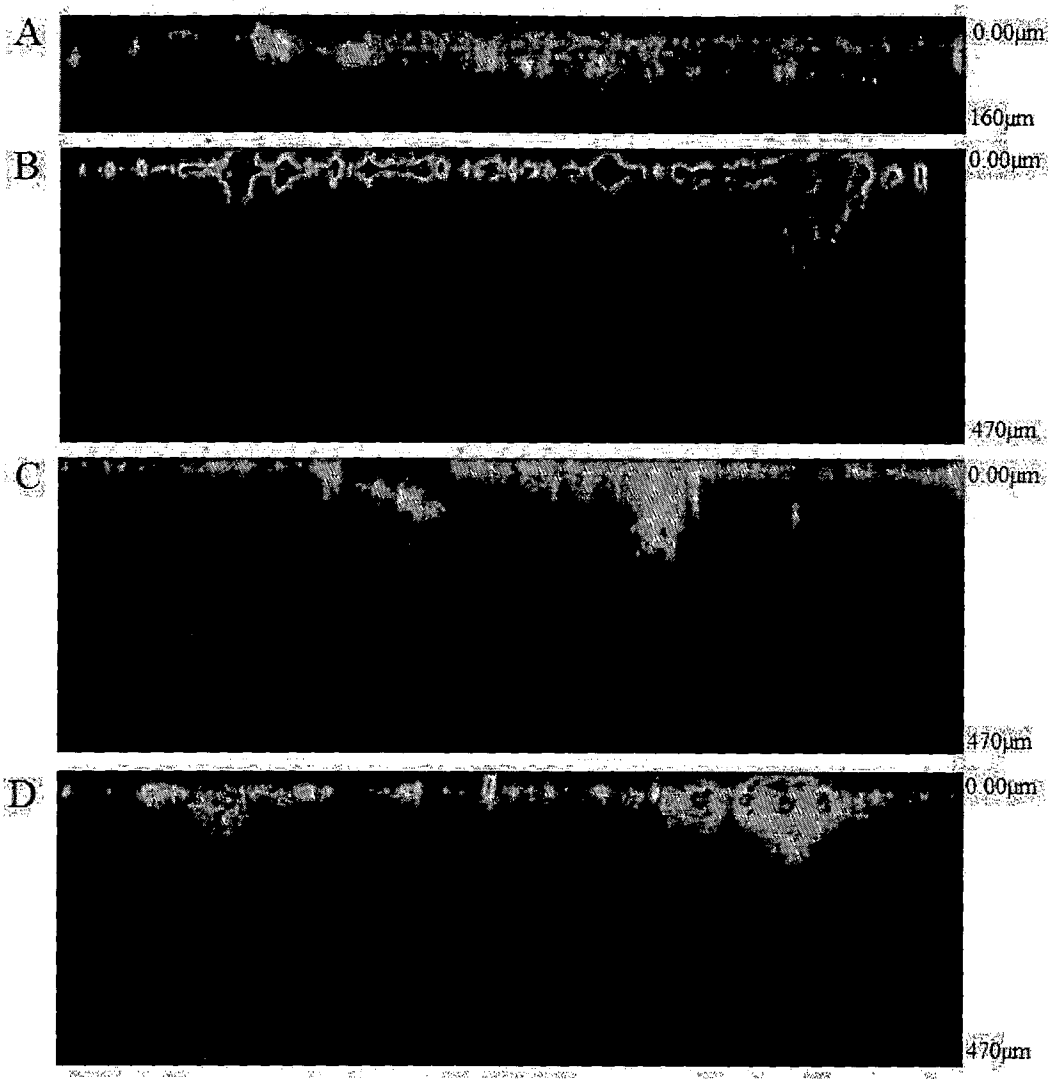


FIG. 27A-D