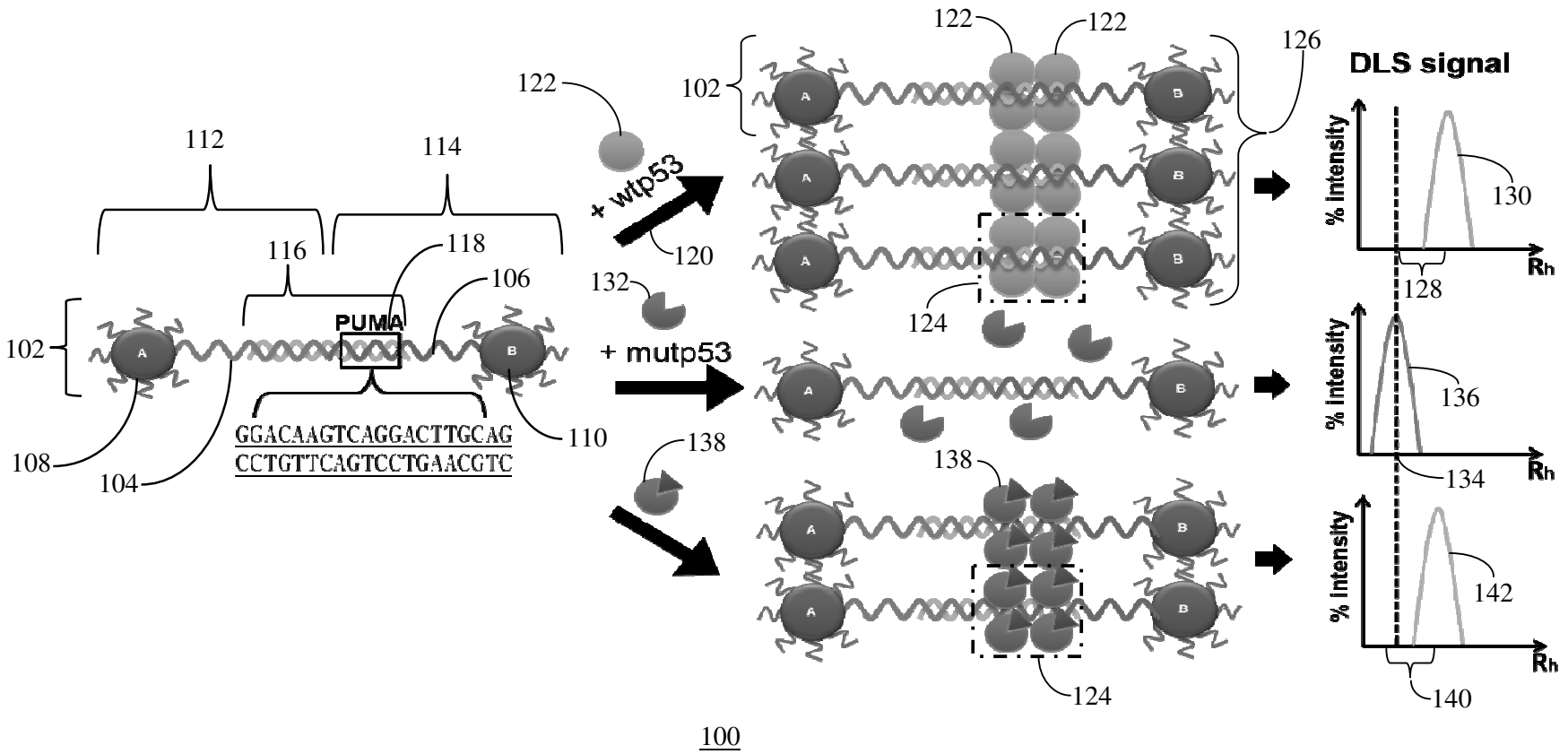

112
114
116
118
106
PUMA
102
A
B
GGACAAGTCAGGACTTGCAG
CCTGTTCAGTCCTGAACGTC
108
104
110
122
+ wtp53
120
132
+ mutp53
138
122
122
126
102
124
138
124
DLS signal
% Intensity
Rh
130
128
136
134
142
140
100

FIG. 1

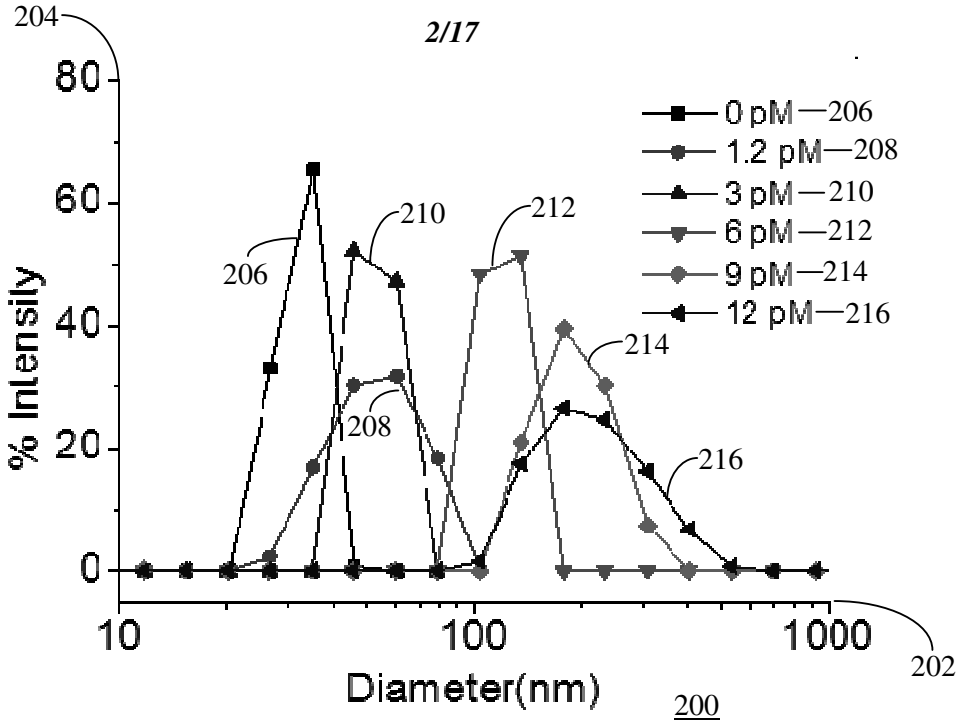

204
80
60
40
20
0
% Intensily
0 pM—206
1.2 pM—208
3 pM—210
6 pM—212
9 pM—214
12 pM—216
206
210
212
214
208
216
10
100
1000
202
Diameter(nm)
200

FIG. 2A

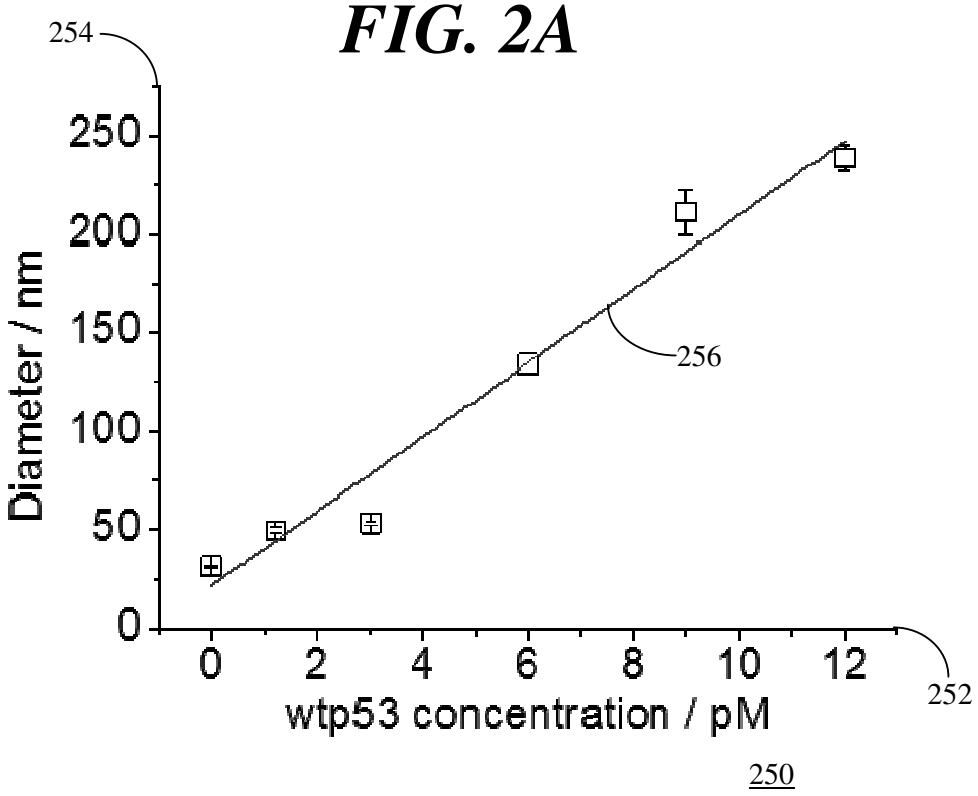

254
250
200
150
100
50
0
Diameter / nm
256
0
2
4
6
8
10
12
252
wtp53 concentration / pM
250

FIG. 2B

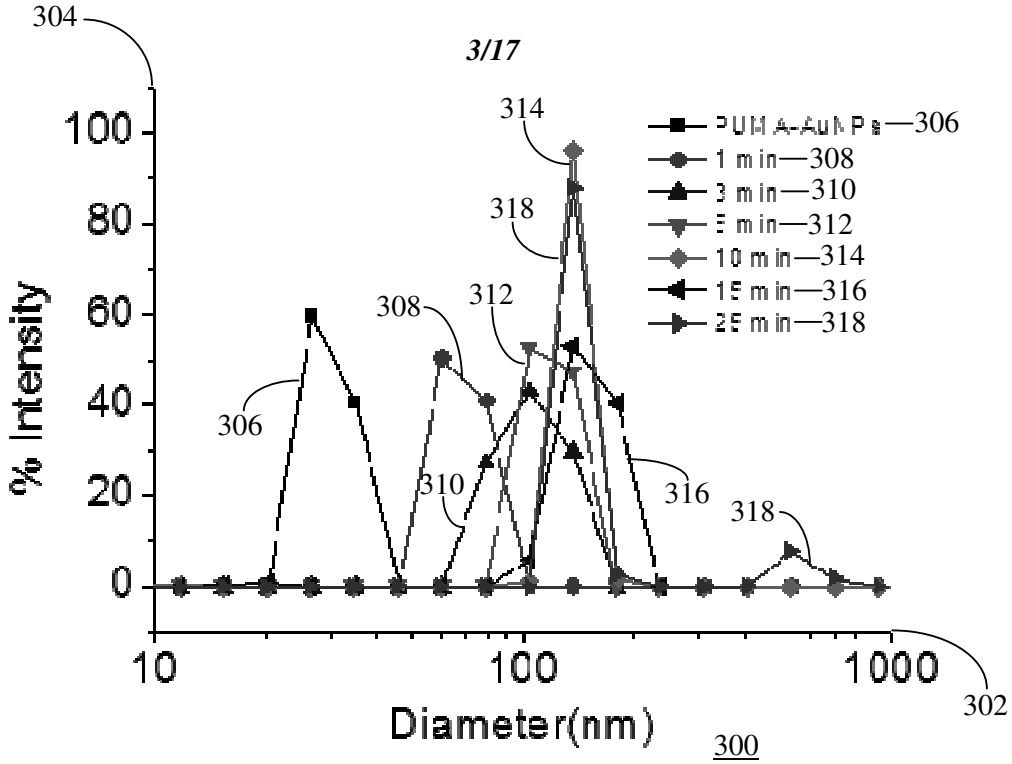

304
314
318
308
312
306
310
316
318
302
% Intensity
Diameter(nm)
PUMA-AuNPs—306
1 min—308
3 min—310
5 min—312
10 min—314
15 min—316
25 min—318
100
80
60
40
20
0
10
100
1000
300

FIG. 3A

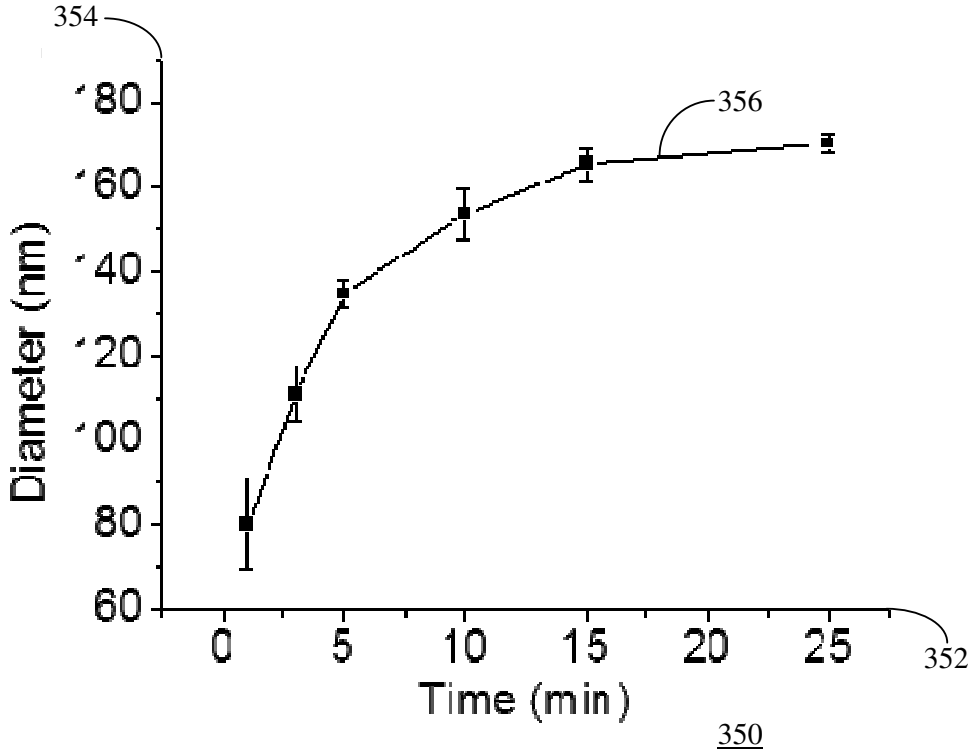
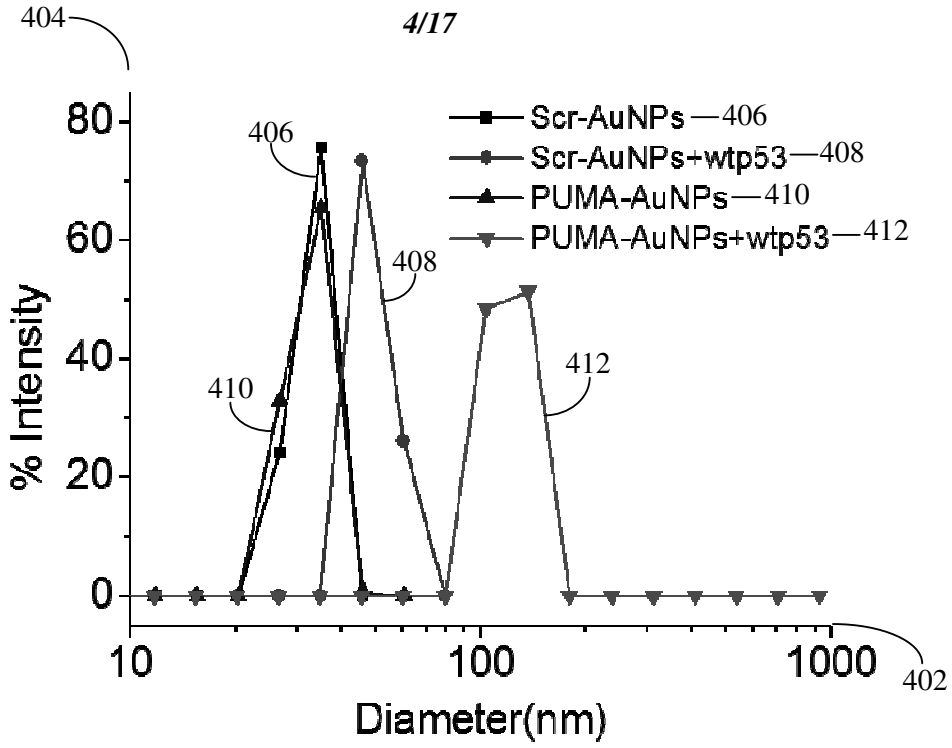
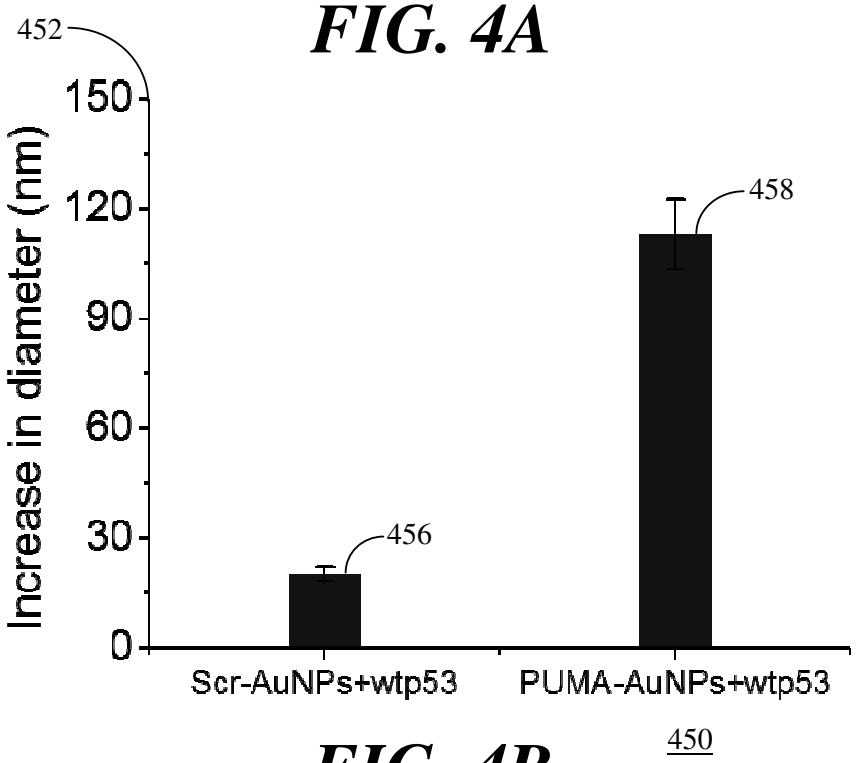

354
356
352
Diameter (nm)
Time (min)
80
60
40
20
00
80
60
0
5
10
15
20
25
350

FIG. 3B



400

FIG. 4A



450

FIG. 4B

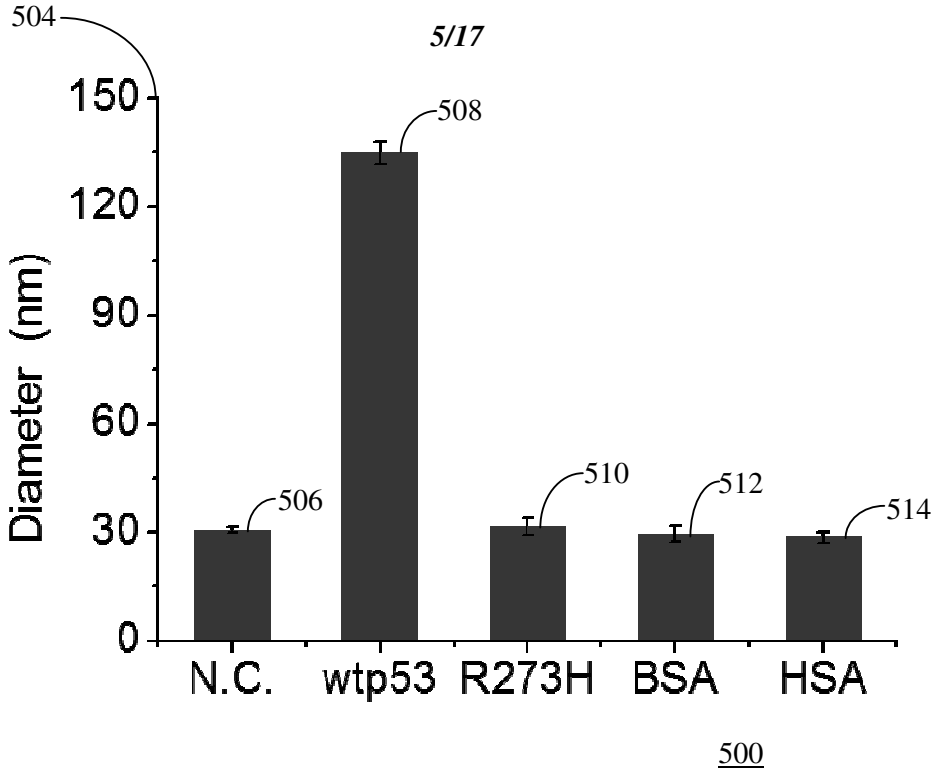

504
150
120
90
60
30
0
Diameter (nm)
508
506
510
512
514
N.C.
wtp53
R273H
BSA
HSA
500

FIG. 5A

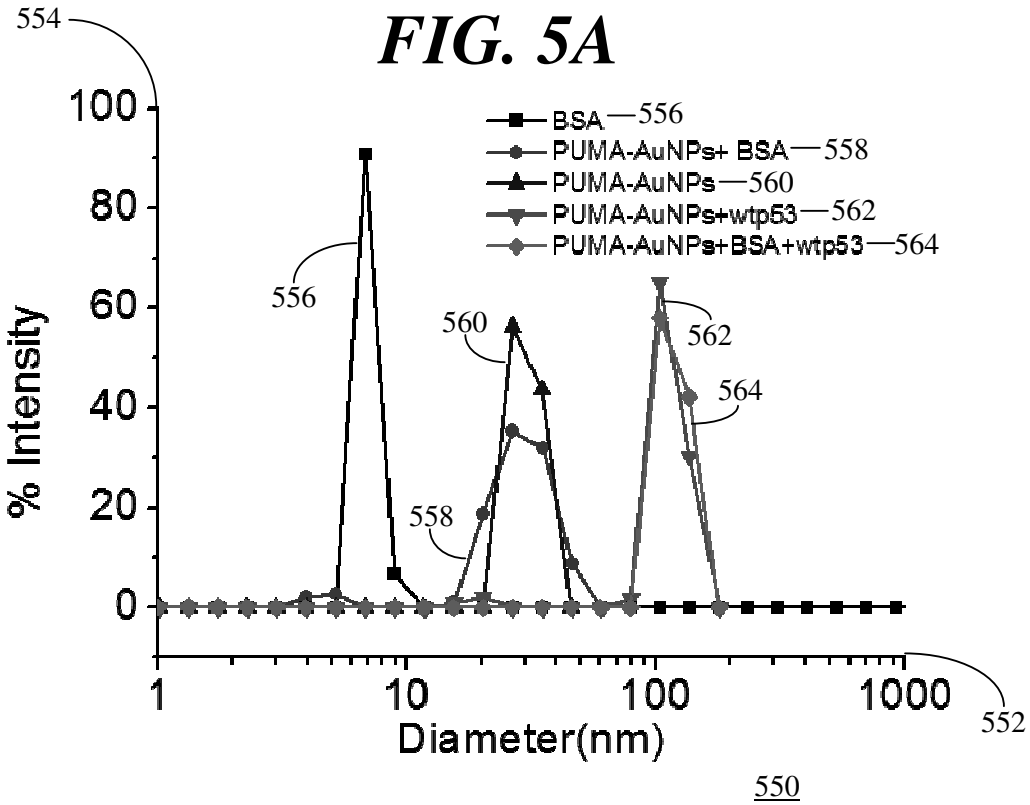
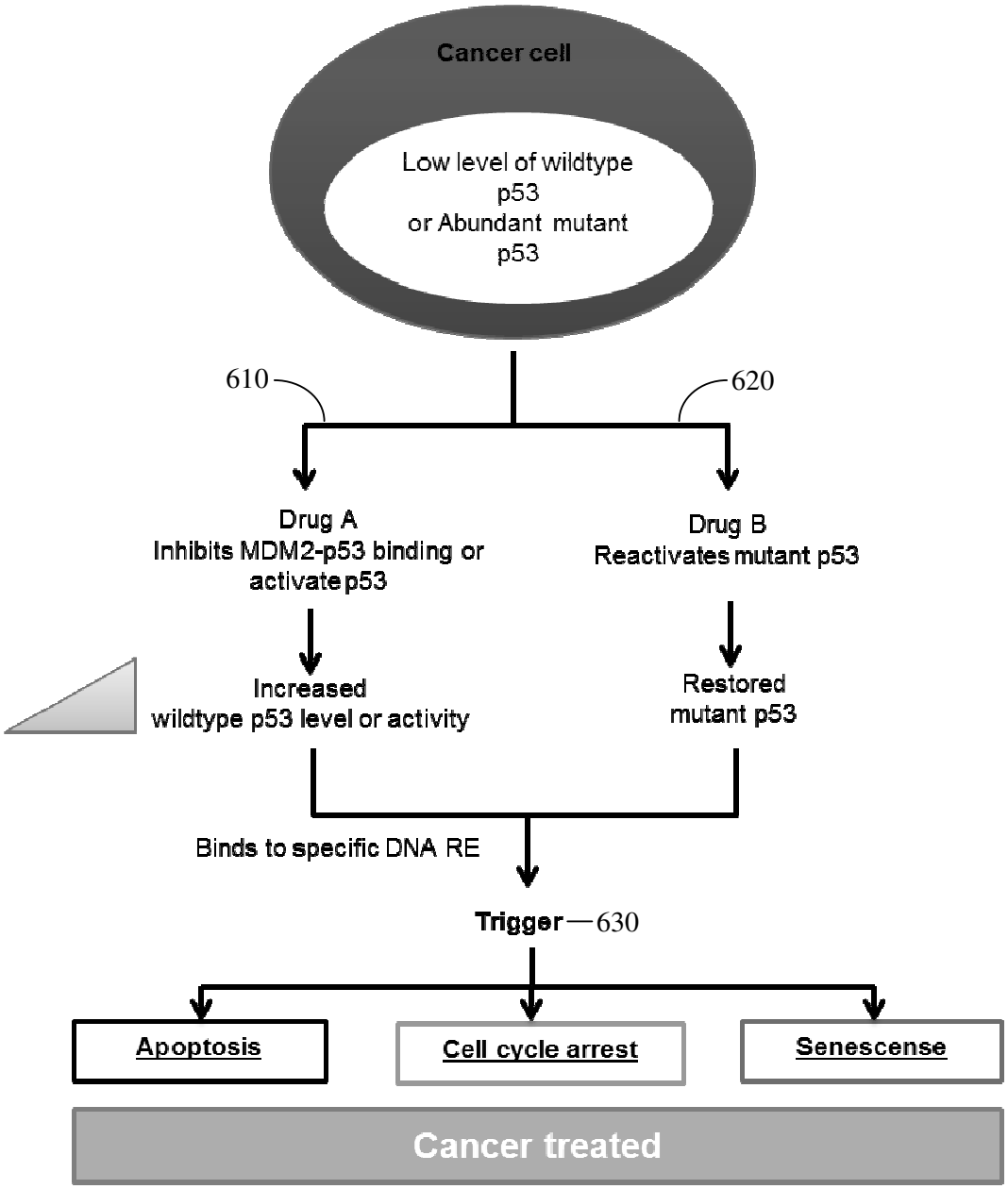

554
100
80
60
40
20
0
% Intensity
BSA —556
PUMA-AuNPs+ BSA —558
PUMA-AuNPs —560
PUMA-AuNPs+wtp53 —562
PUMA-AuNPs+BSA+wtp53 —564
556
560
562
564
558
1
10
100
1000
Diameter(nm)
552
550

FIG. 5B


Cancer cell
Low level of wildtype p53
or Abundant mutant p53
610
620
Drug A
Inhibits MDM2-p53 binding or activate p53
Drug B
Reactivates mutant p53
Increased wildtype p53 level or activity
Restored mutant p53
Binds to specific DNA RE
Trigger
630
Apoptosis
Cell cycle arrest
Senescense
Cancer treated

600

FIG. 6

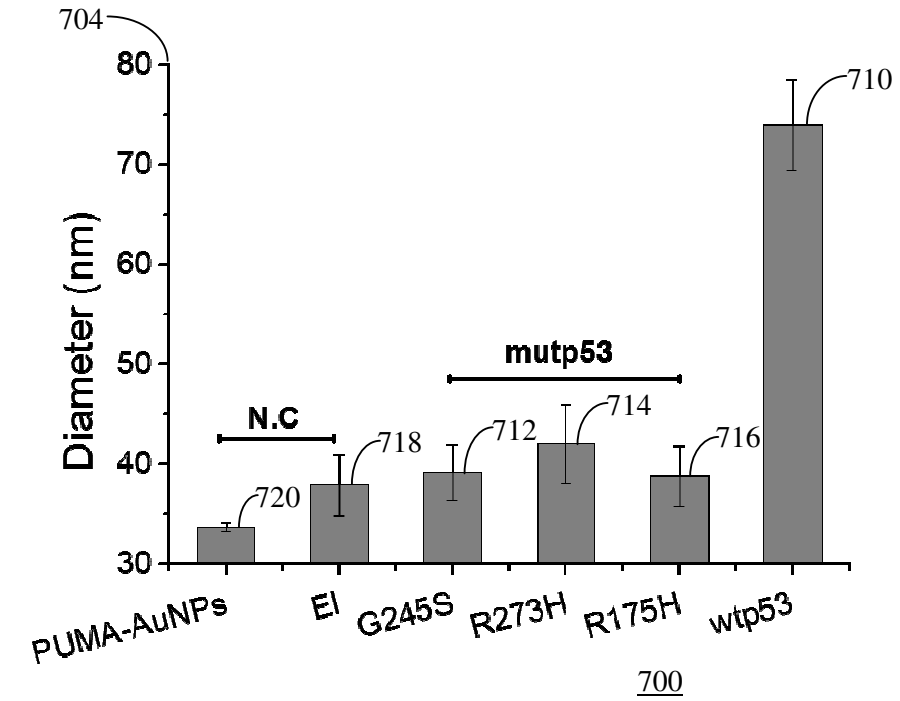

704
80
70
60
50
40
30
Diameter (nm)
N.C
mutp53
720
718
712
714
716
710
PUMA-AuNPs
EI
G245S
R273H
R175H
wtp53
700

FIG. 7A

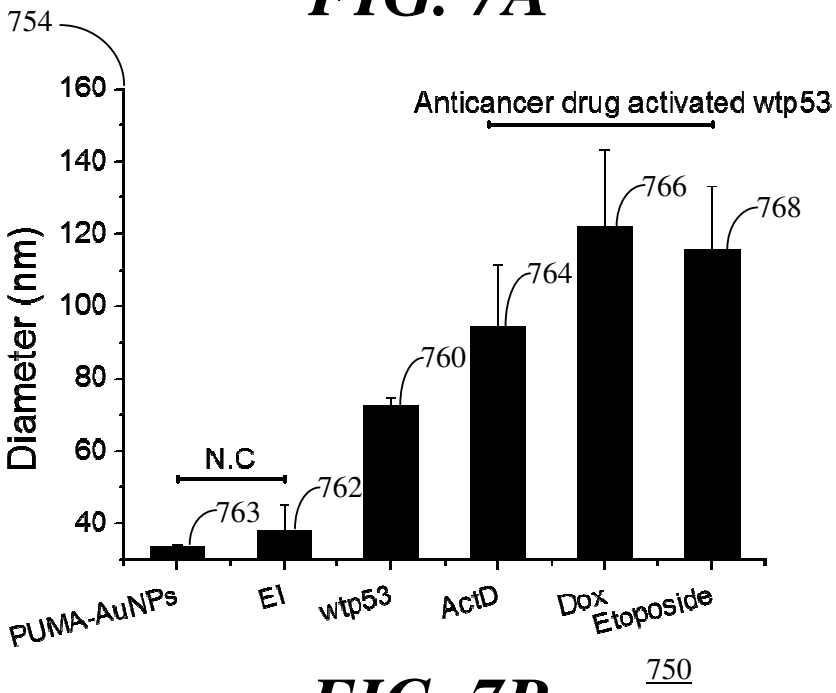

754
160
140
120
100
80
60
40
Diameter (nm)
Anticancer drug activated wtp53
N.C
763
762
760
764
766
768
PUMA-AuNPs
EI
wtp53
ActD
Dox
Etoposide
750

FIG. 7B

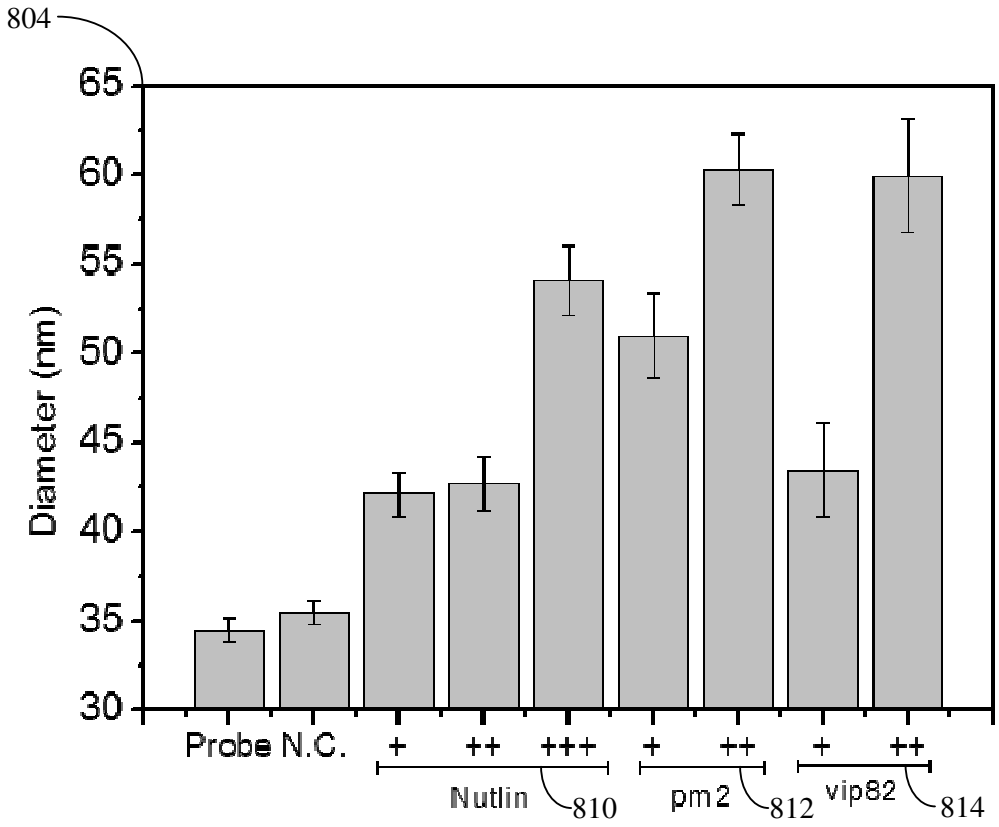

804
65
60
55
50
45
40
35
30
Diameter (nm)
Probe N.C.
+
++
+++
+
++
+
++
Nutlin
810
pm2
812
vip82
814

FIG. 8 800

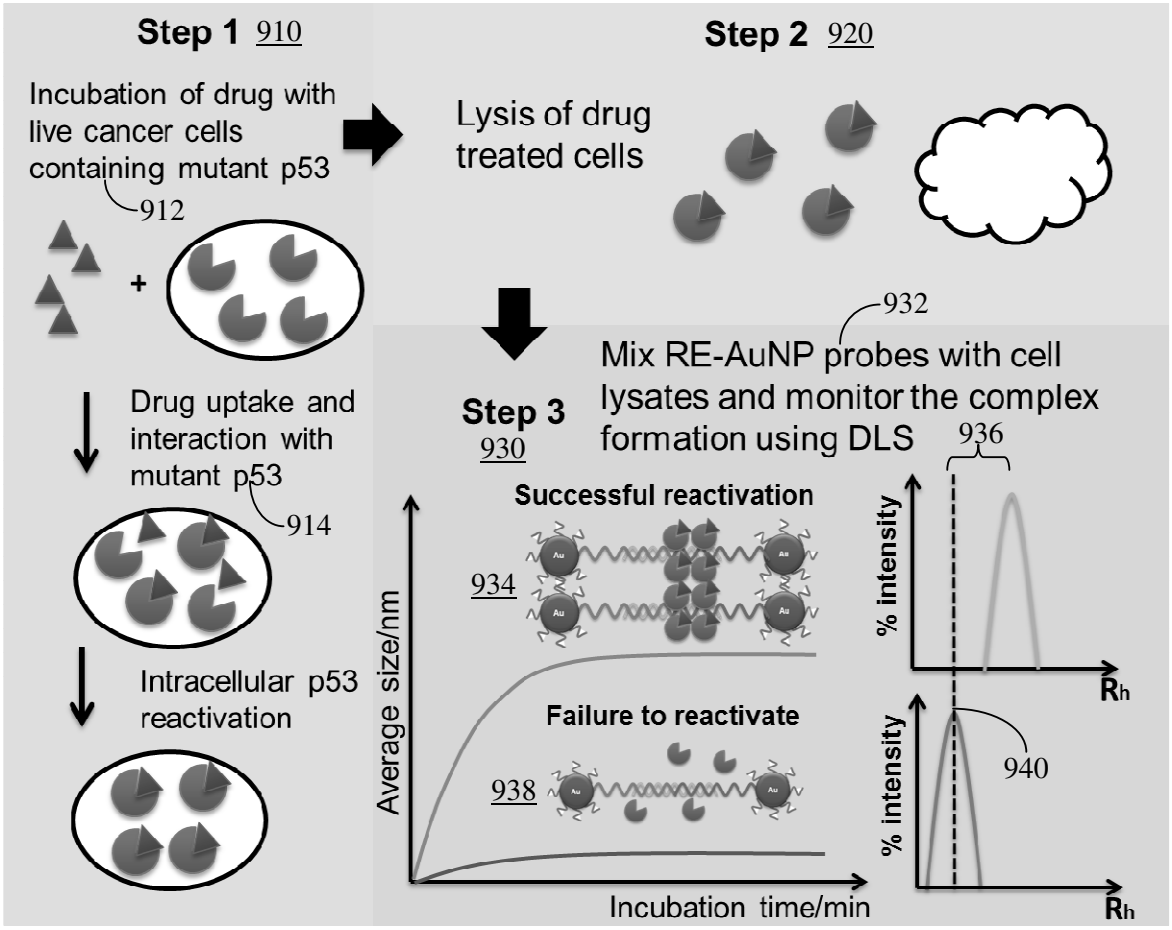

Step 1 910
Incubation of drug with live cancer cells containing mutant p53
912
+
Drug uptake and interaction with mutant p53
914
Intracellular p53 reactivation
Step 2 920
Lysis of drug treated cells
932
Mix RE-AuNP probes with cell lysates and monitor the complex formation using DLS
Step 3
930
936
Successful reactivation
934
Failure to reactivate
938
Average size/nm
Incubation time/min
% intensity
Rh
940
900

FIG. 9

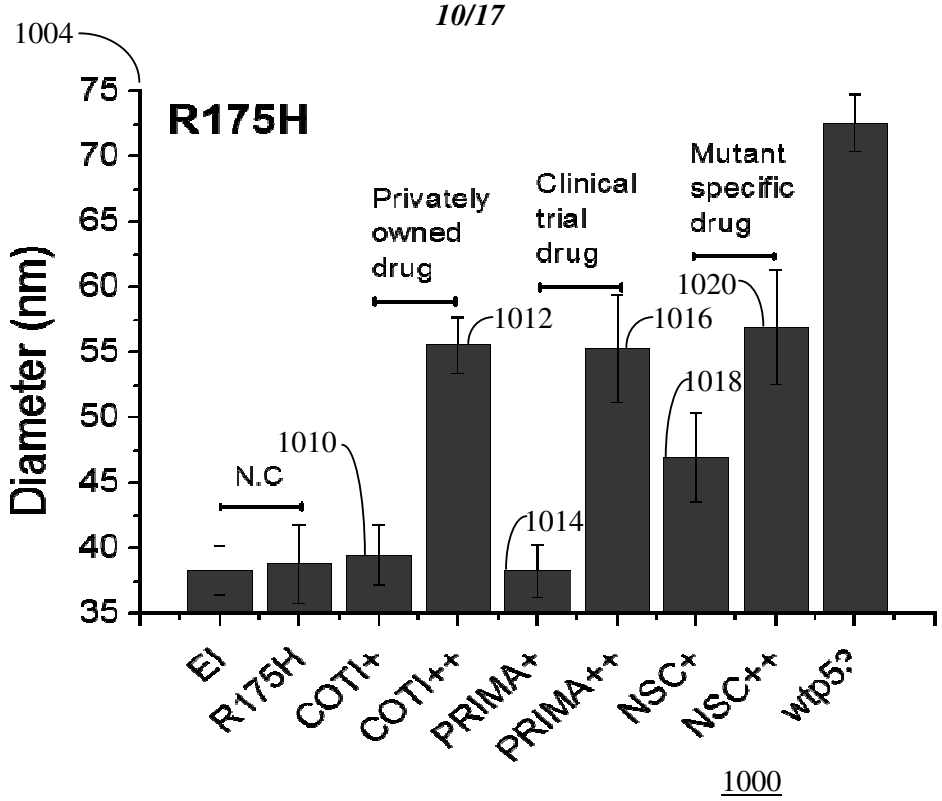


FIG. 10A

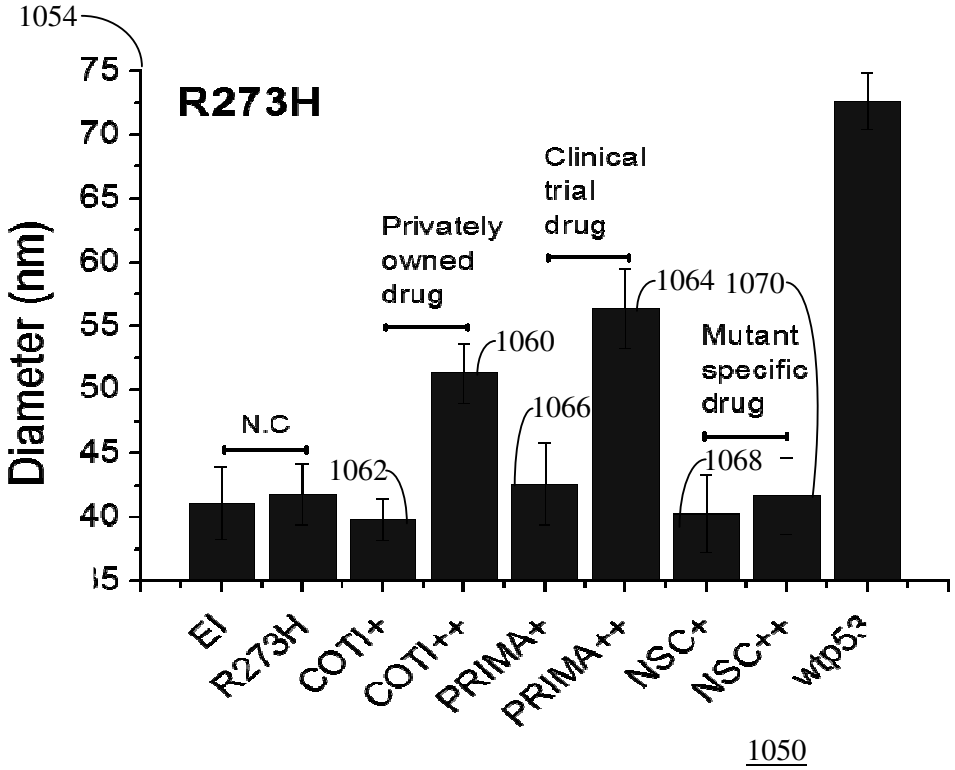


FIG. 10B

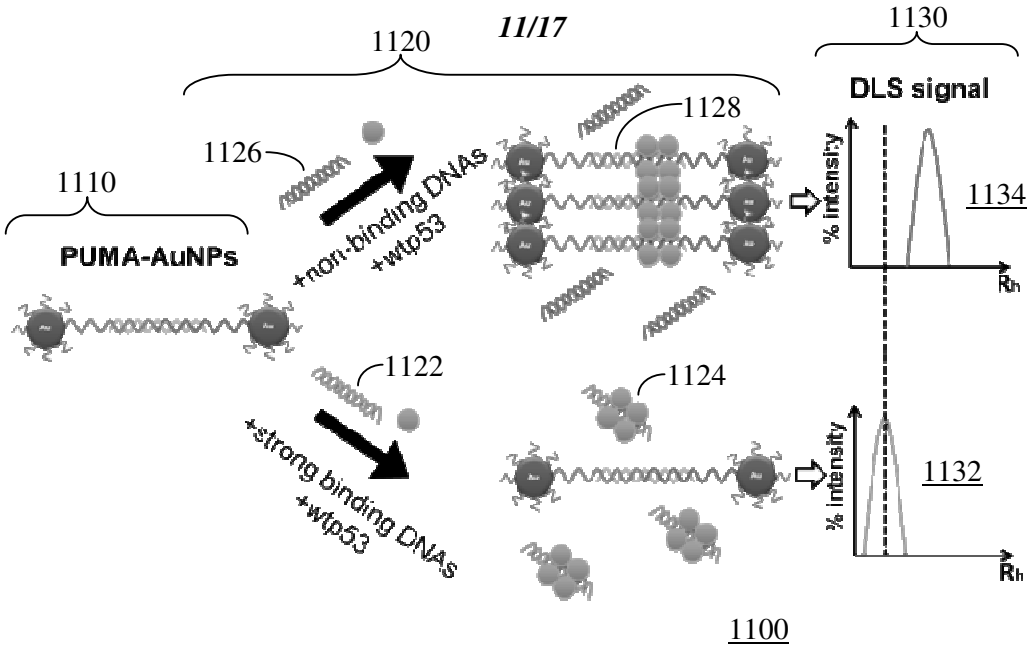


FIG. 11A

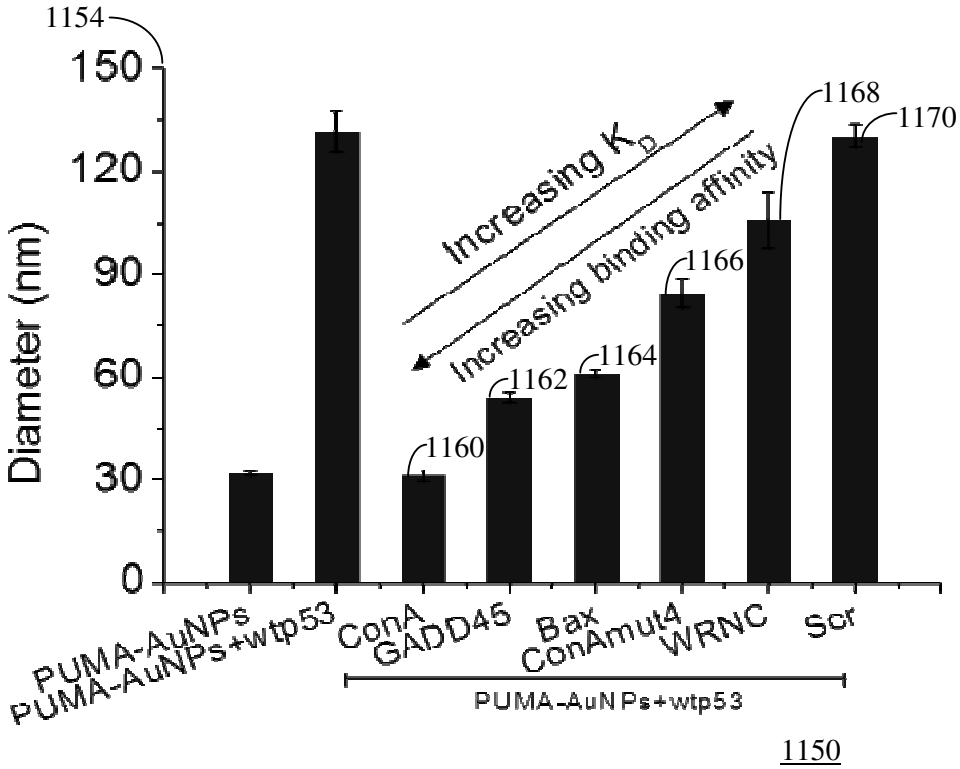


FIG. 11B

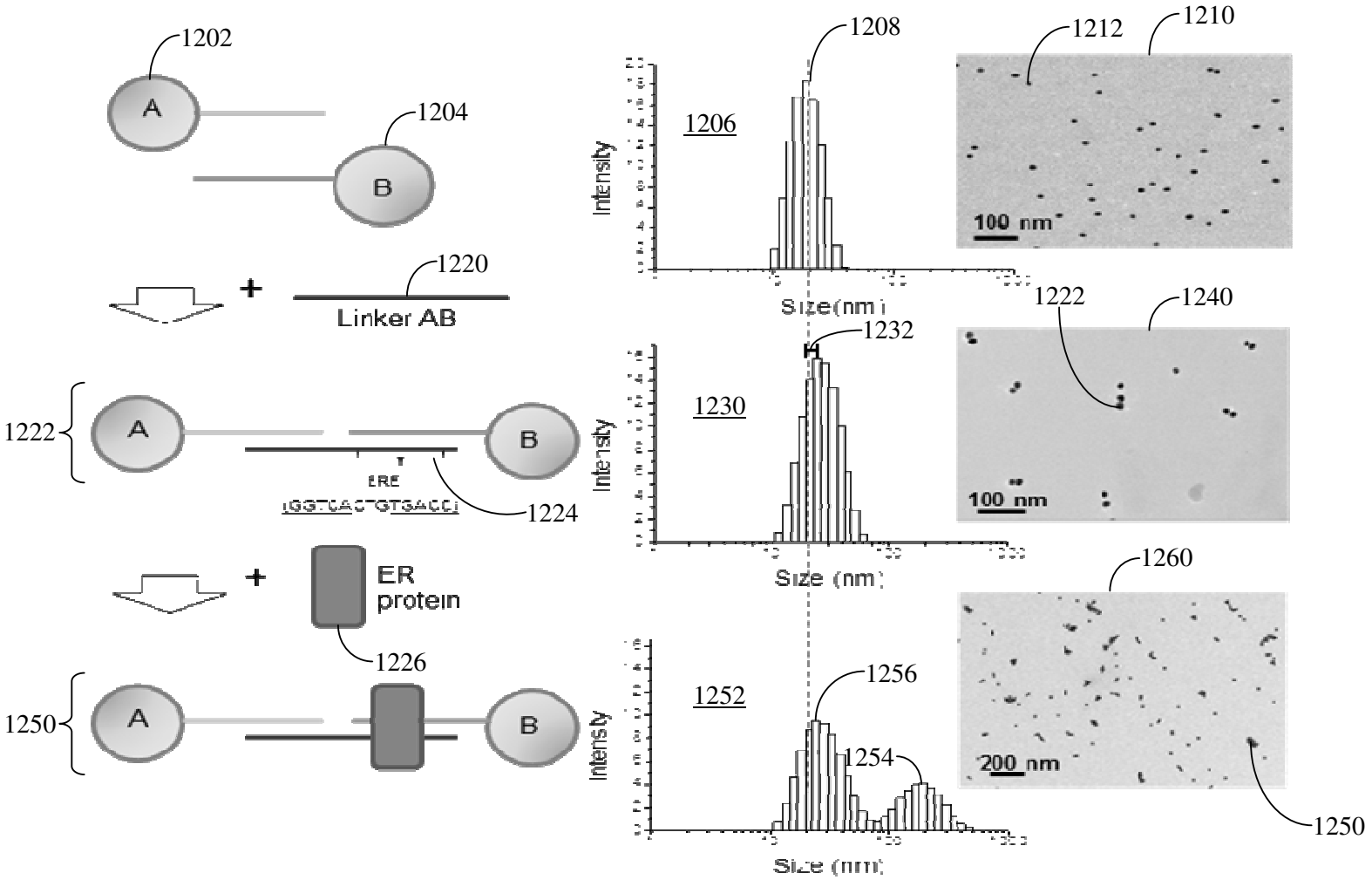

1202
A
1204
B
1220
Linker AB
1222
A
B
ERE
1224
ER
protein
1226
1250
A
B
1206
1208
Intensity
Size(nm)
1212
1210
100 nm
1222
1240
1230
1232
Intensity
Size (nm)
100 nm
1260
1252
1256
1254
Intensity
Size (nm)
200 nm
1250

FIG. 12

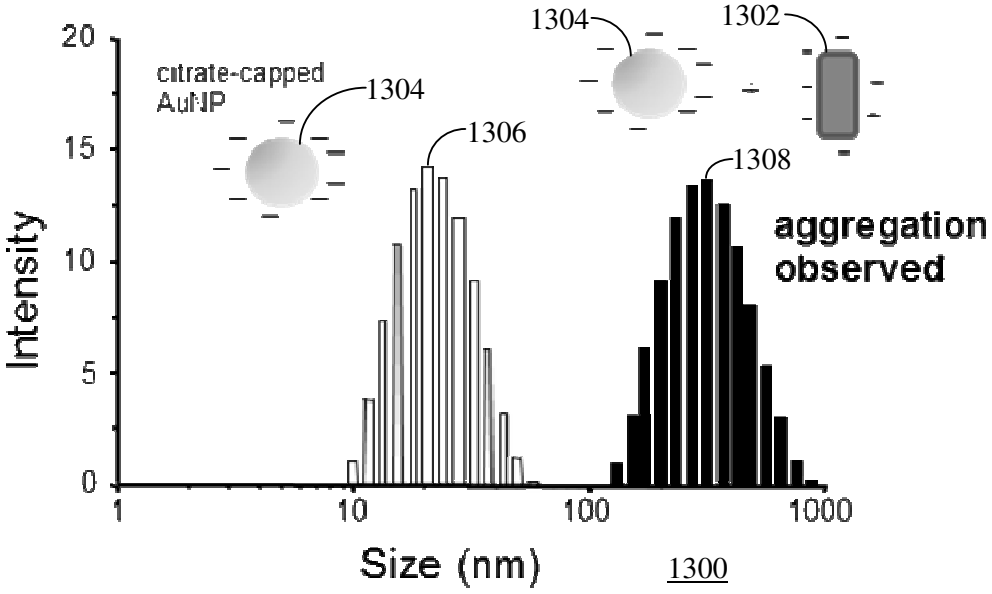


FIG. 13A

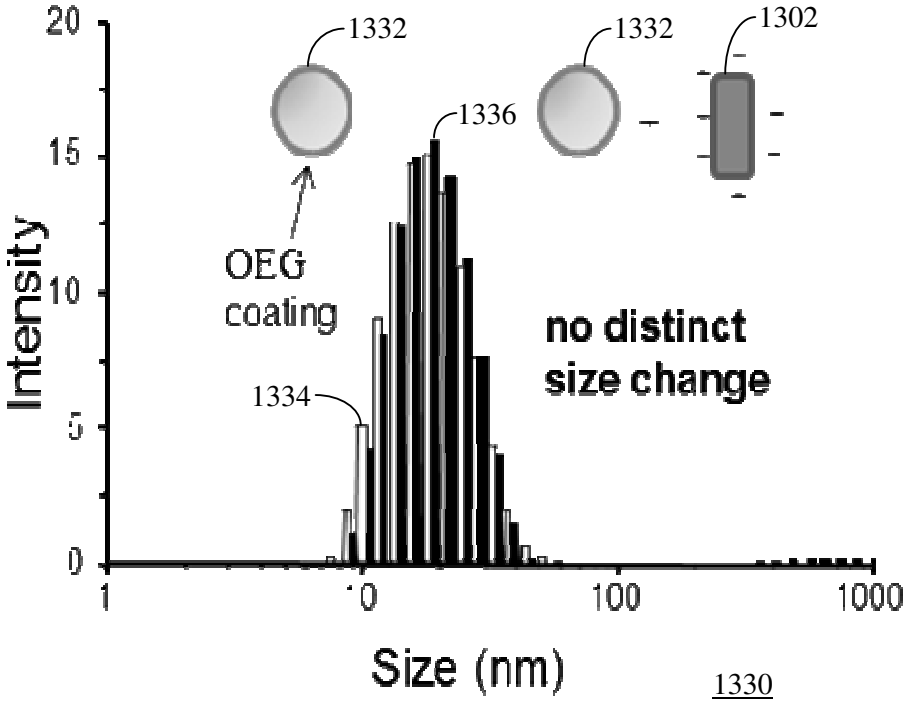


FIG. 13B

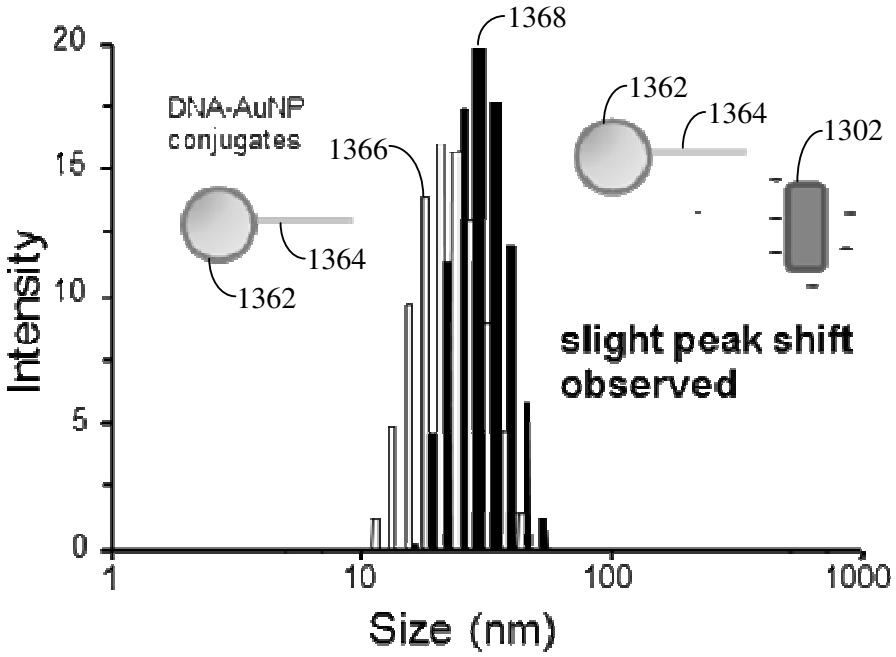

1368
20
15
10
5
0
Intensity
DNA-AuNP
conjugates
1366
1362
1364
1362
1364
1302
slight peak shift
observed
1
10
100
1000
Size (nm)
1360

FIG. 13C

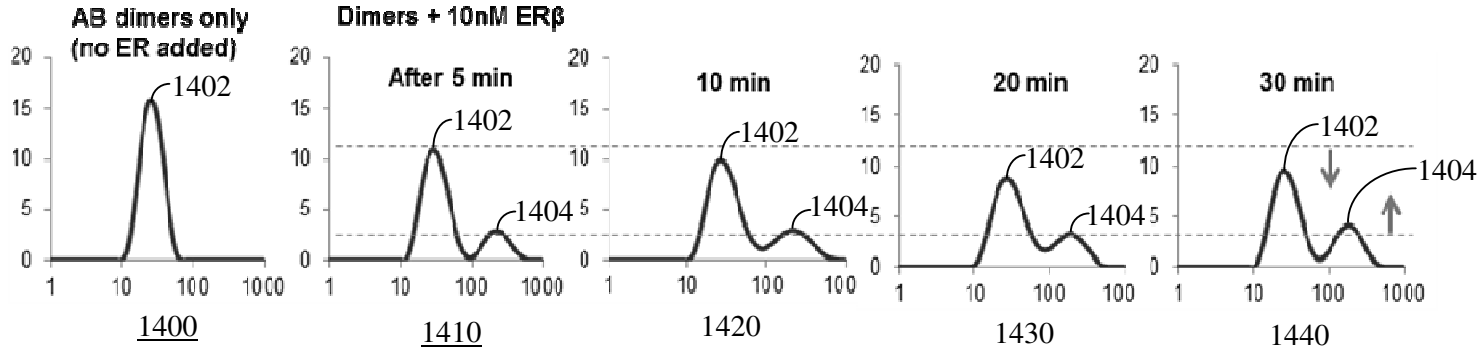


FIG. 14A

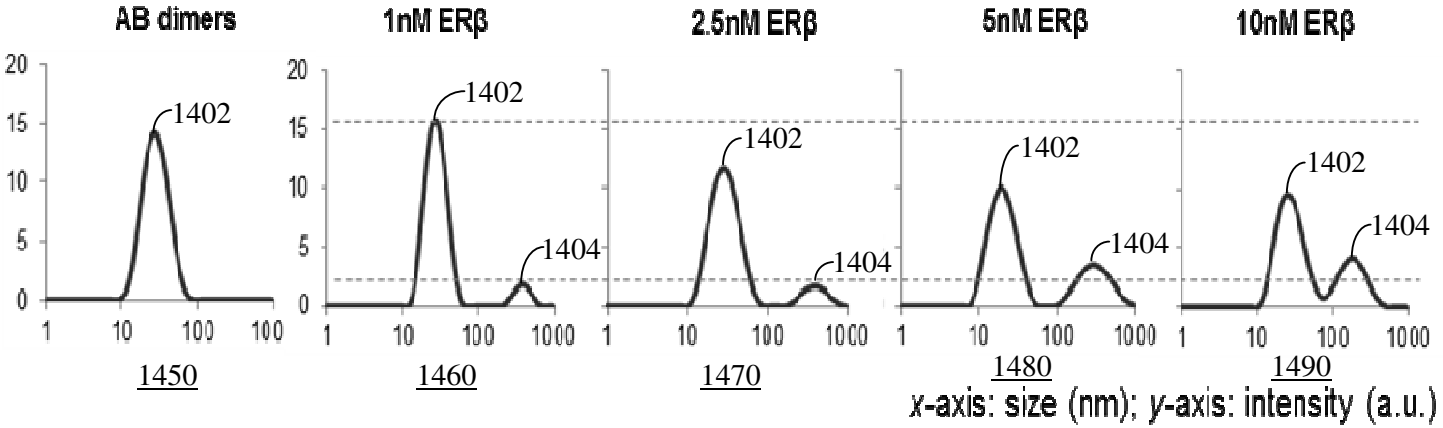


FIG. 14B

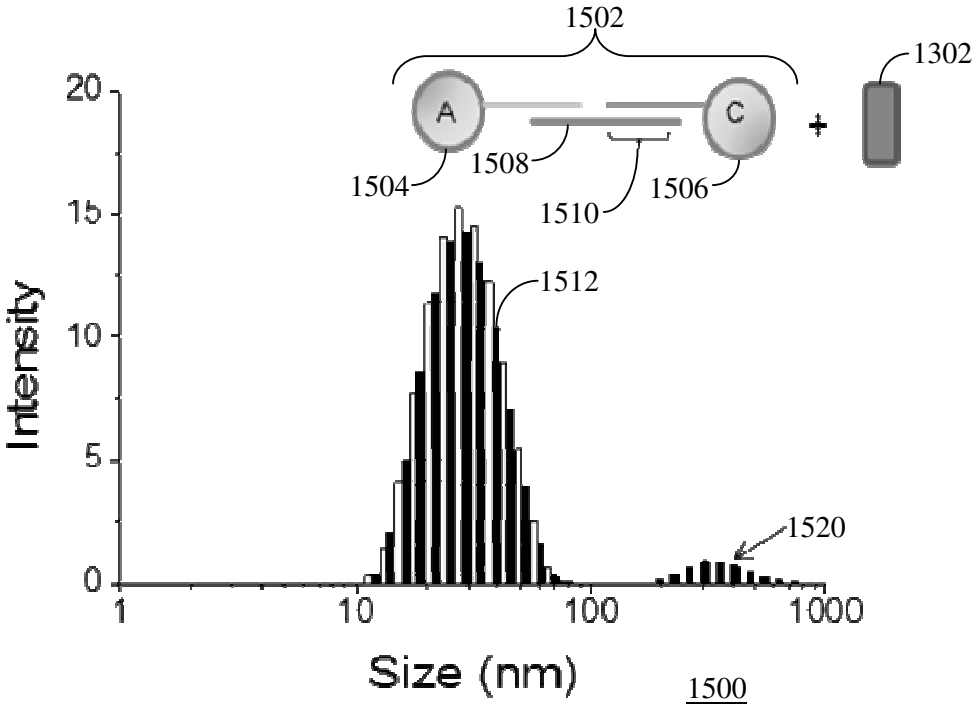


FIG. 15A

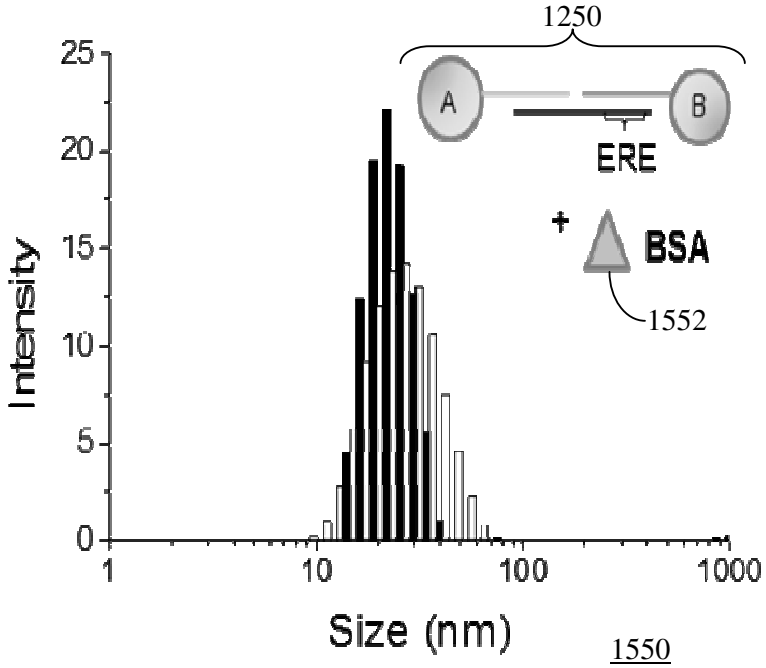


FIG. 15B

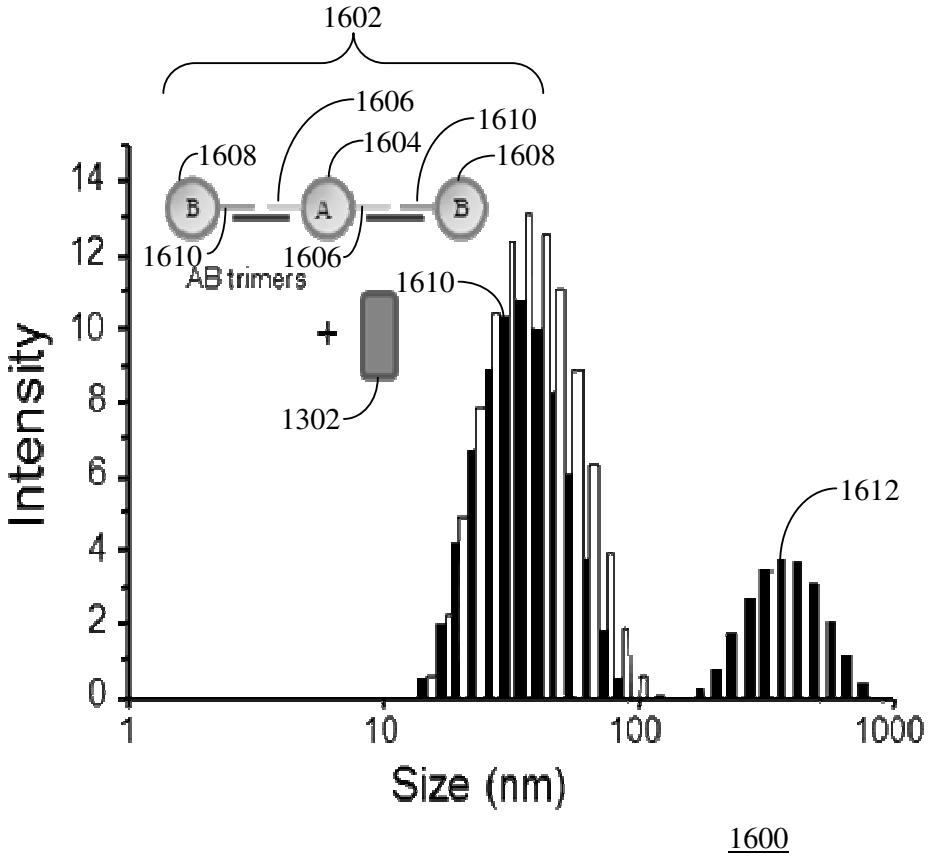

1602
1606
1610
1608
1604
1608
B
A
B
1610
1606
AB trimers
1610
+
1302
1612
Intensity
0
2
4
6
8
10
12
14
1
10
100
1000
Size (nm)
1600

FIG. 16