Fig. 1

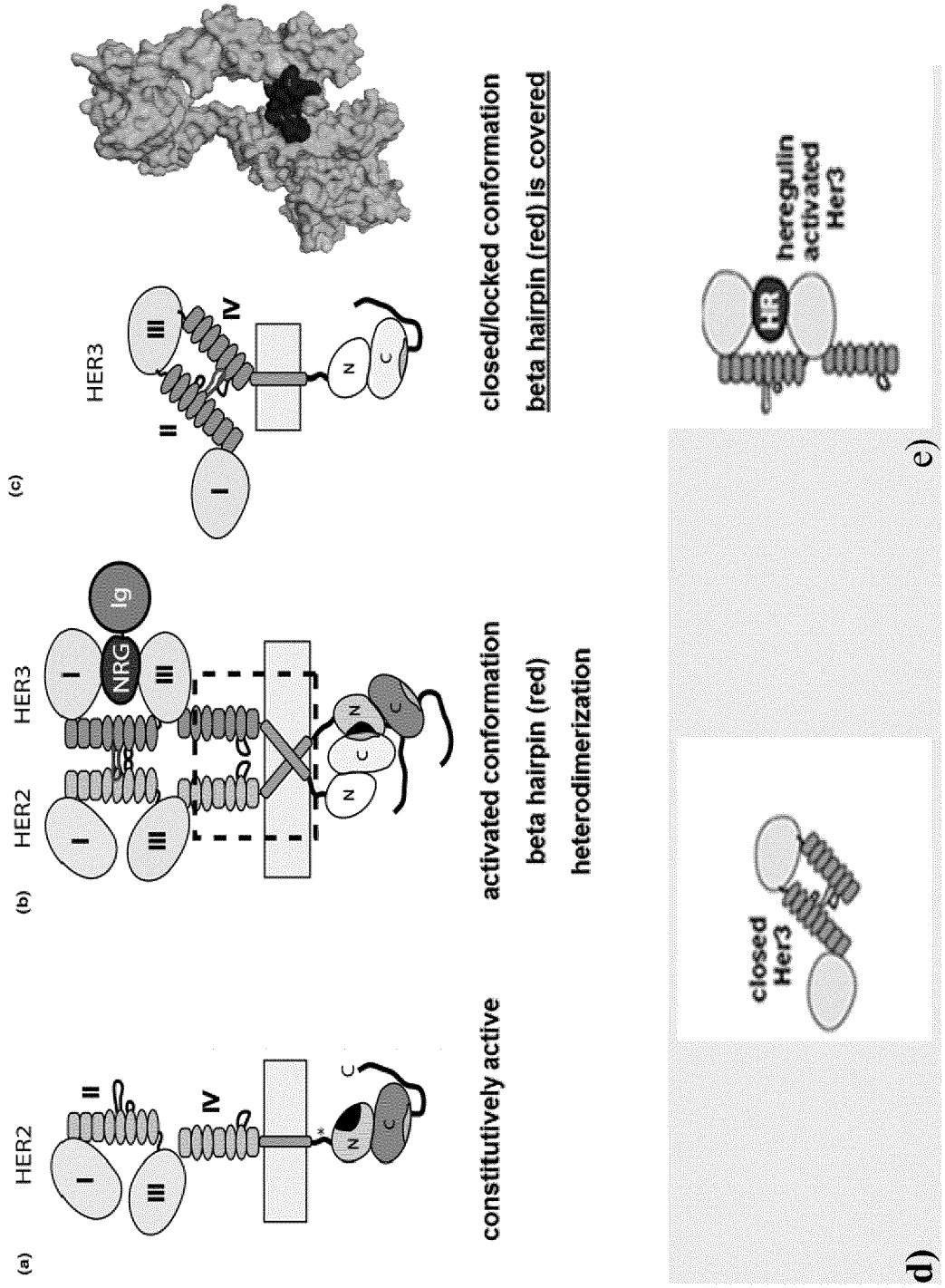

(a)
HER2
I
II
III
IV
constitutively active
(b)
HER2
HER3
I
III
NRG
Ig
activated conformation
beta hairpin (red)
heterodimerization
(c)
HER3
I
II
III
IV
N
C
closed/locked conformation
beta hairpin (red) is covered
d)
closed Her3
e)
HR
heregulin activated Her3

Fig. 2

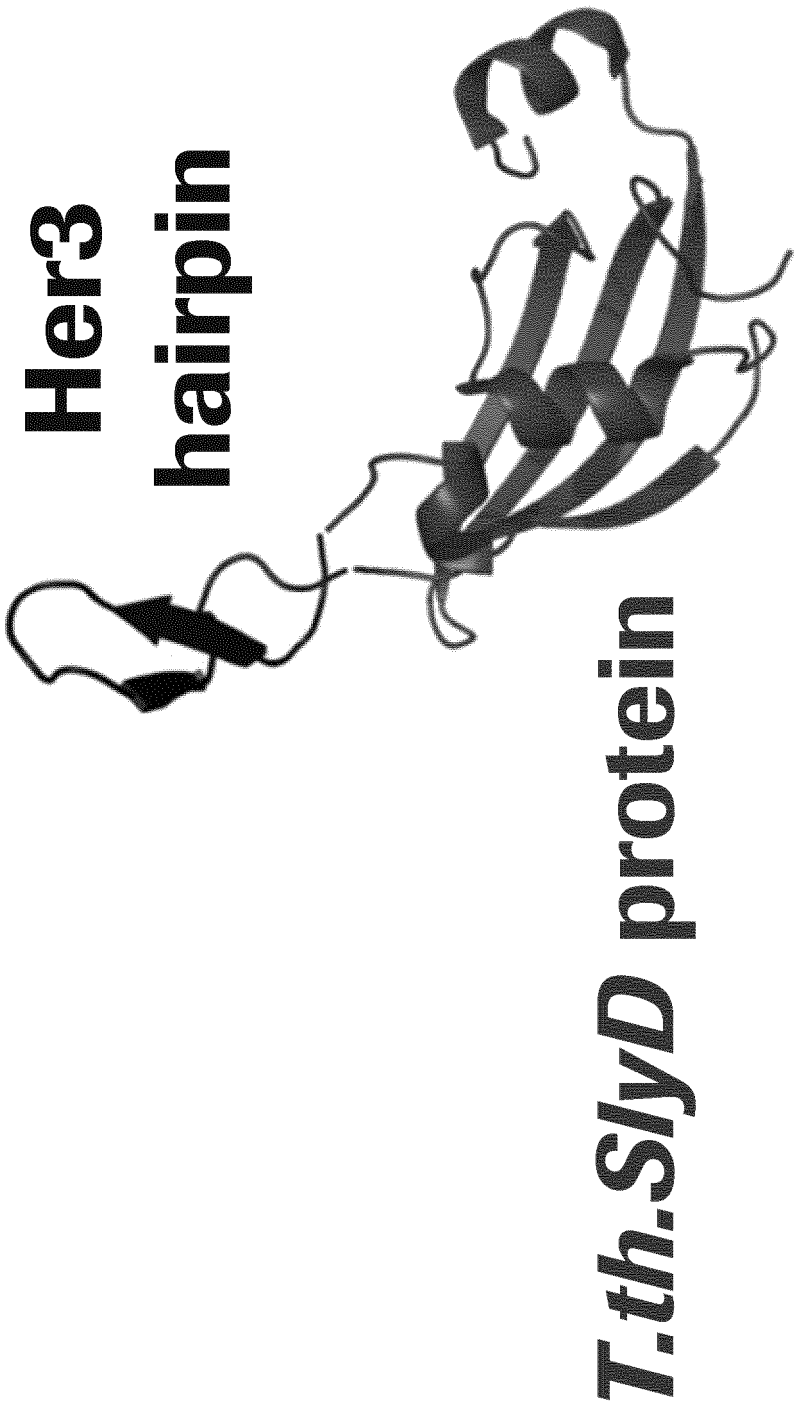


Fig. 3

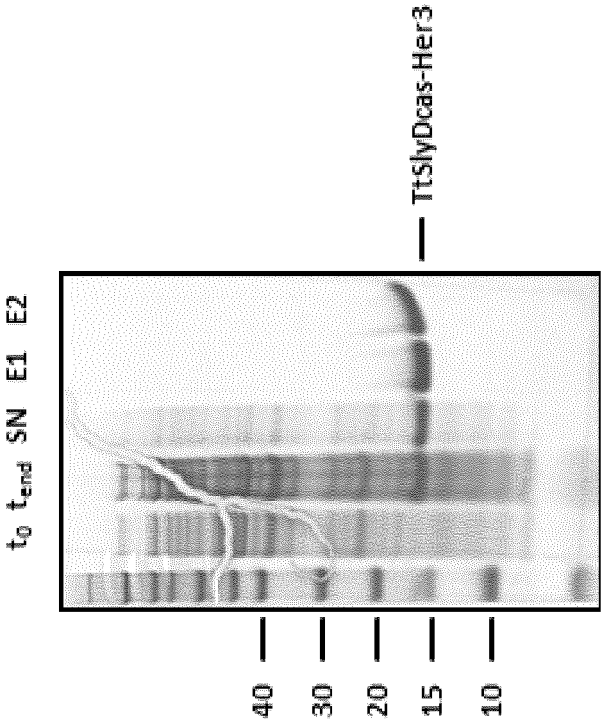


Fig. 4

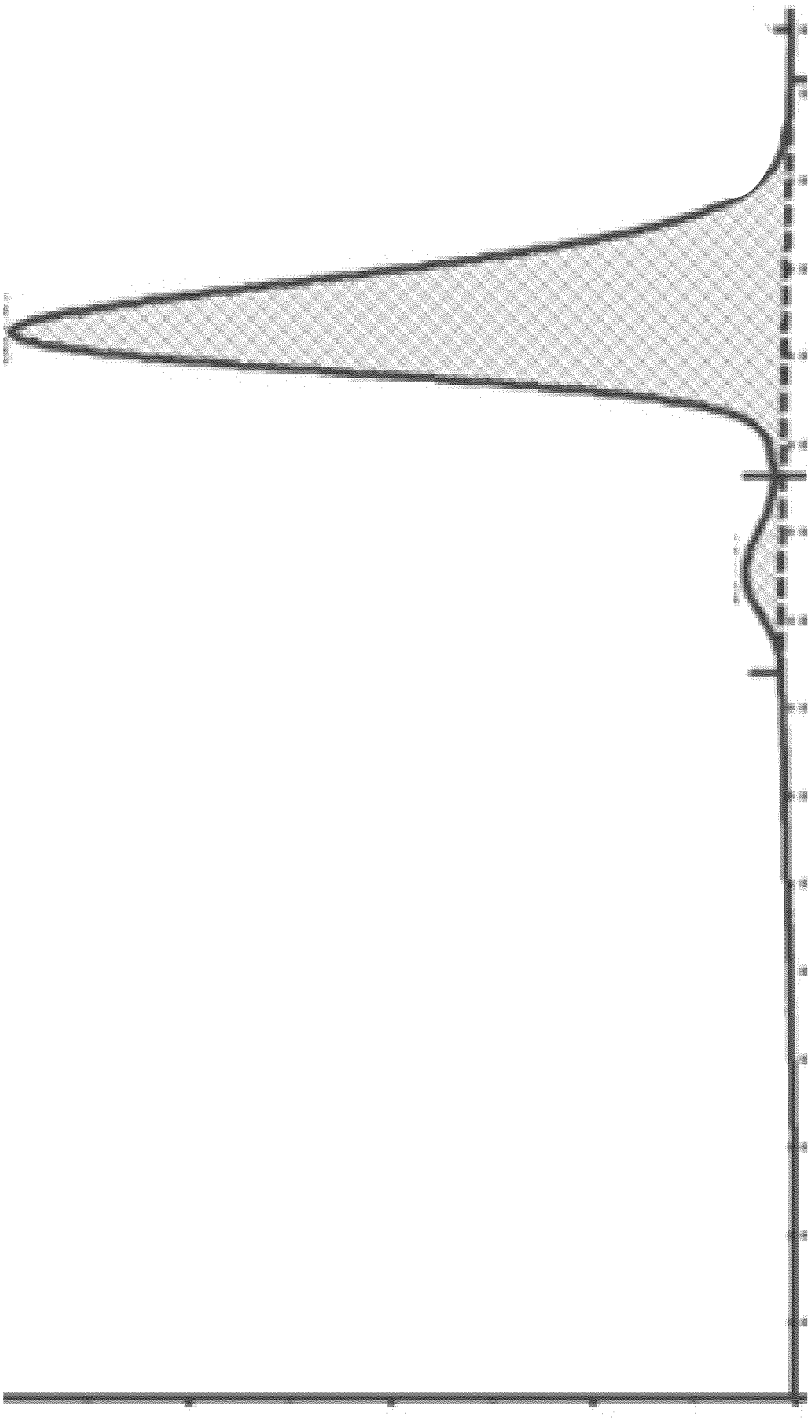


Fig. 5A



Fig. 5B

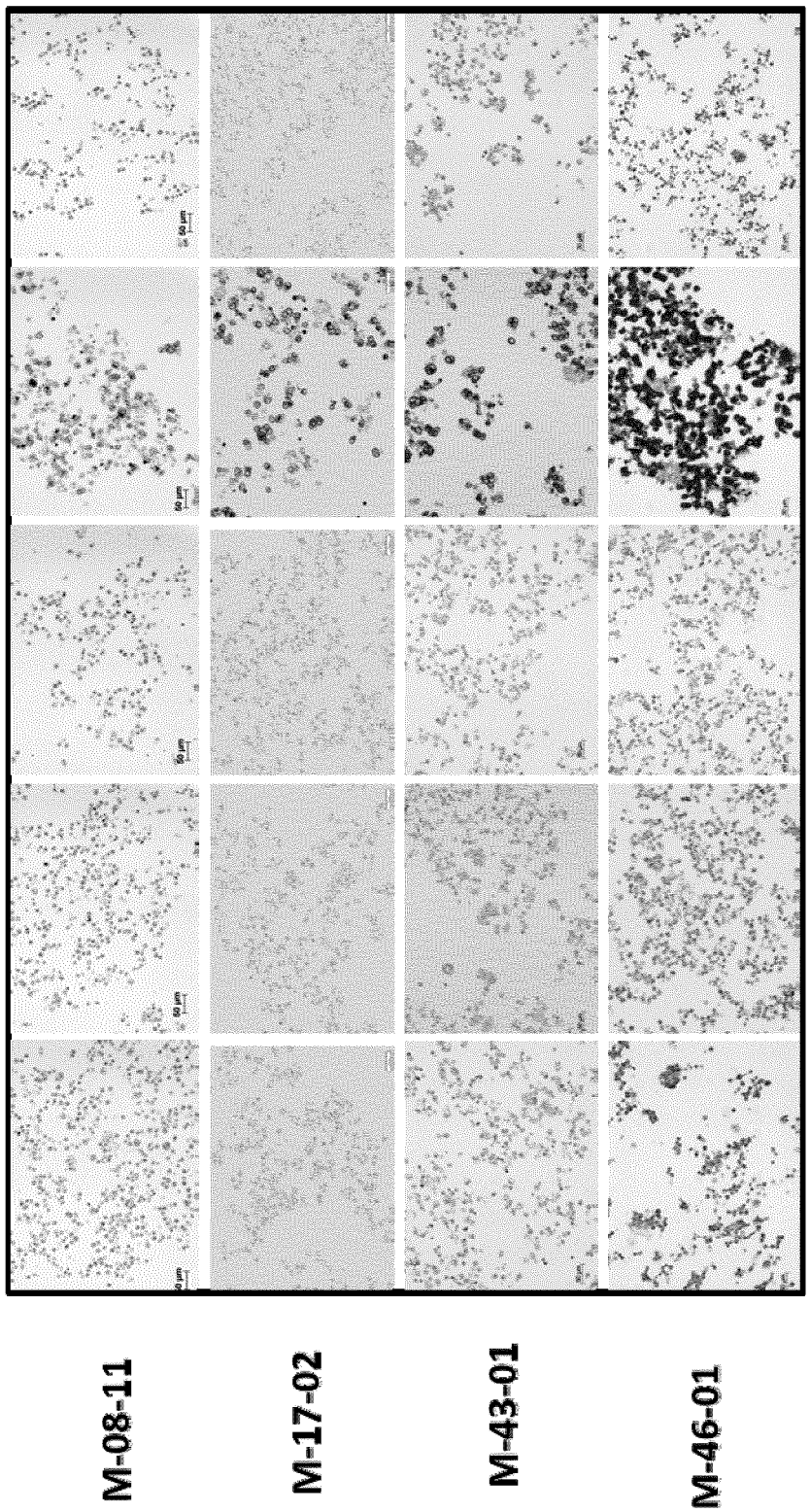


Fig. 6

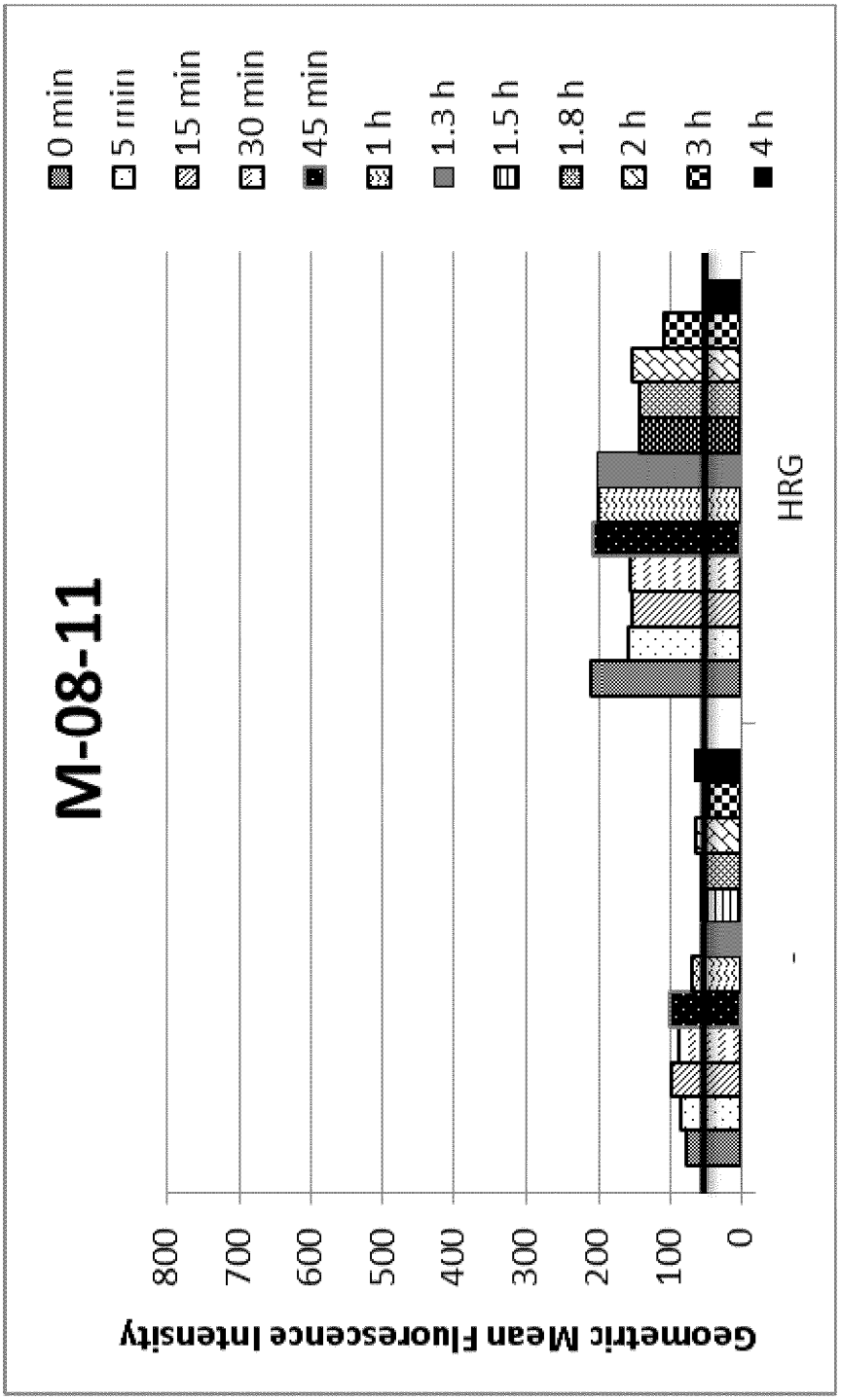

M-08-11
0 min
5 min
15 min
30 min
45 min
1 h
1.3 h
1.5 h
1.8 h
2 h
3 h
4 h
Geometric Mean Fluorescence Intensity
800
700
600
500
400
300
200
100
0
HRG
-

Fig. 7a

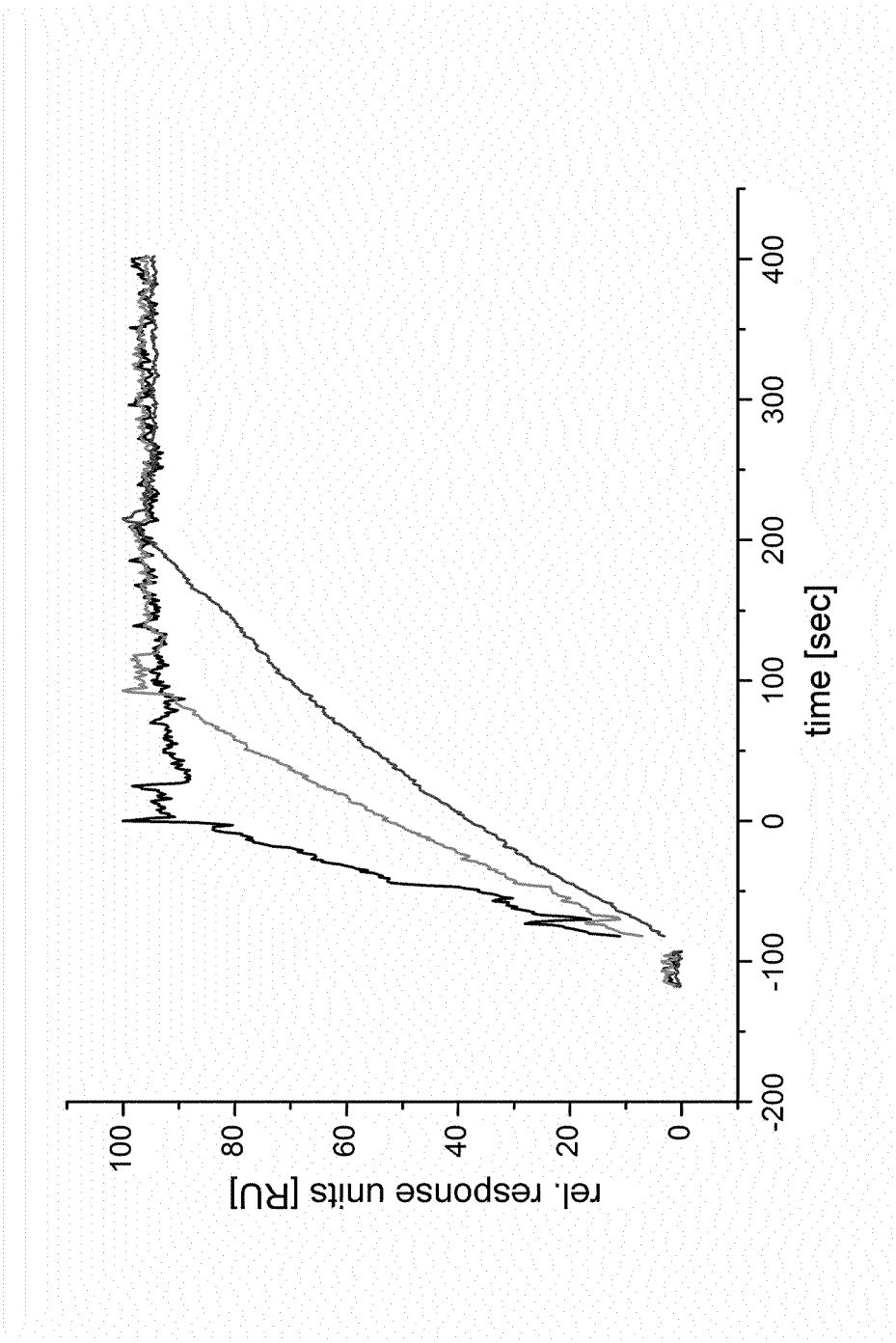

rel. response units [RU]
0
20
40
60
80
100
-200
-100
0
100
200
300
400
time [sec]

Fig. 7b

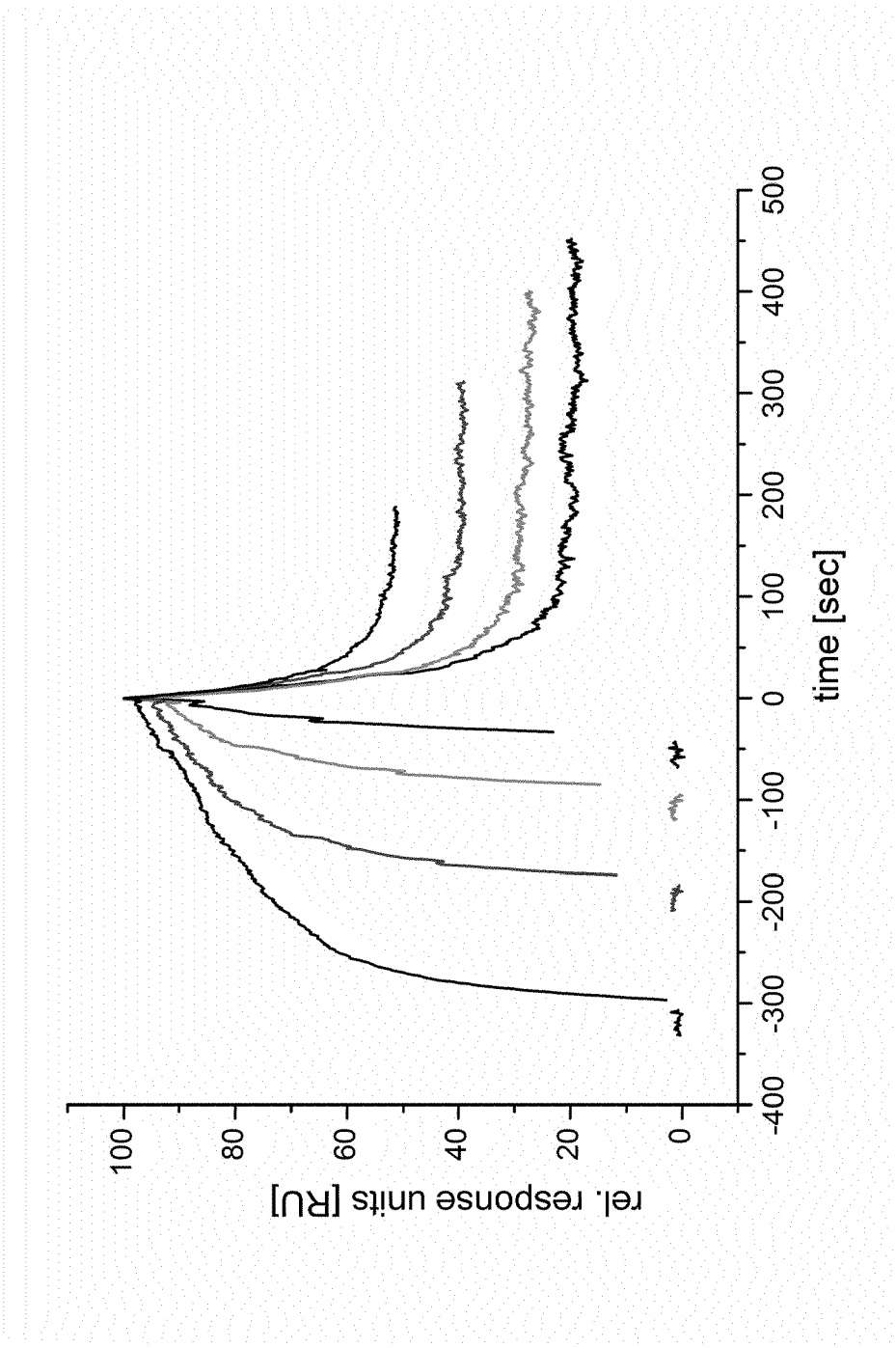

rel. response units [RU]
0
20
40
60
80
100
-400
-300
-200
-100
0
100
200
300
400
500
time [sec]

Fig. 7c

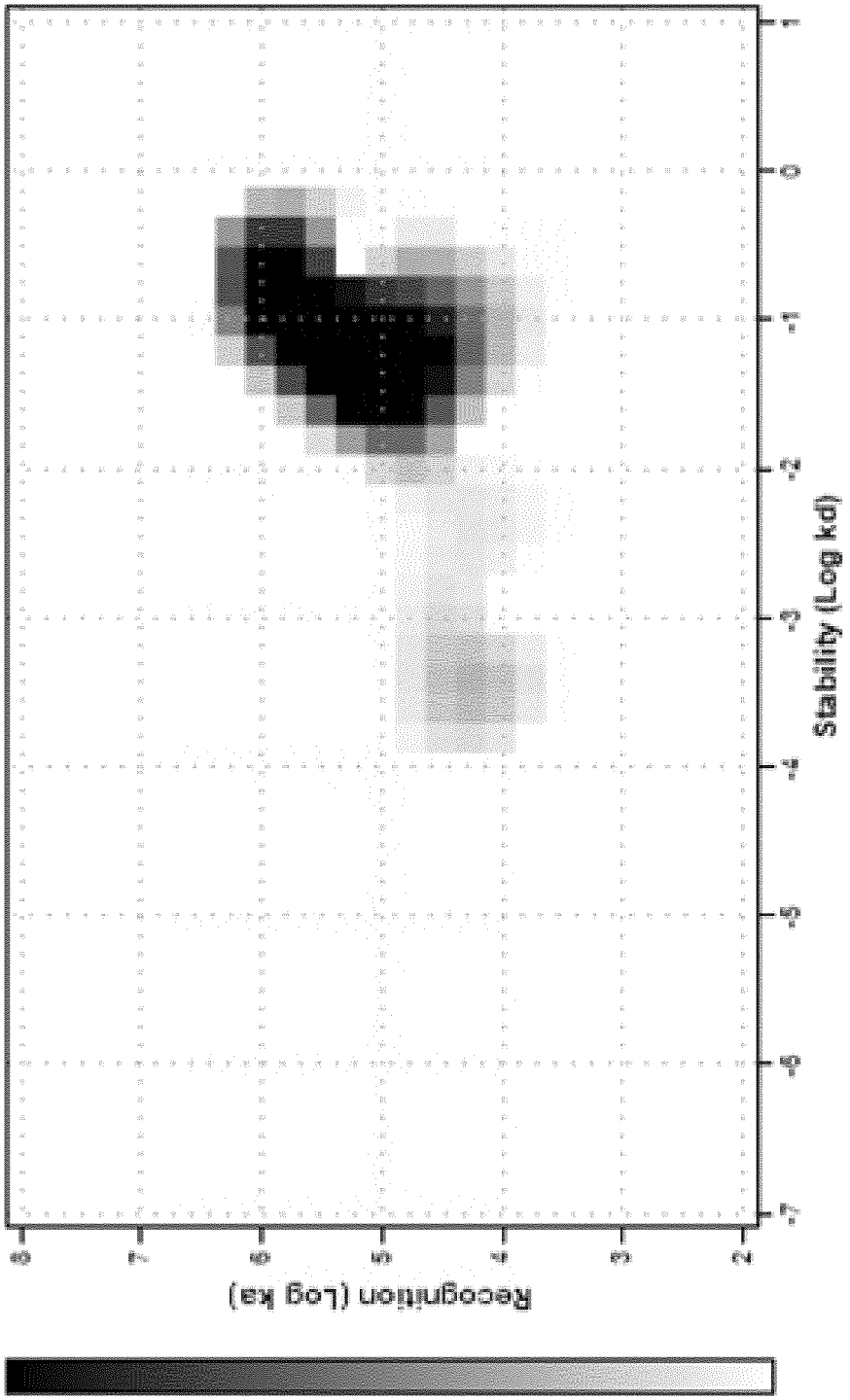


Fig. 7d

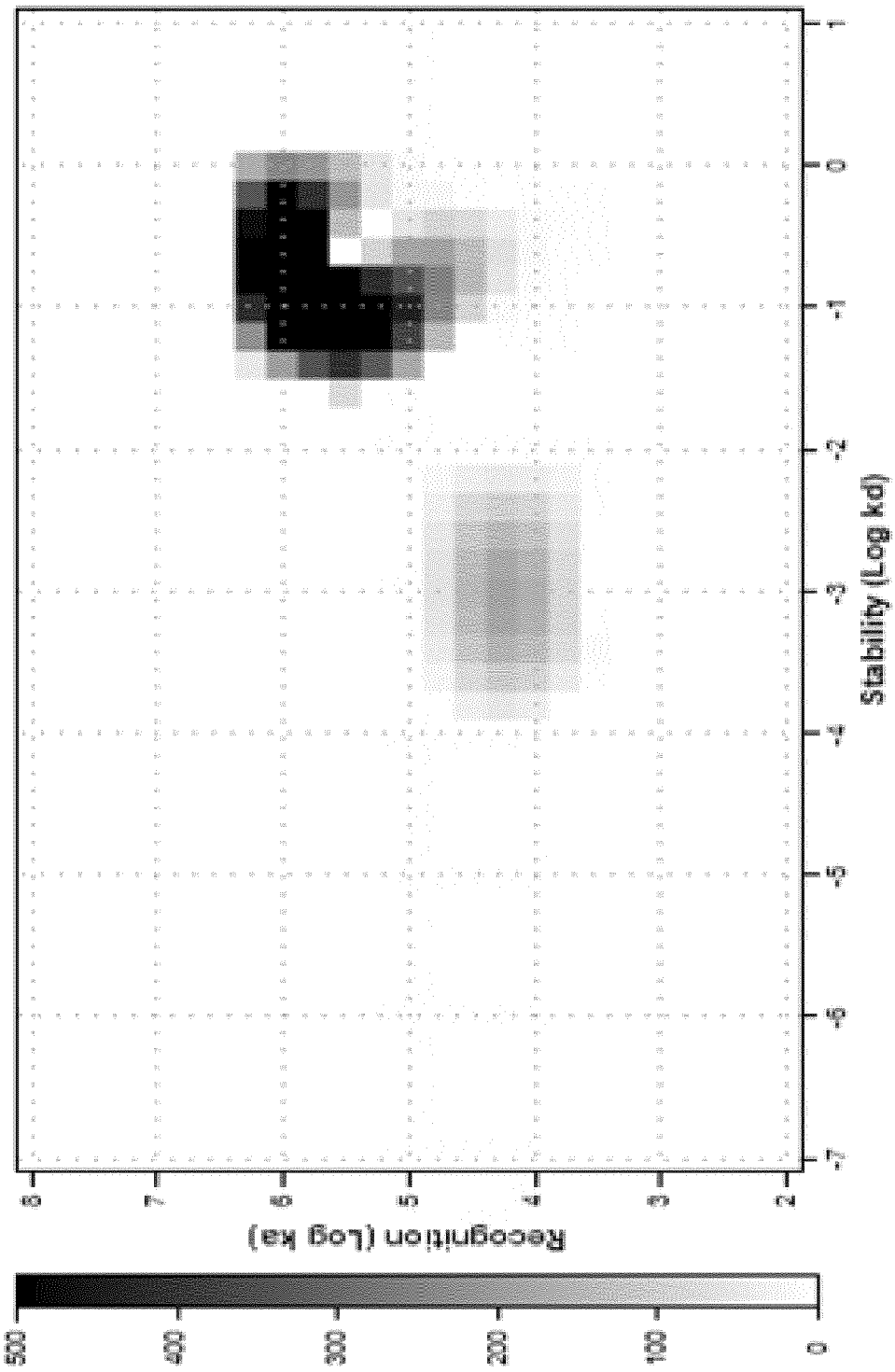

Stability (Log kd)
0
-1
-2
-3
-4
-5
-6
-7
Recognition (Log ka)
3
4
5
6
7
500
400
300
200
100
0

Fig. 7e

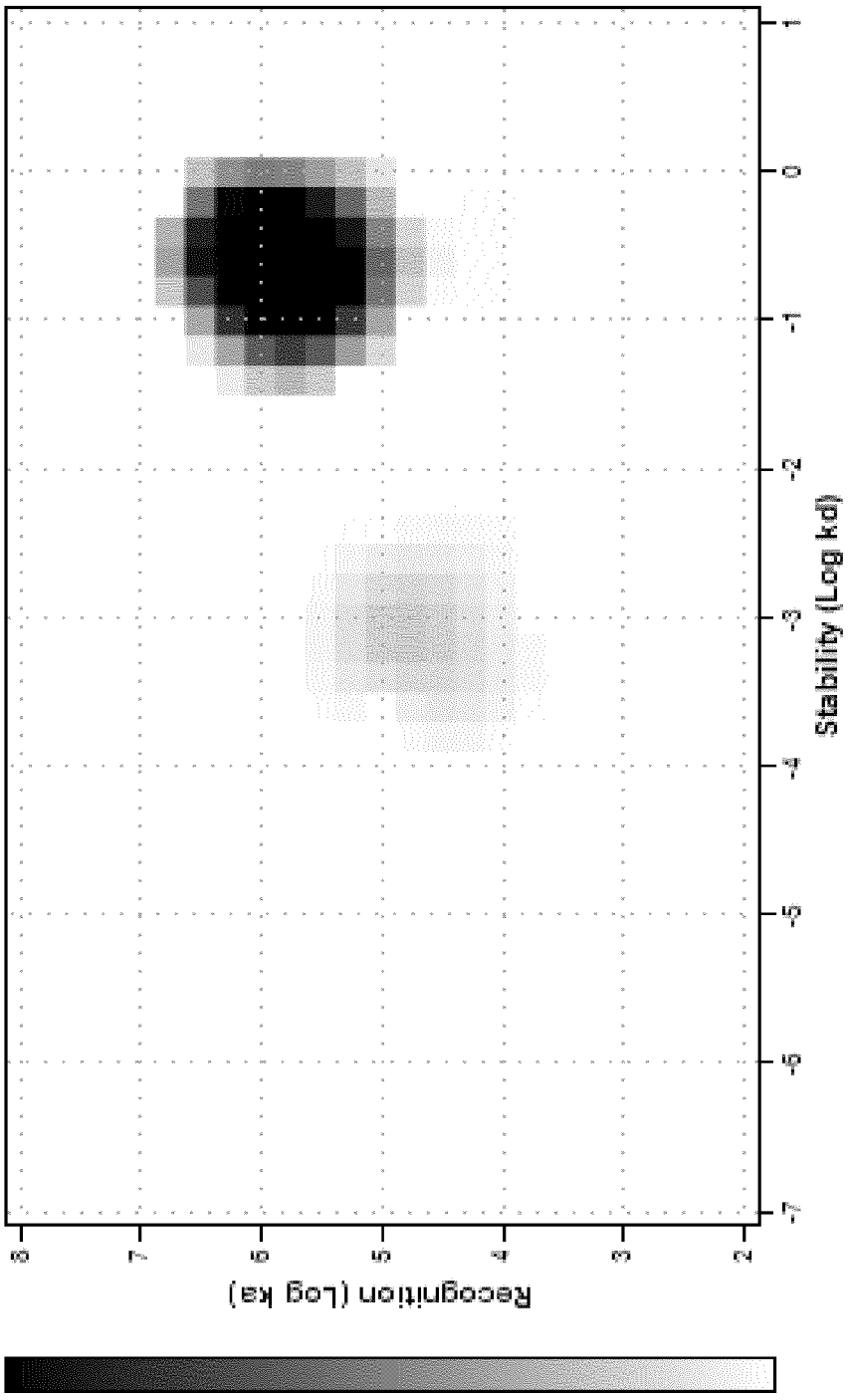


Fig. 8

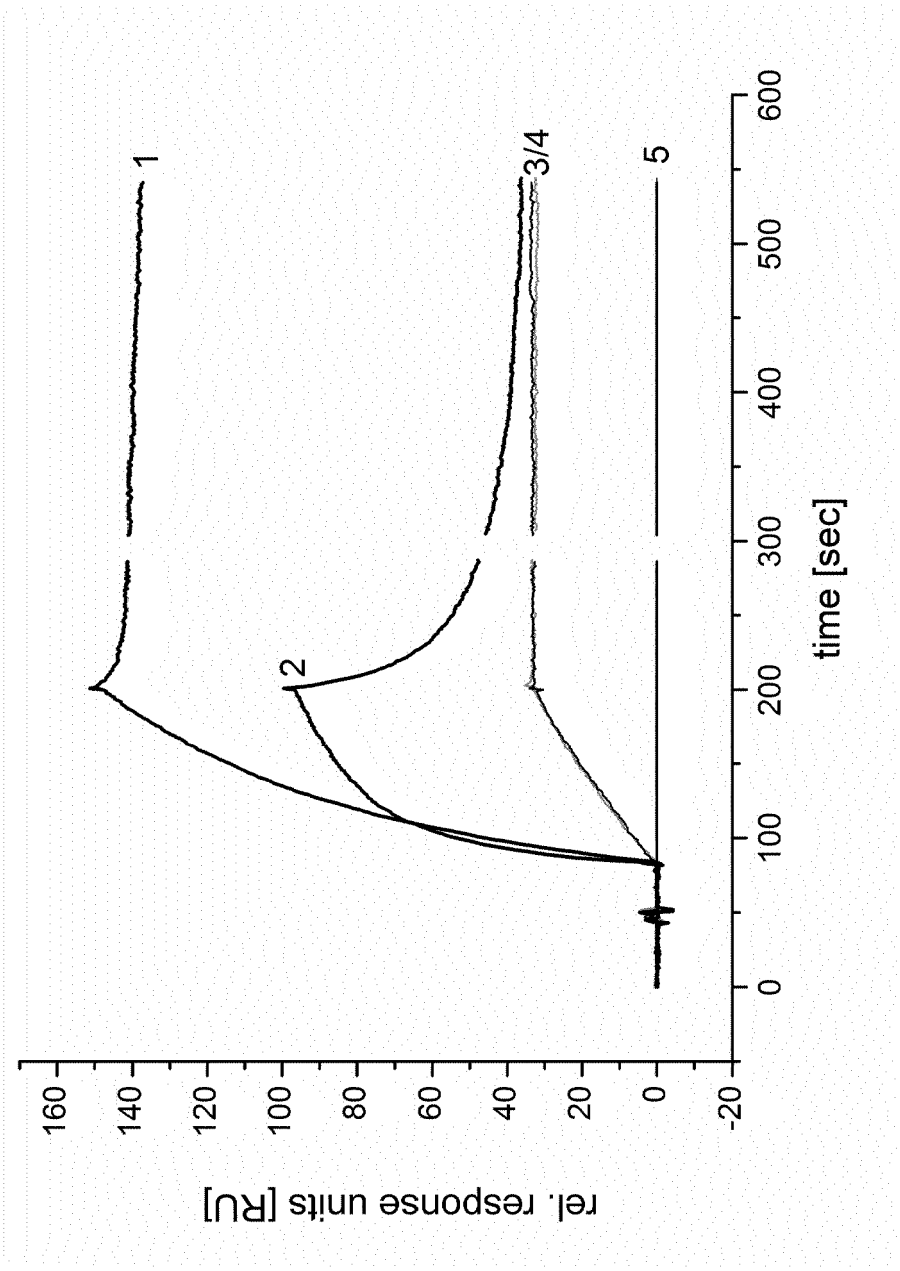

rel. response units [RU]
time [sec]
1
2
3/4
5
160
140
120
100
80
60
40
20
0
-20
0
100
200
300
400
500
600

Fig. 9

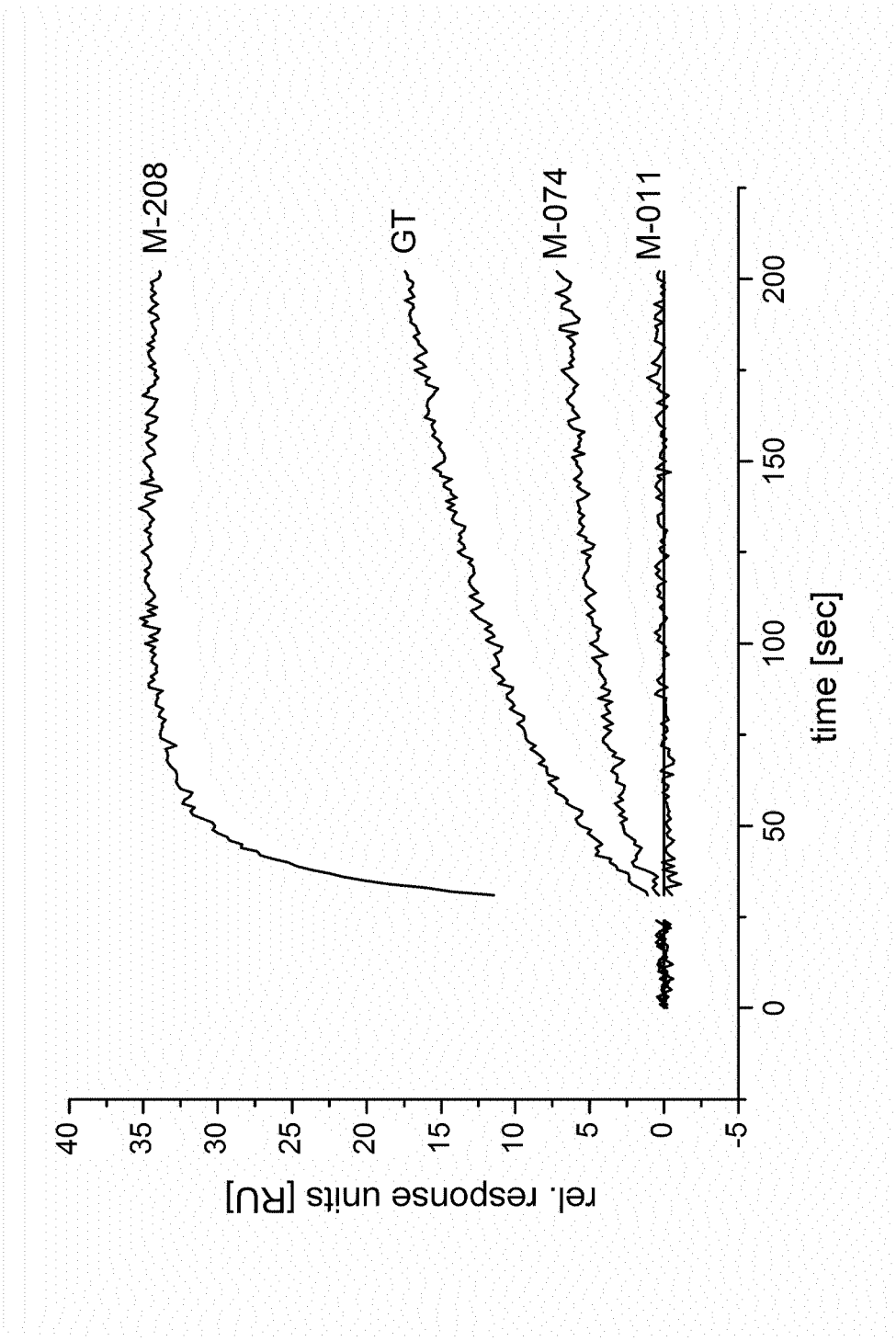

M-208
GT
M-074
M-011
rel. response units [RU]
time [sec]
40
35
30
25
20
15
10
5
0
-5
0
50
100
150
200

Fig. 10

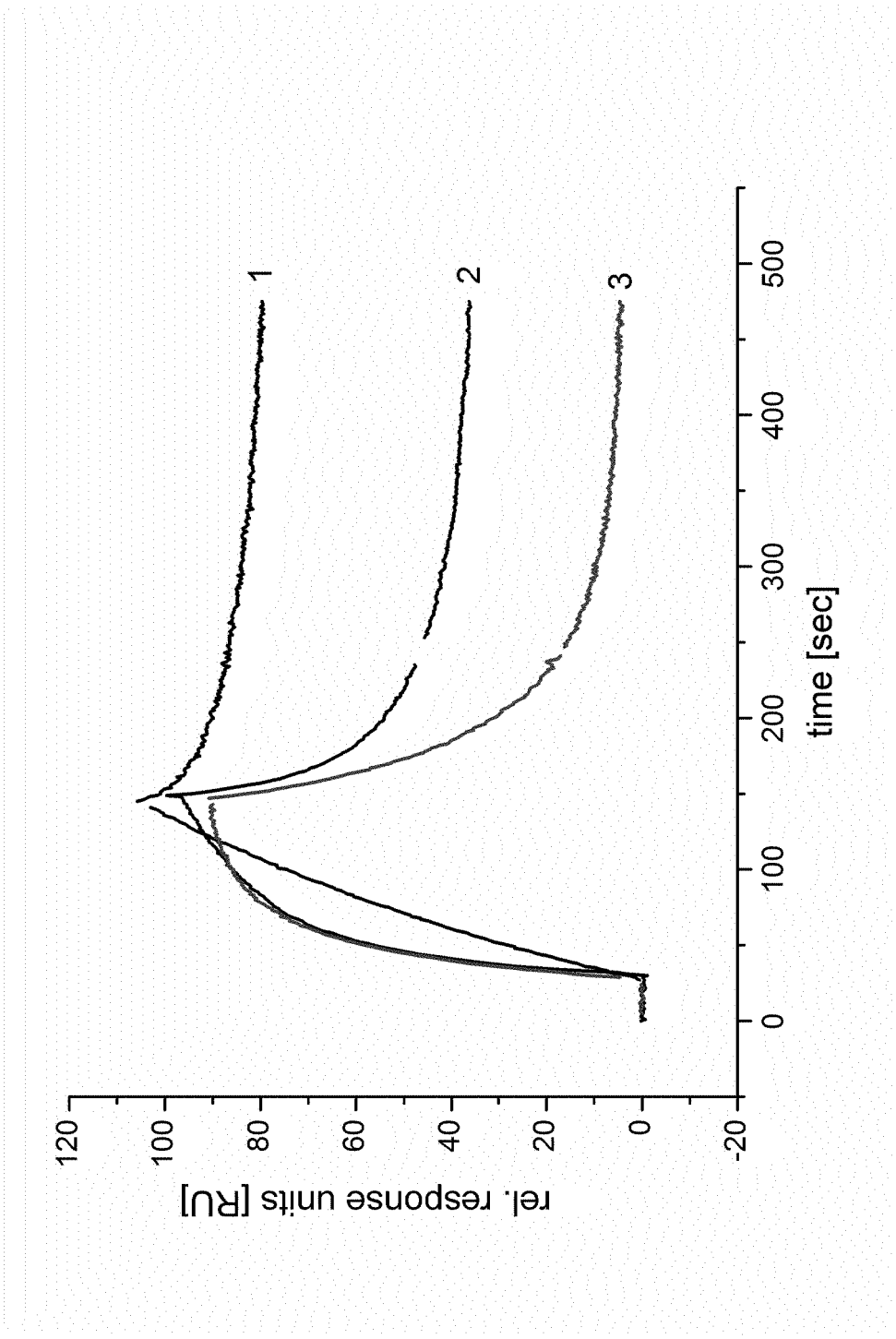

rel. response units [RU]
120
100
80
60
40
20
0
-20
0
100
200
300
400
500
time [sec]
1
2
3

Fig. 11

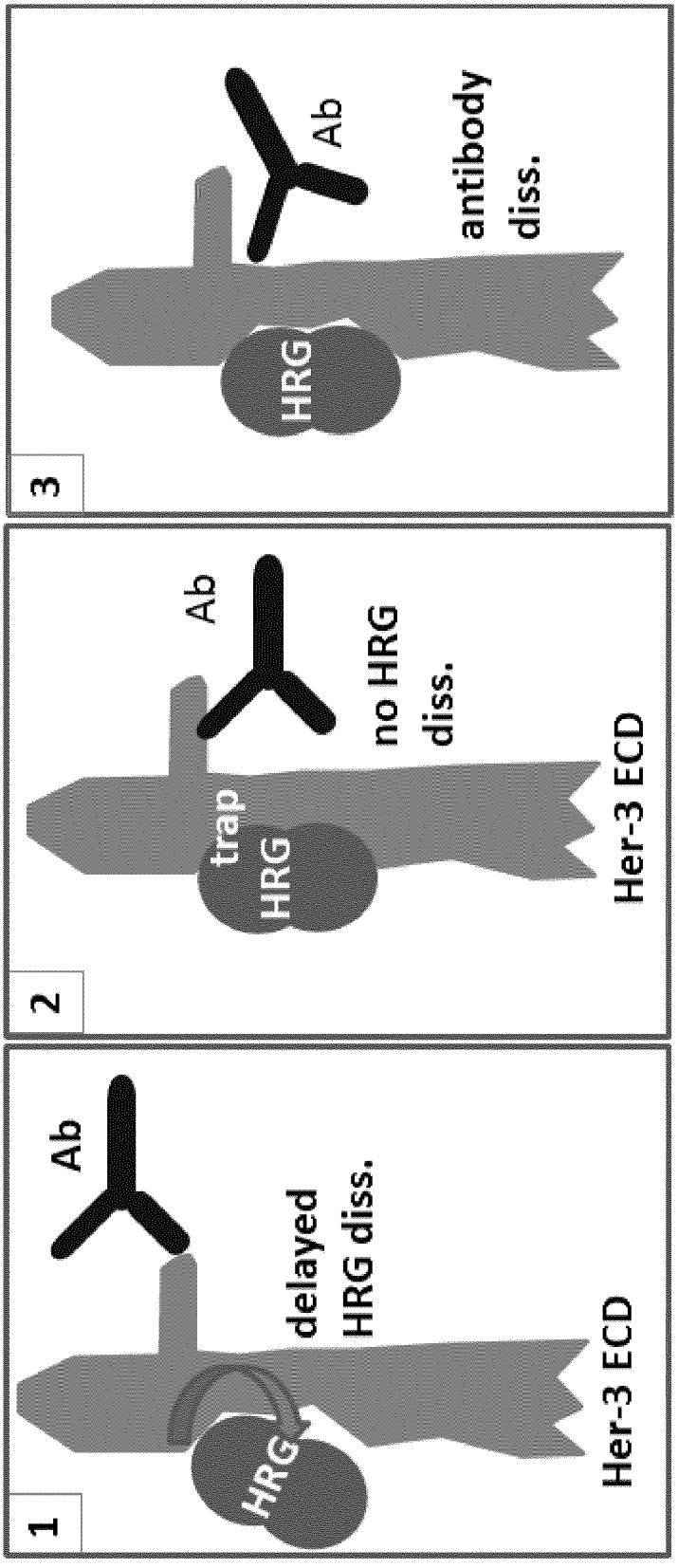

1
Ab
delayed
HRG diss.
HRG
Her-3 ECD
2
Ab
trap
HRG
no HRG
diss.
Her-3 ECD
3
Ab
antibody
diss.
HRG

Fig. 12


structural
peptide-hairpin
structural
EGFR DEATCKDTCP PLMLYNPTTY QMDVNPEGKY SFGATCVKKC
HER3 DSGACVPRCP QPLVYNKLTF QLEPNPHTKY QYGGVCVASC
HER4 DSGACVTQCP QTFVYNPTTF QLEHNFNAKY TYGAFCVKKC
HER2 HSGICELHCP ALVTYNTDTF ESMPNPEGRY TFGASCVTAC
Her3 Ala-Scan
Epitope Mapping
*Cys were exchanged to Ser

Fig. 13

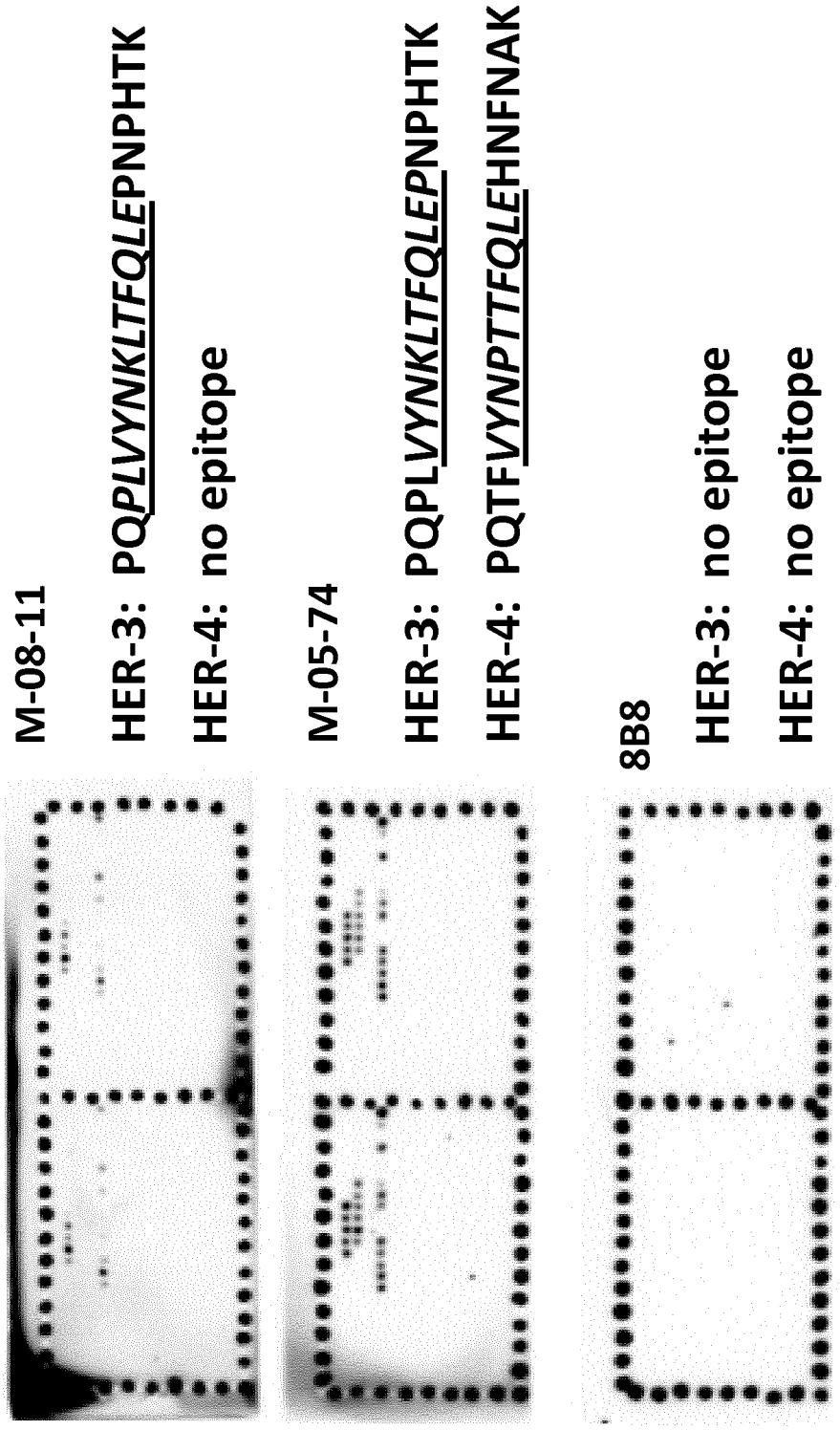

M-08-11
HER-3: PQPLVYNKLTFQLEPNPHTK
HER-4: no epitope
M-05-74
HER-3: PQPLVYNKLTFQLEPNPHTK
HER-4: PQTFVYNPTTFQLEHNFNAK
8B8
HER-3: no epitope
HER-4: no epitope

Fig. 14

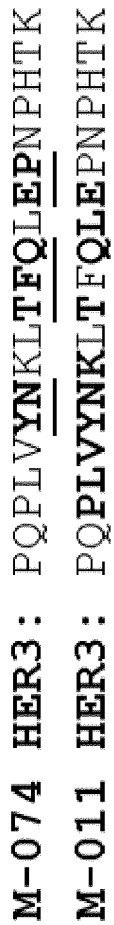

M-074 HER3: PQPLVYNKLTFQLEPNPHTK
M-011 HER3: PQPLVYNKLTFQLEPNPHTK

Fig. 15A

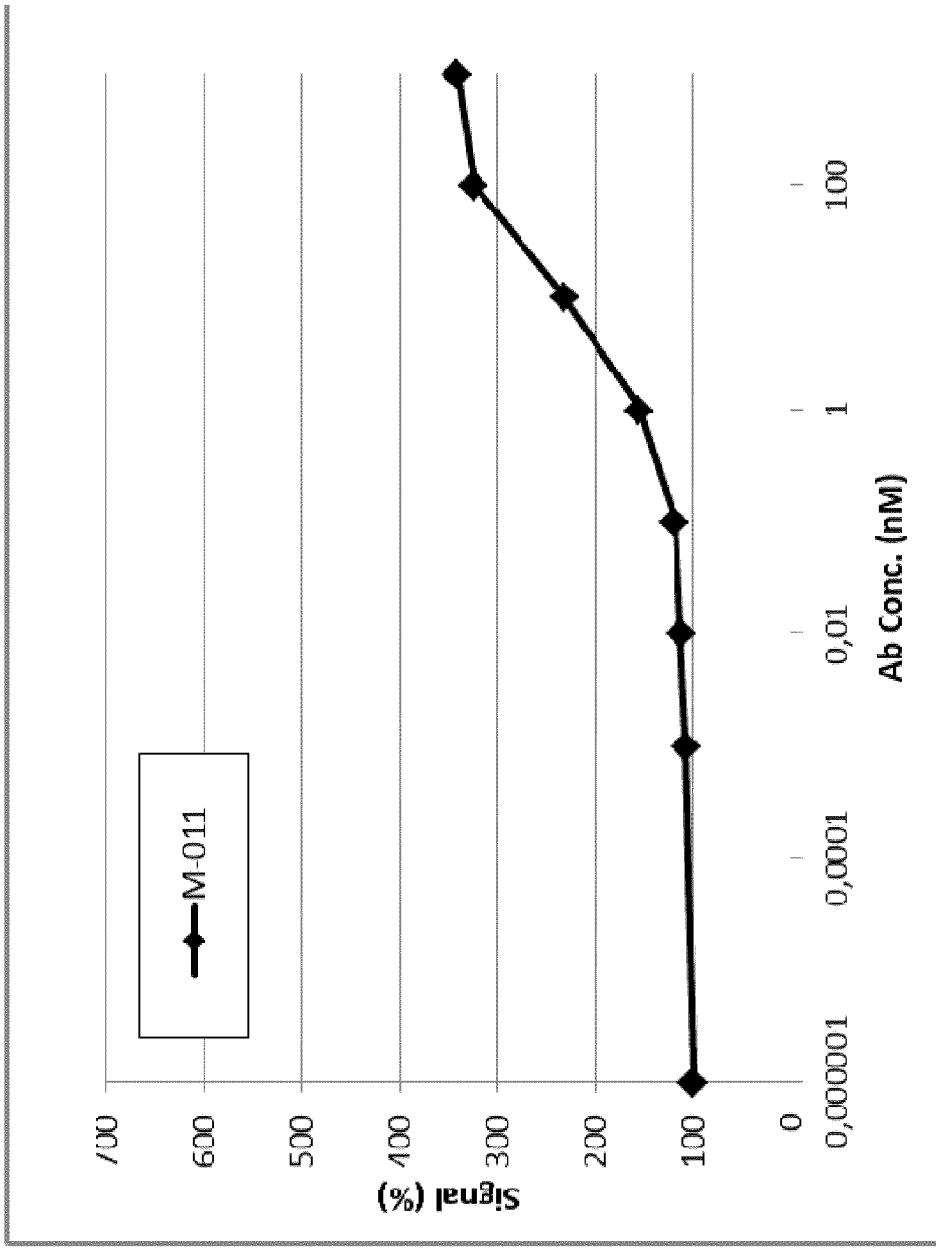

Signal (%)
700
600
500
400
300
200
100
0
0,000001
0,0001
0,01
1
100
Ab Conc. (nM)
M-011

Fig. 15B

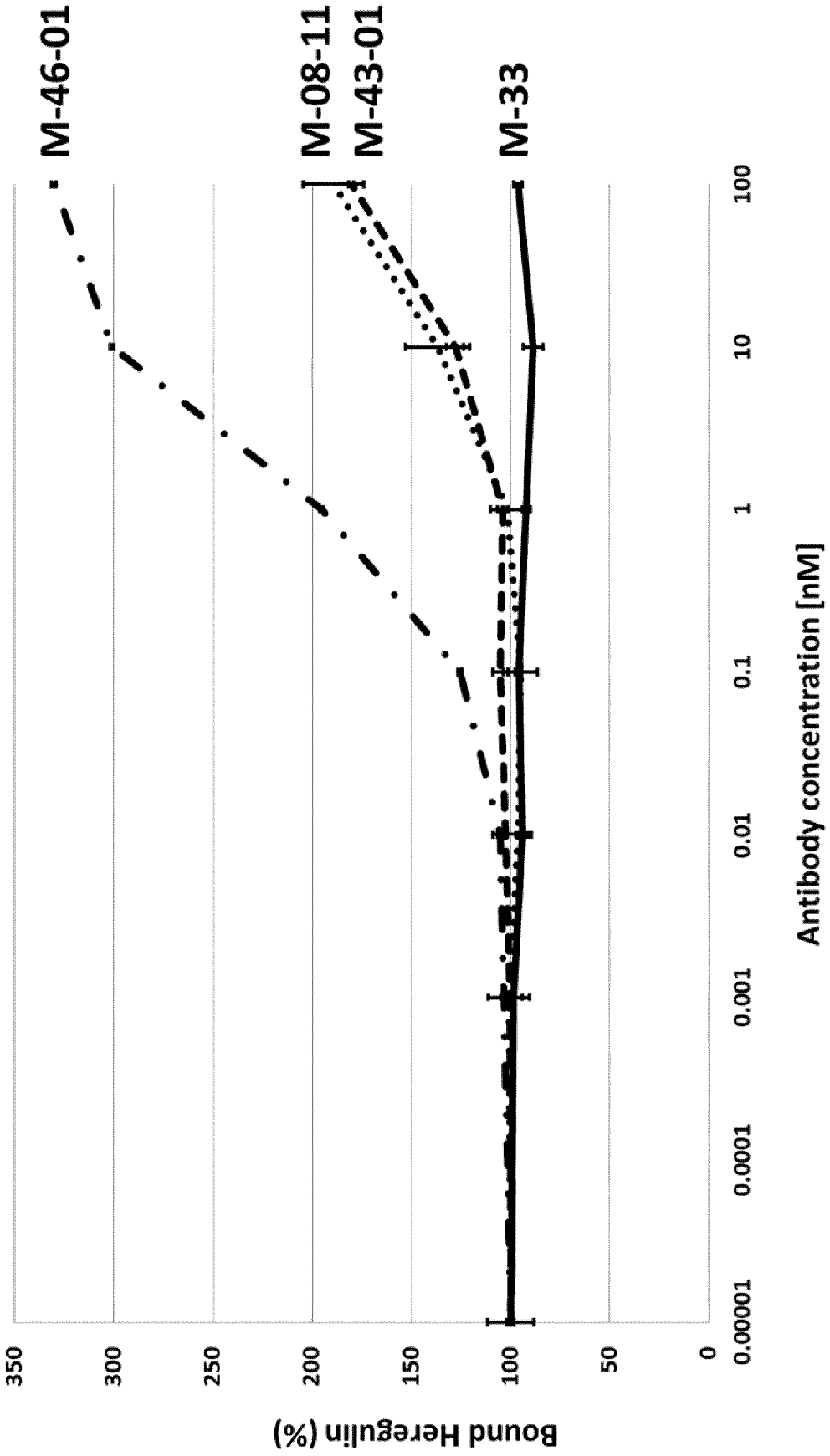

M-46-01
M-08-11
M-43-01
M-33
Bound Heregulin (%)
350
300
250
200
150
100
50
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Antibody concentration [nM]

Fig. 16

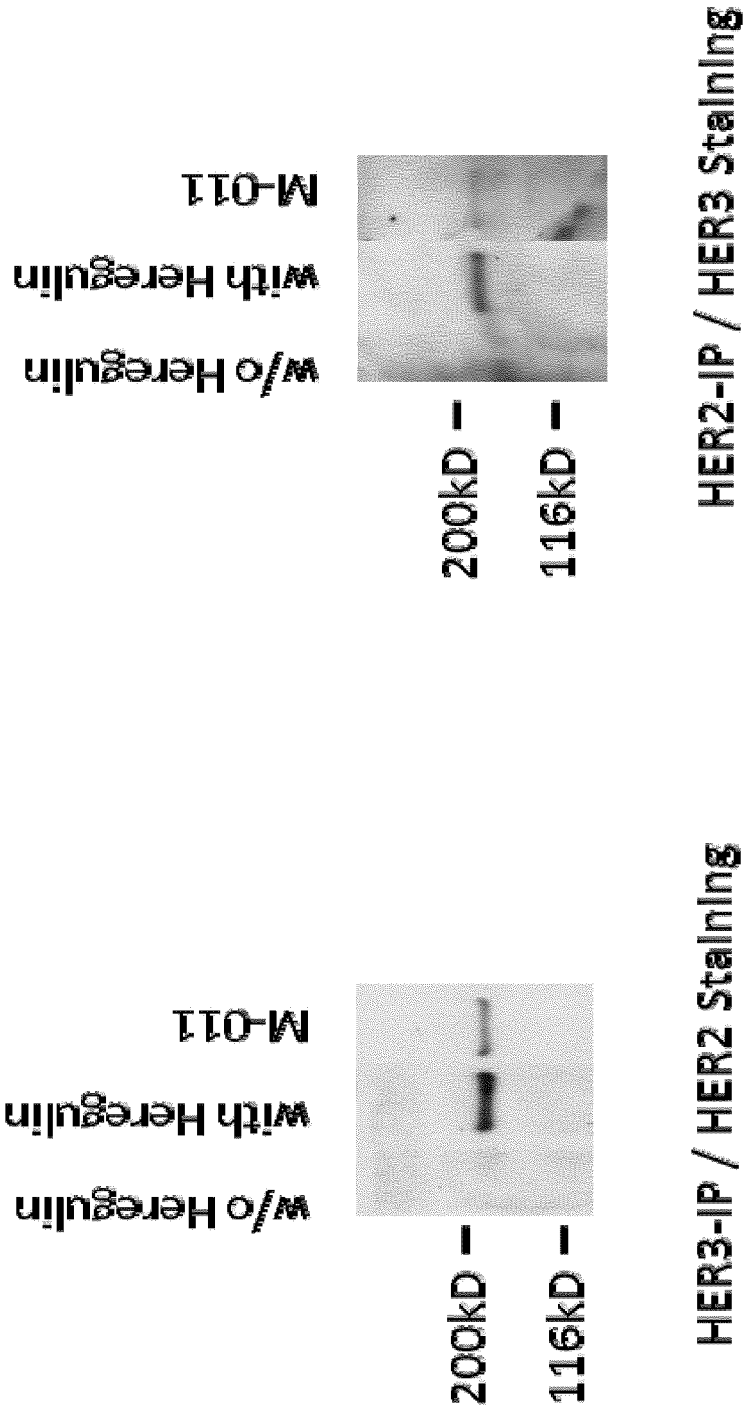
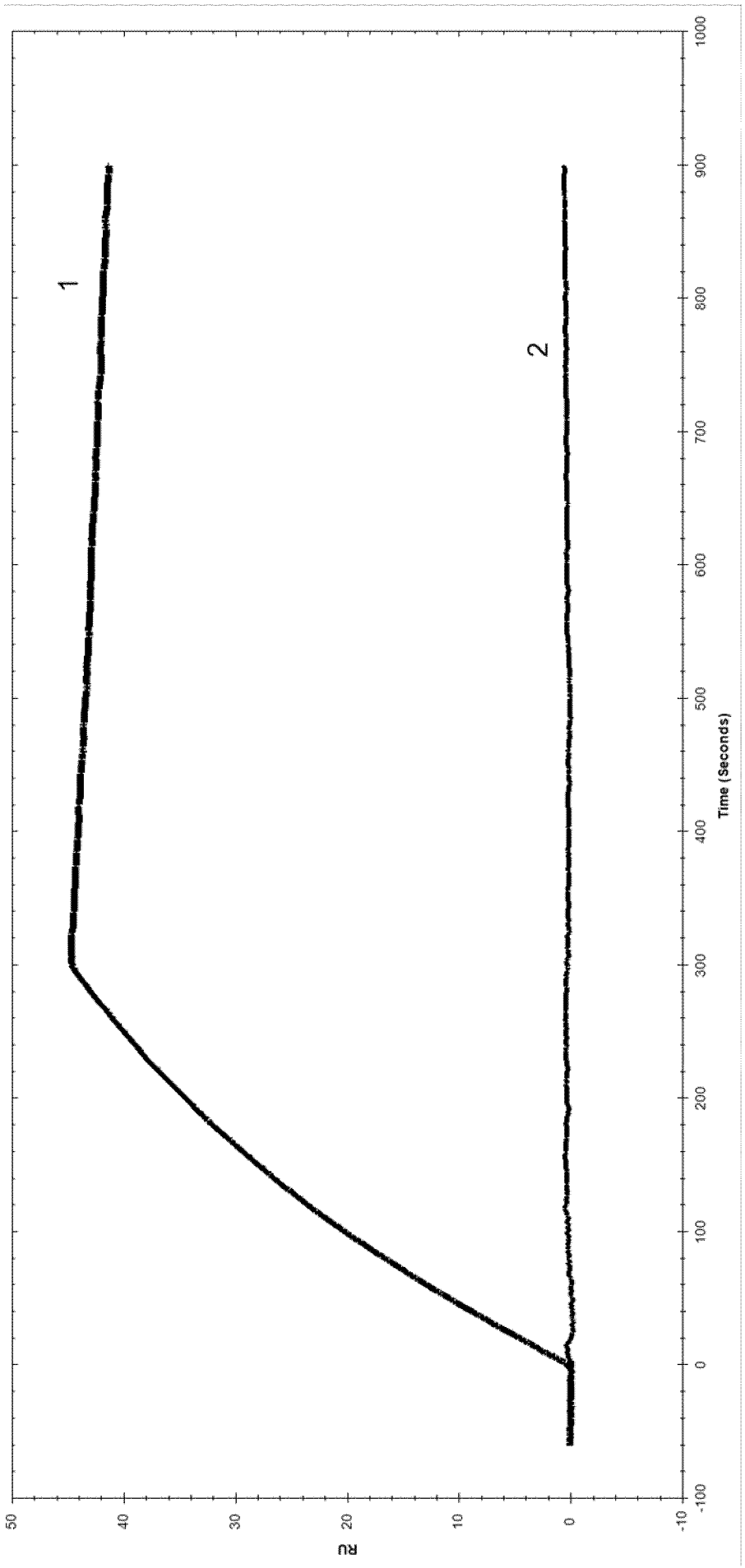

HER3-IP / HER2 Stalning
200kD
116kD
w/o Heregulin
with Heregulin
M-011
HER2-IP / HER3 Stalning
200kD
116kD
w/o Heregulin
with Heregulin
M-011

Fig. 17


RU
50
40
30
20
10
0
-10
-100
0
100
200
300
400
500
600
700
800
900
1000
Time (Seconds)
1
2