FIGURE 1

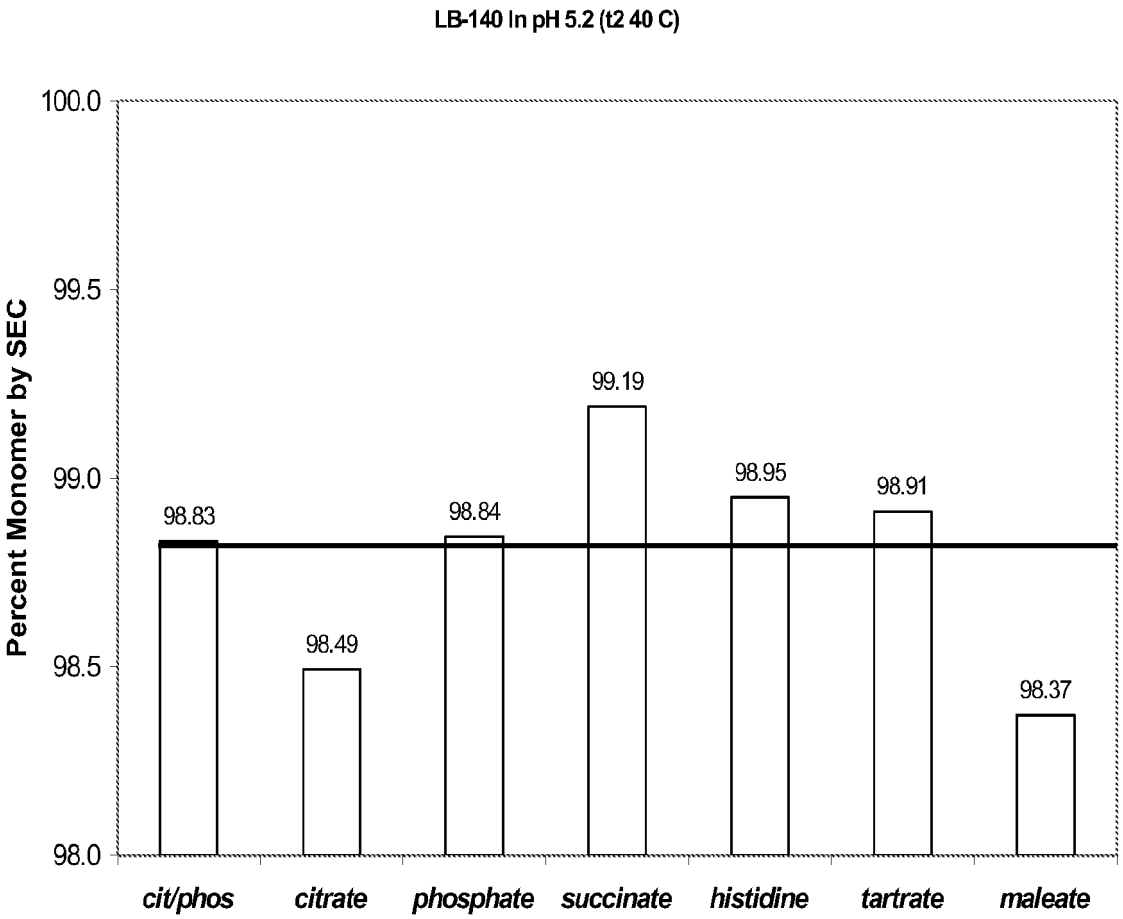

LB-140 In pH 5.2 (t2 40 C)
Percent Monomer by SEC
100.0
99.5
99.0
98.5
98.0
98.83
98.49
98.84
99.19
98.95
98.91
98.37
cit/phos
citrate
phosphate
succinate
histidine
tartrate
maleate

FIGURE 2

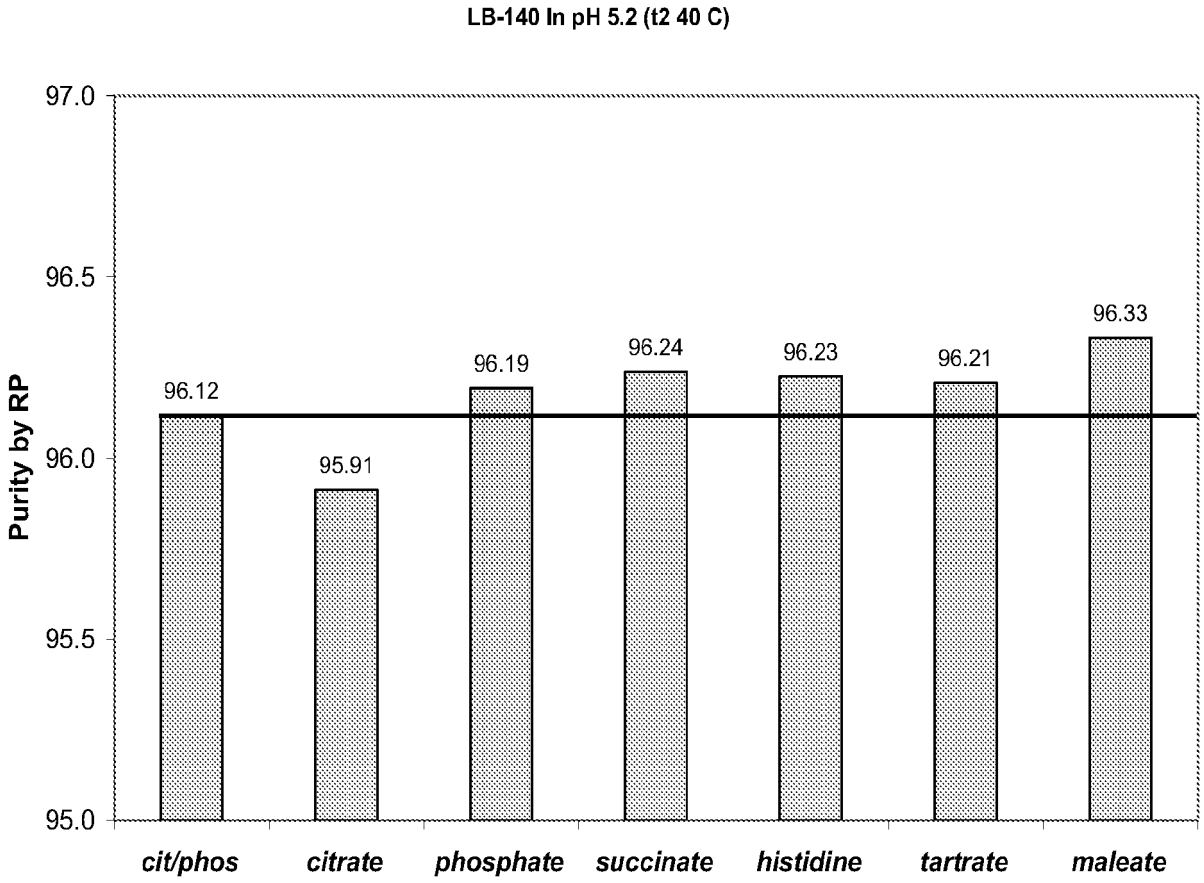
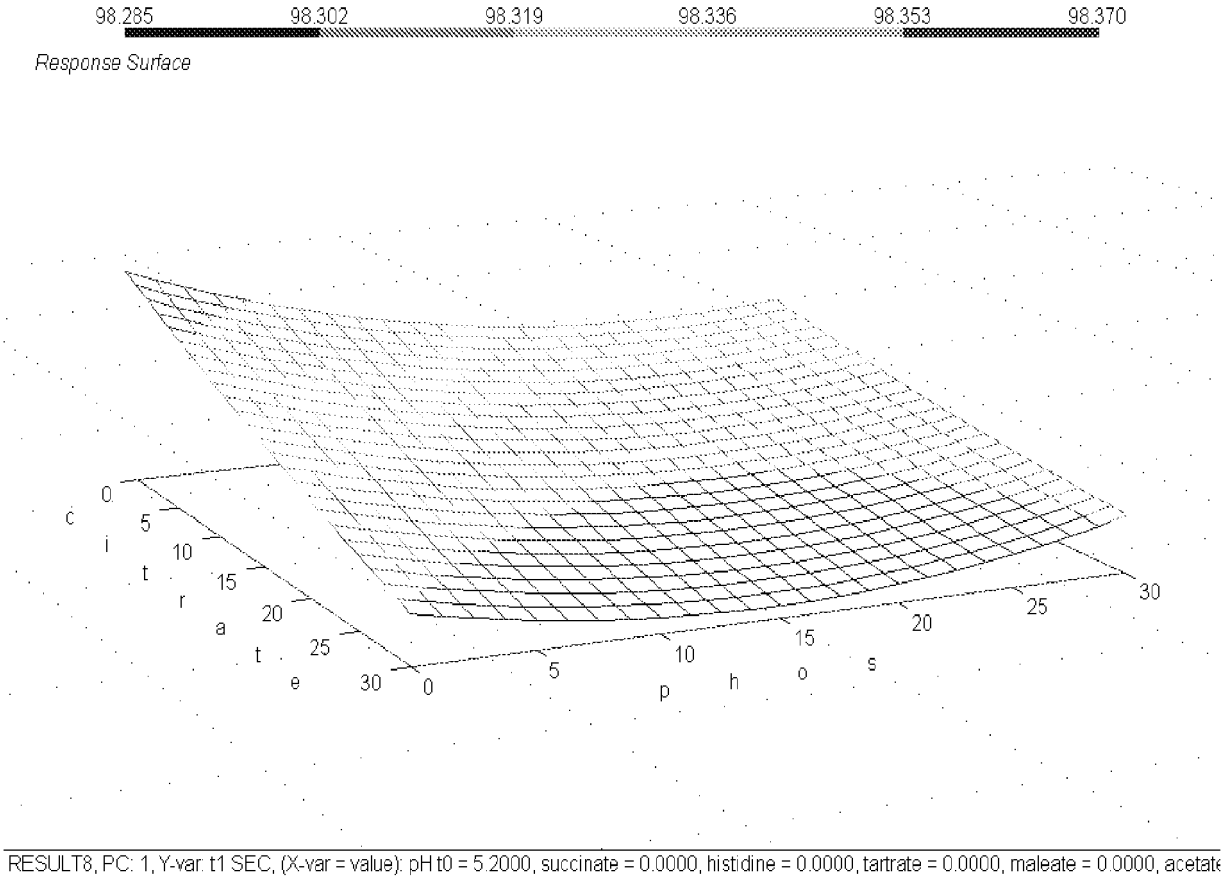

LB-140 In pH 5.2 (t2 40 C)
Purity by RP
97.0
96.5
96.0
95.5
95.0
96.12
95.91
96.19
96.24
96.23
96.21
96.33
cit/phos
citrate
phosphate
succinate
histidine
tartrate
maleate

FIGURE 3

Effect of Citrate/Phosphate (PLS Model 1)



RESULT8, PC: 1, Y-var: t1 SEC, (X-var = value): pH t0 = 5.2000, succinate = 0.0000, histidine = 0.0000, tartrate = 0.0000, maleate = 0.0000, acetate

FIGURE 4

Effect of Citrate/Phosphate (PLS Model 2)

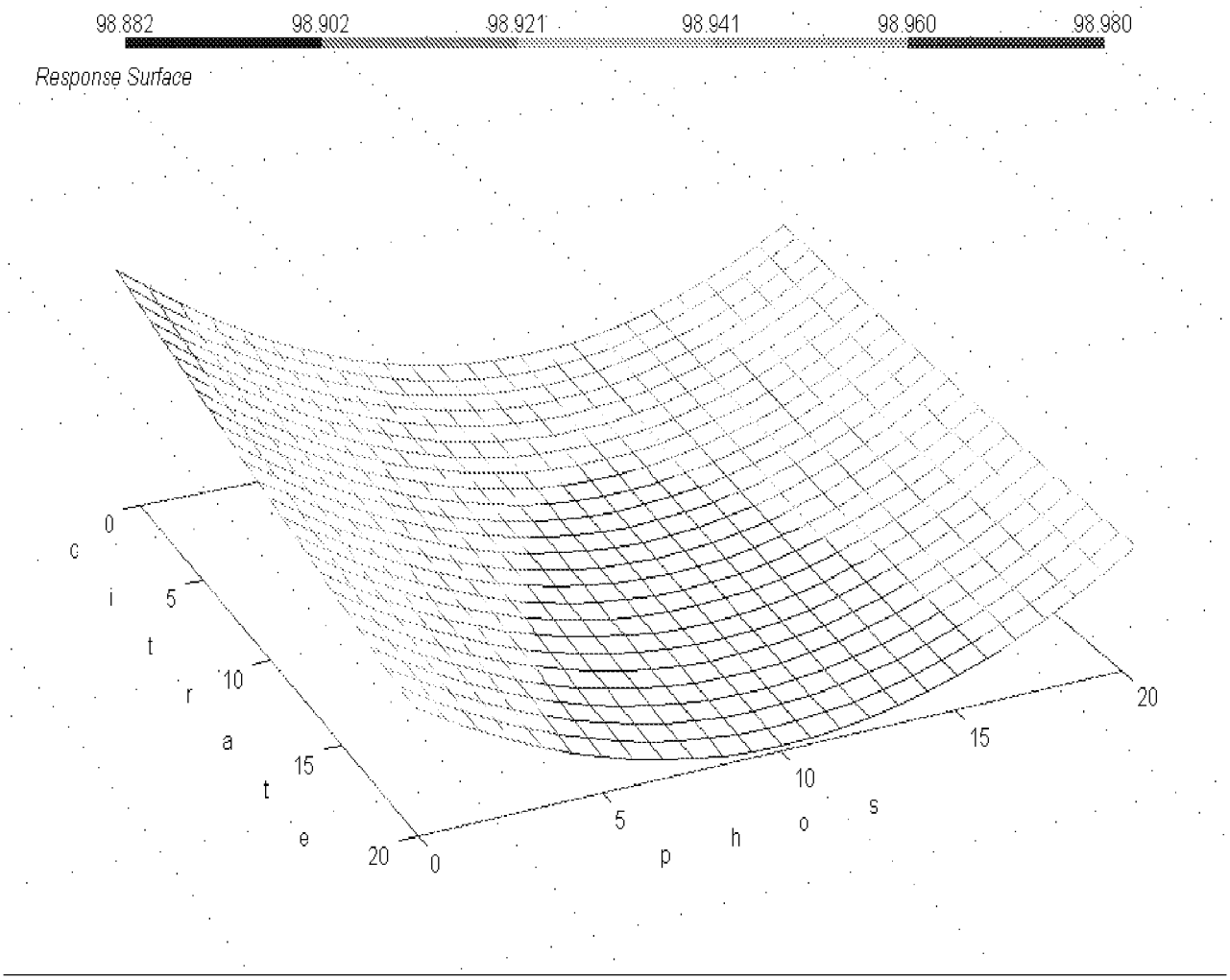
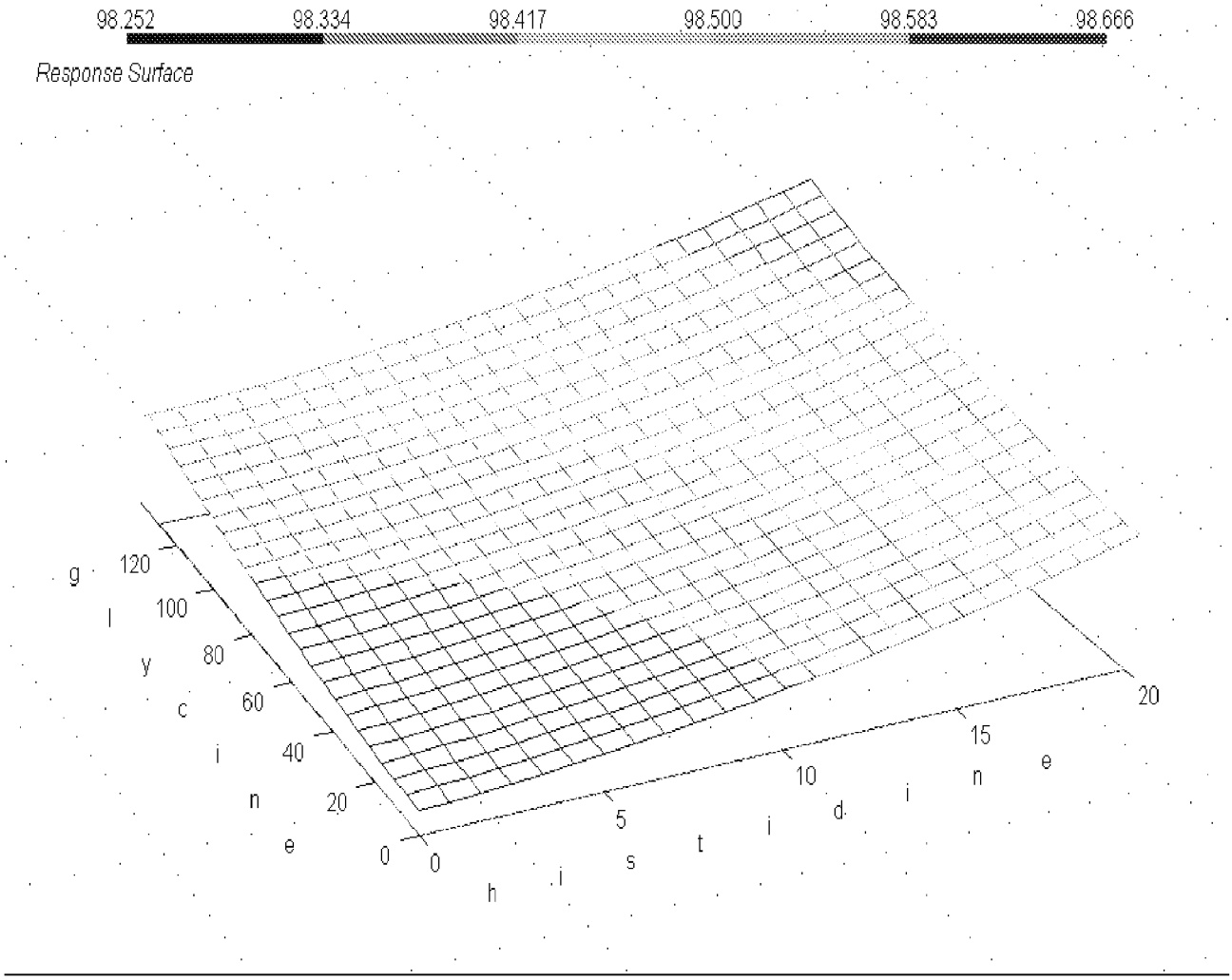


FIGURE 5

Effect of HIS/GLY (PLS Model 1)



LB-140 SEC t1 M..., PC: 1, Y-var: t1 SEC, (X-var = value): pH t0 = 5.2000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, tartrate = 0.0000, m

FIGURE 6

Effect of Arg/sorbitol (PLS Model 1)

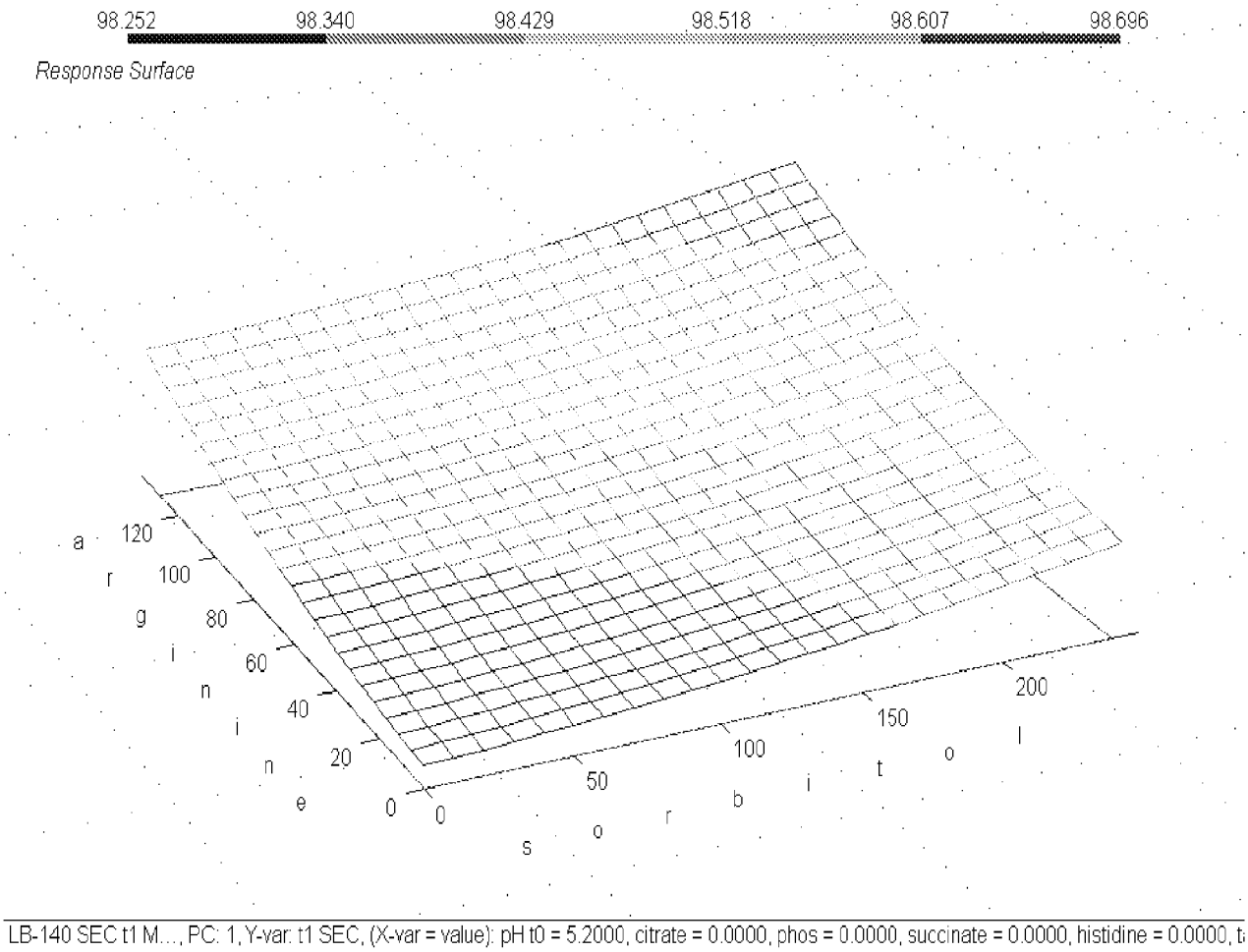


FIGURE 7

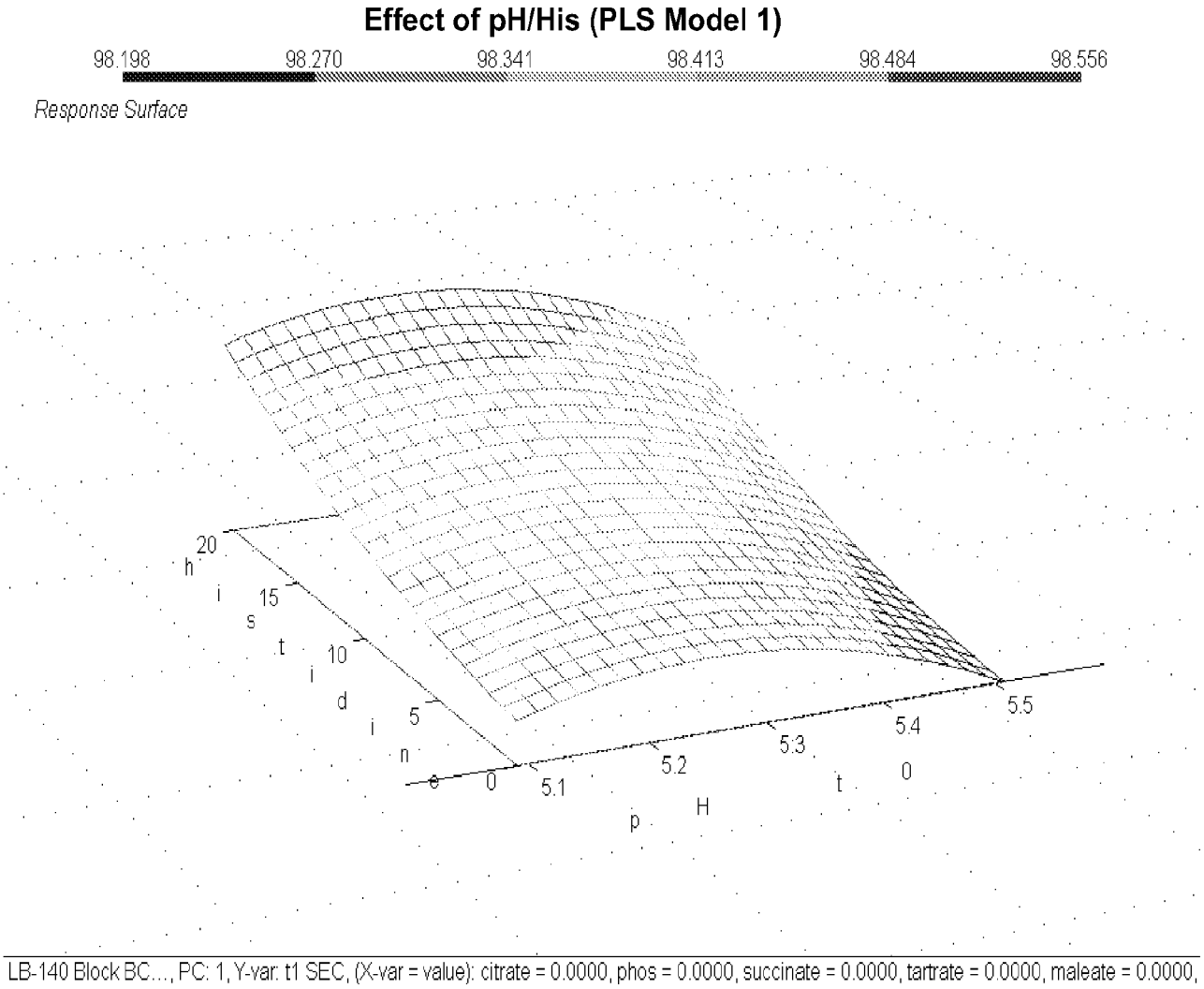

Effect of pH/His (PLS Model 1)
98.198
98.270
98.341
98.413
98.484
98.556
Response Surface
20
h
i
15
s
t
10
i
d
i
5
n
e
0
5.1
5.2
5.3
5.4
5.5
p
H
t
0
LB-140 Block BC..., PC: 1, Y-var: t1 SEC, (X-var = value): citrate = 0.0000, phos = 0.0000, succinate = 0.0000, tartrate = 0.0000, maleate = 0.0000,

FIGURE 8

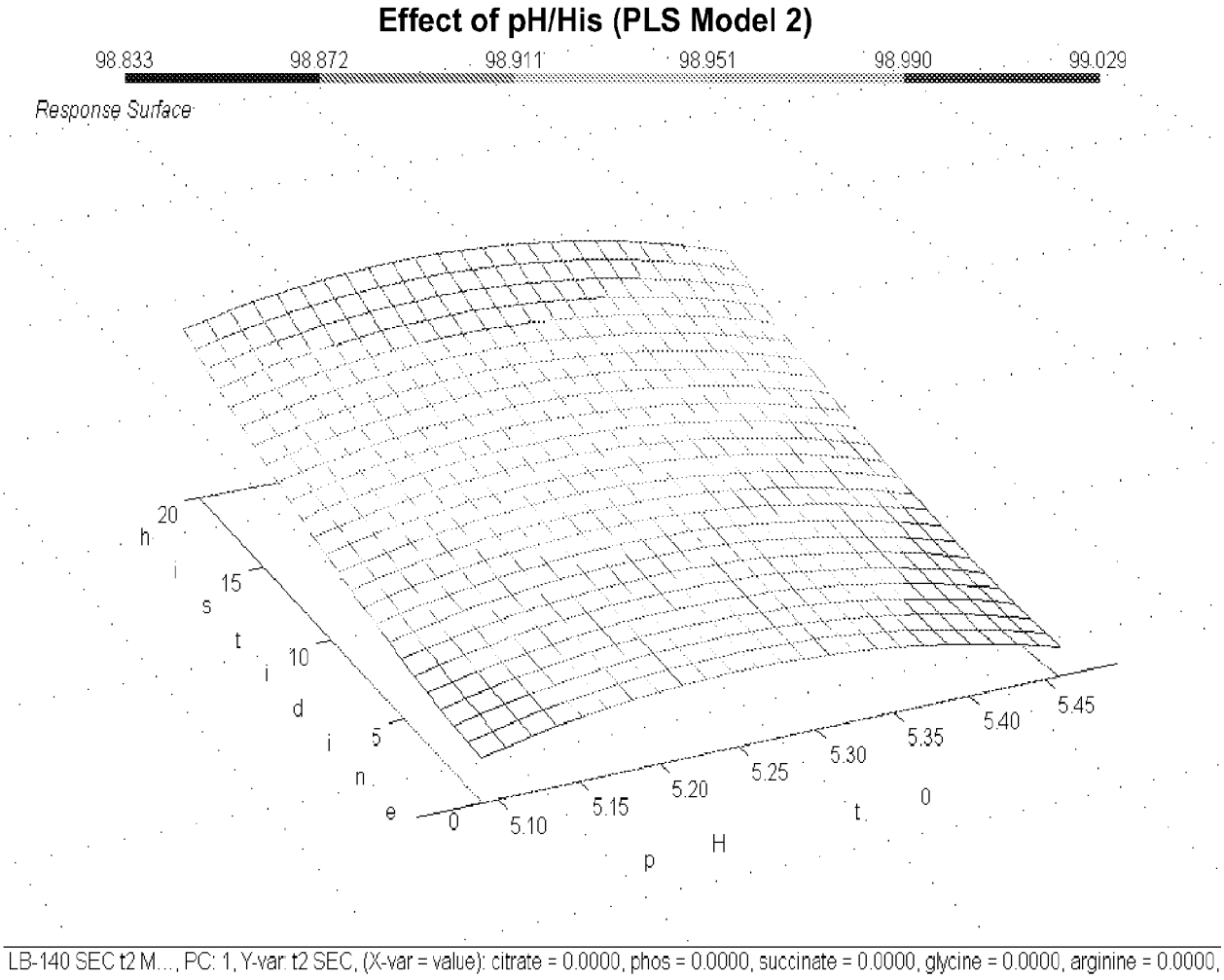

Effect of pH/His (PLS Model 2)
98.833
98.872
98.911
98.951
98.990
99.029
Response Surface
20
h
i
s
15
t
i
10
d
i
5
n
e
0
5.10
5.15
5.20
5.25
5.30
5.35
5.40
5.45
p
H
t
0
LB-140 SEC t2 M..., PC: 1, Y-var: t2 SEC, (X-var = value): citrate = 0.0000, phos = 0.0000, succinate = 0.0000, glycine = 0.0000, arginine = 0.0000,

FIGURE 9

Effect of trehalose/PS 80 (PLS Model 2)

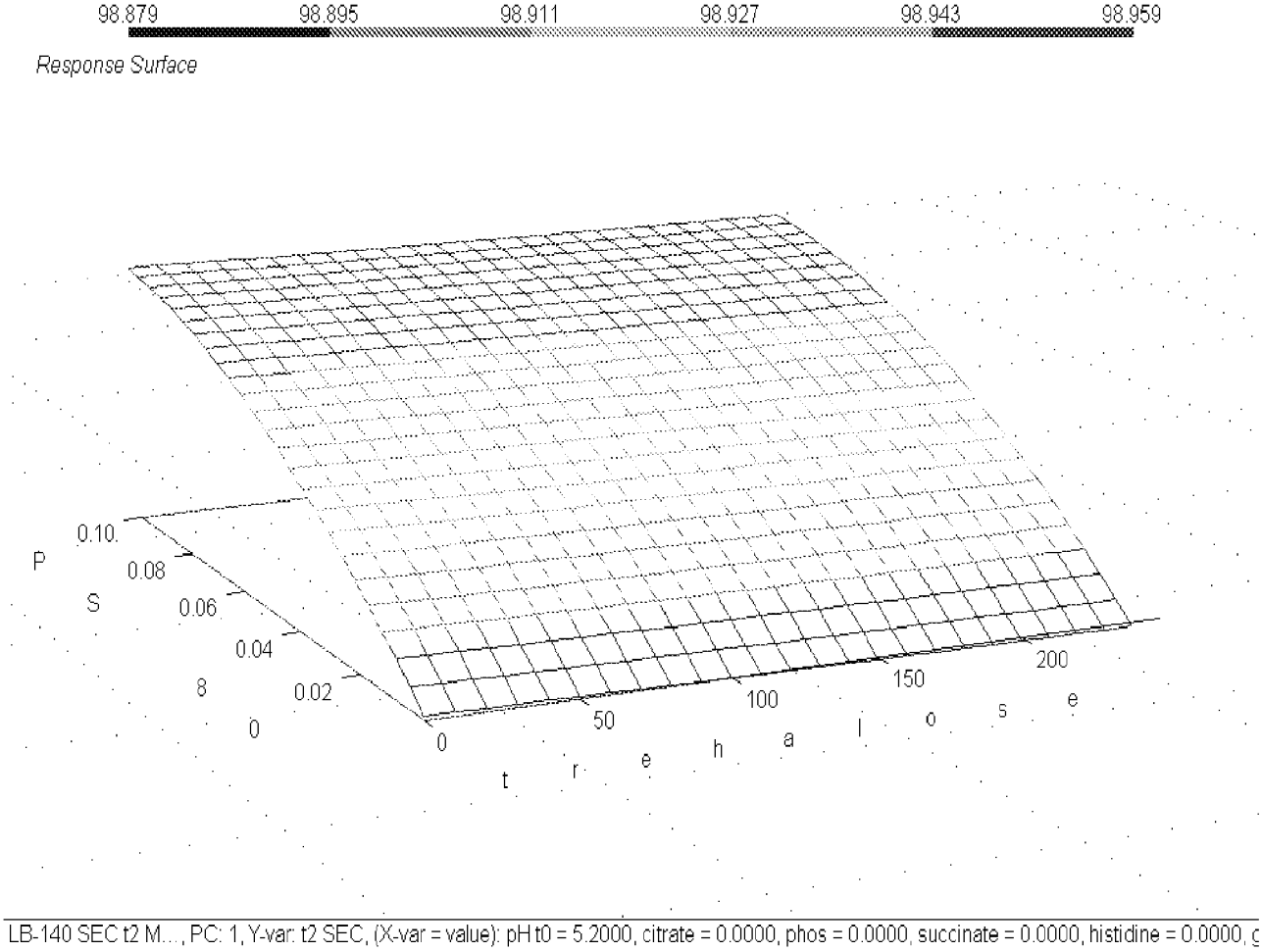


FIGURE 10

Effect of mannitol/PS80 (pH 5.2) (PLS Model 2)

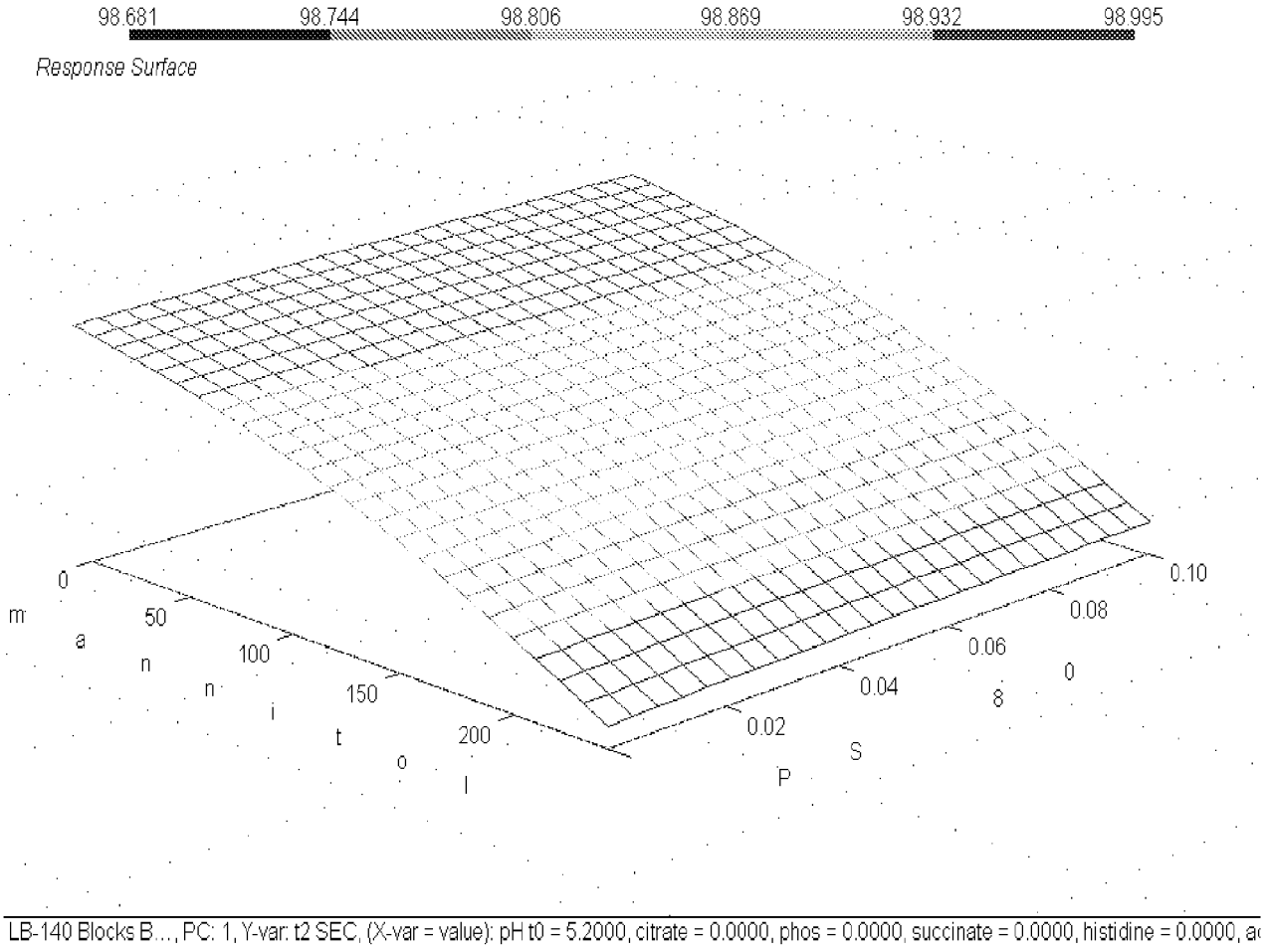


FIGURE 11

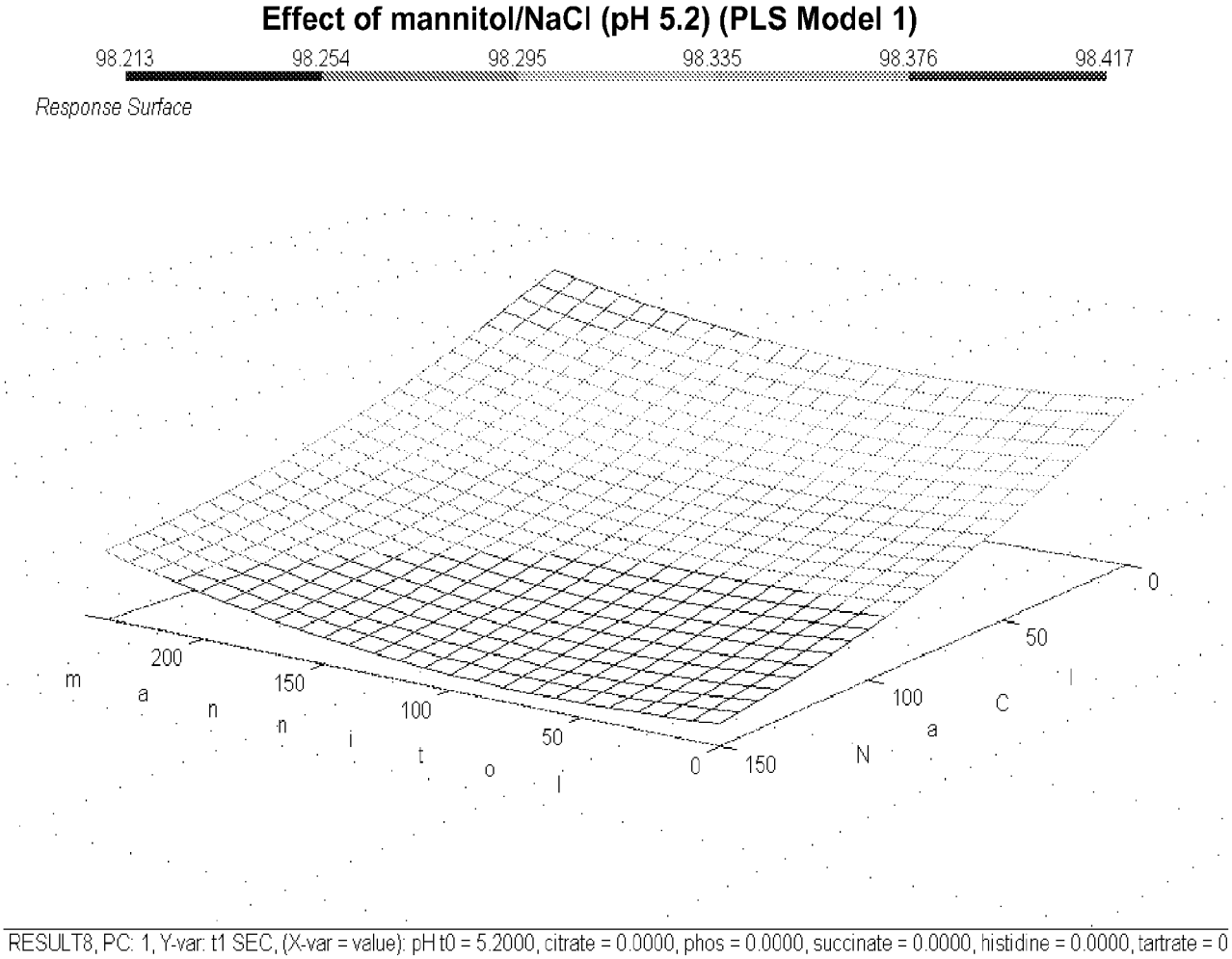

Effect of mannitol/NaCl (pH 5.2) (PLS Model 1)
98.213
98.254
98.295
98.335
98.376
98.417
Response Surface
mannitol
200
150
100
50
0
NaCl
0
50
100
150
RESULT8, PC: 1, Y-var: t1 SEC, (X-var = value): pH t0 = 5.2000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, histidine = 0.0000, tartrate = 0

FIGURE 12

Effect of EDTA/Met (pH 5.2) (PLS Model 1)

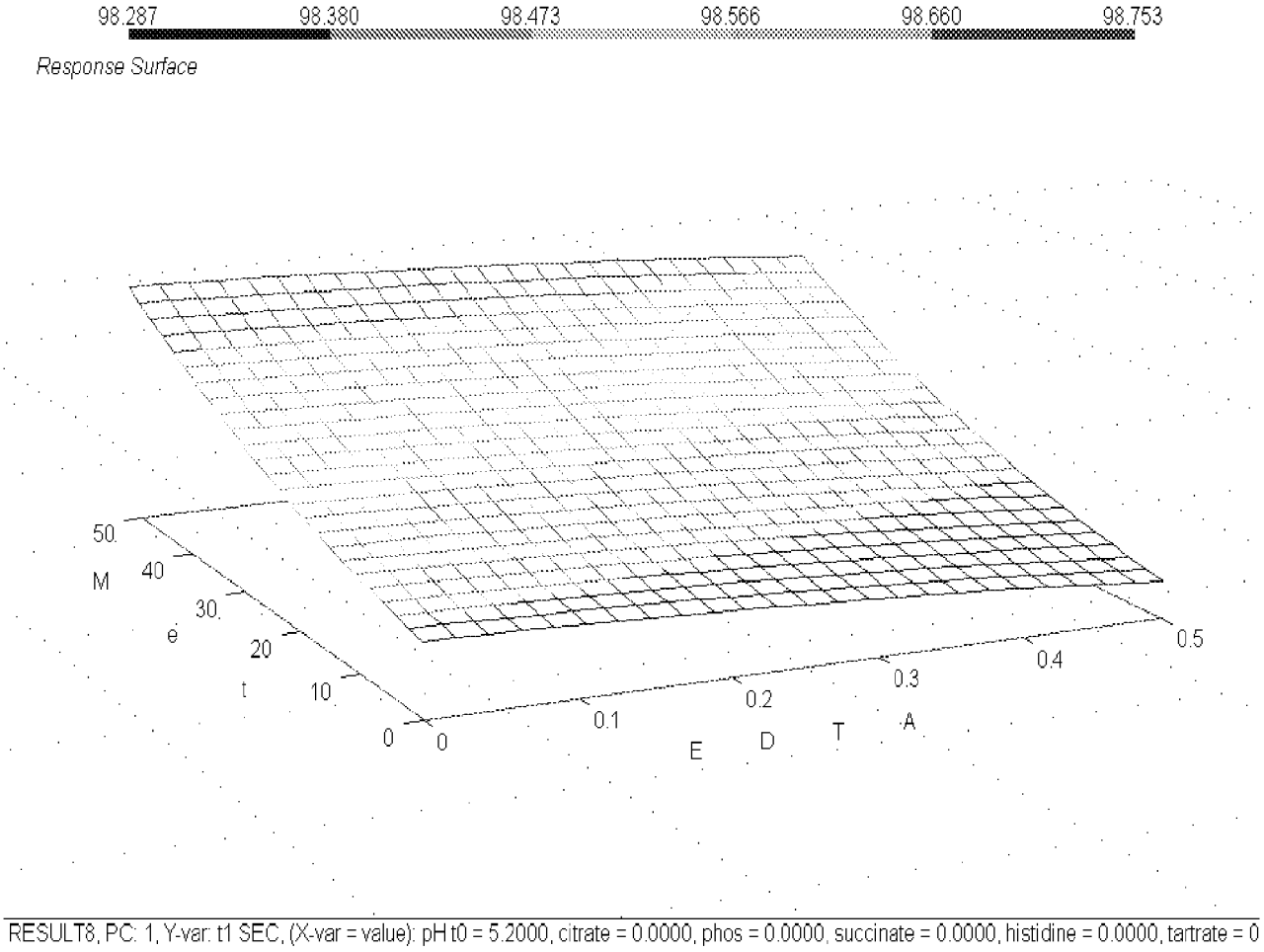


FIGURE 13

Effect of citrate and phosphate according to the PLS model A using the difference in monomer content at t1 as the endpoint. The pH is fixed at 5.2 and the protein at 50 mg/ml.

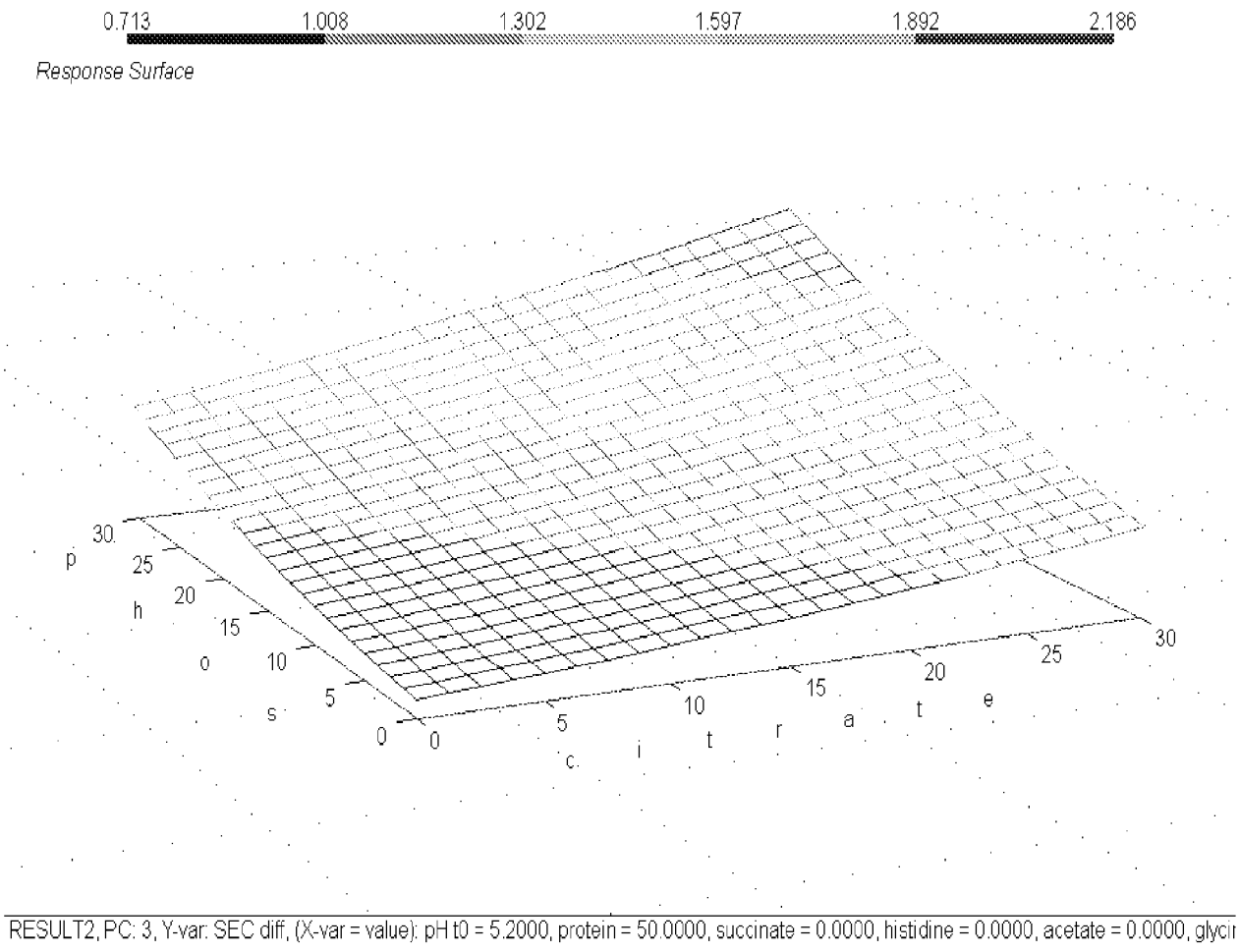
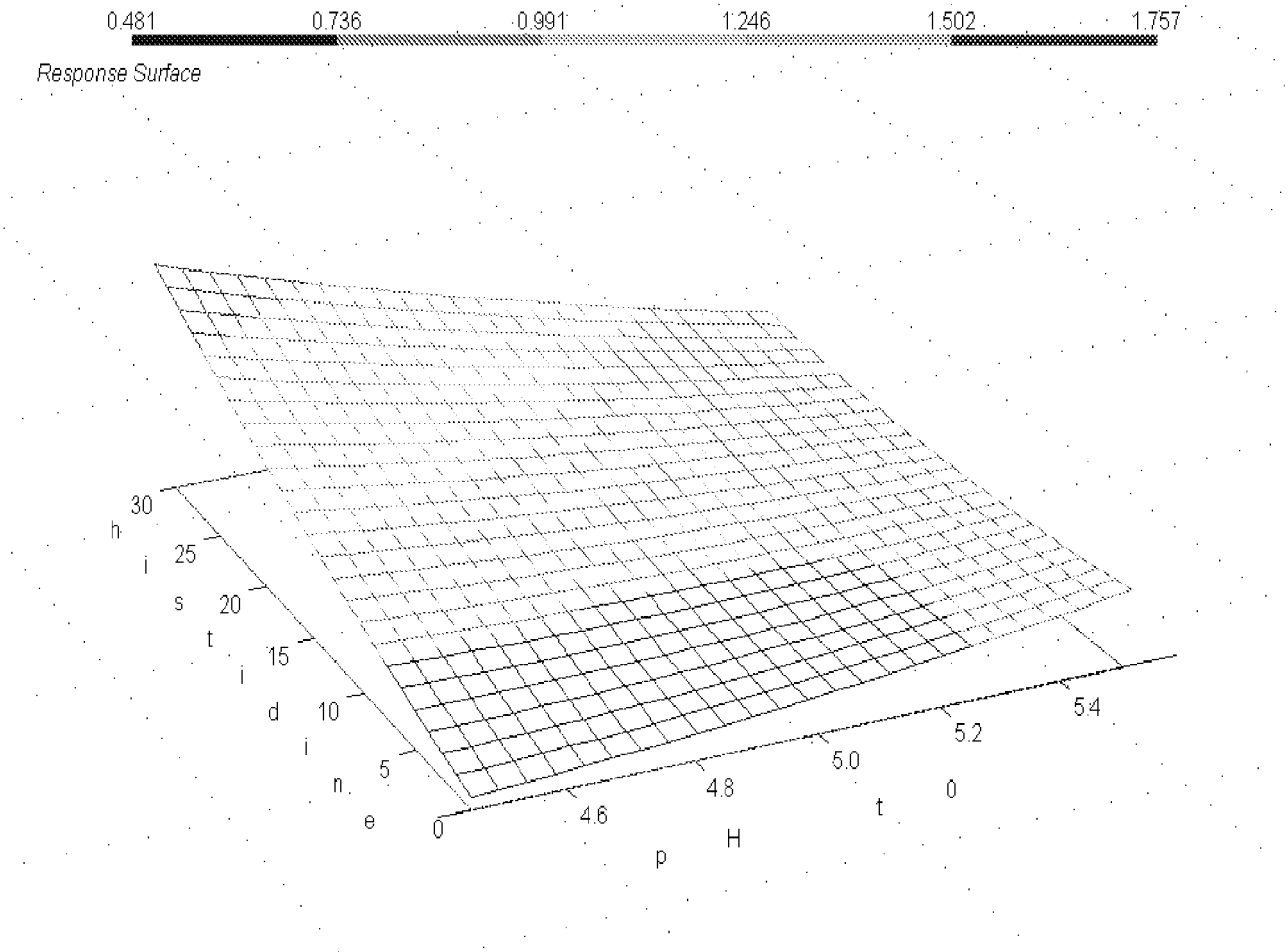


FIGURE 14

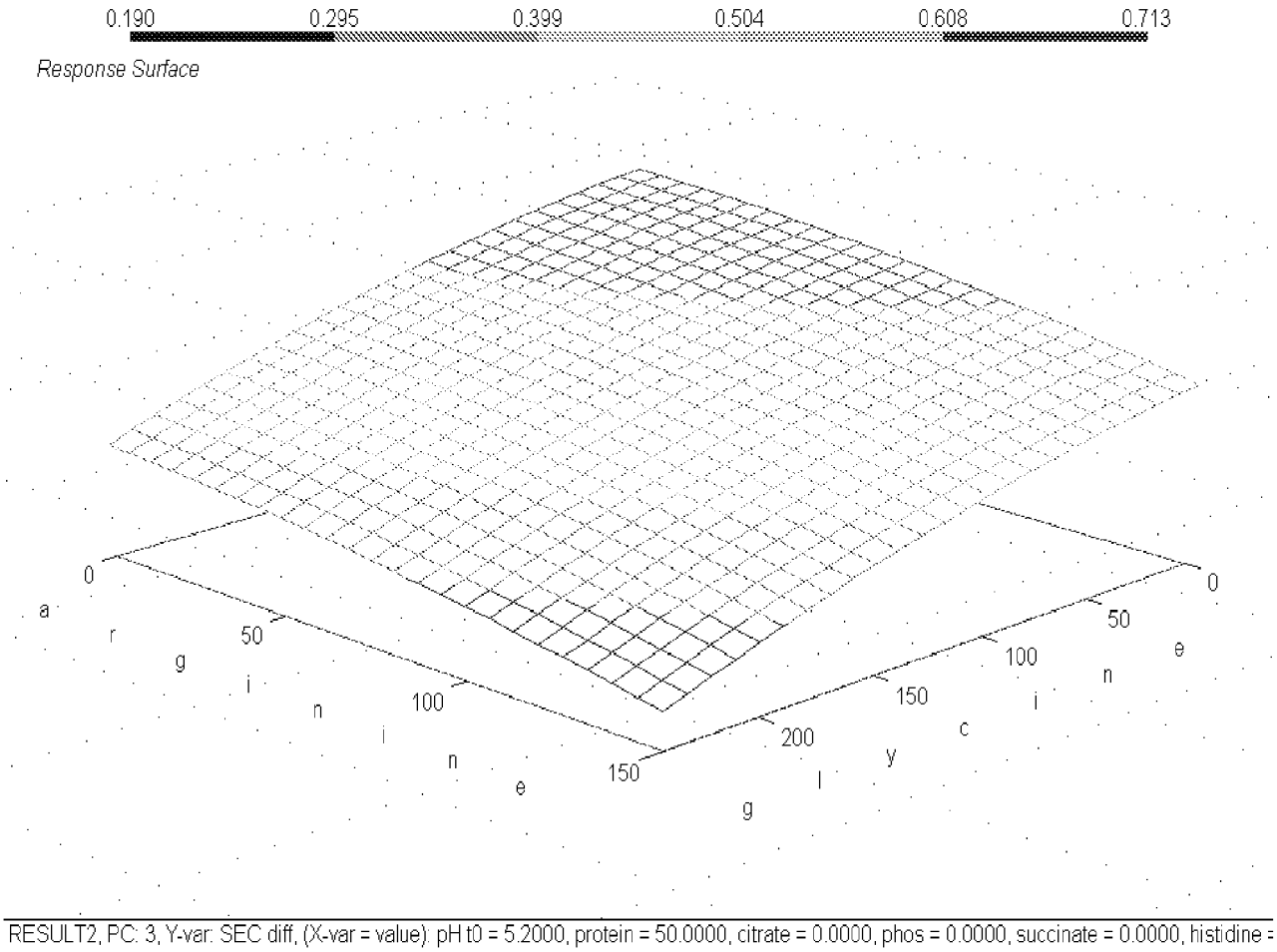
Effect of pH and His according to the PLS model A using the difference in monomer content at t1 as the endpoint. The protein concentration is fixed at 50 mg/ml



RESULT2, PC: 3, Y-var: SEC diff, (X-var = value): protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, acetate = 0.0000, glycine

FIGURE 15

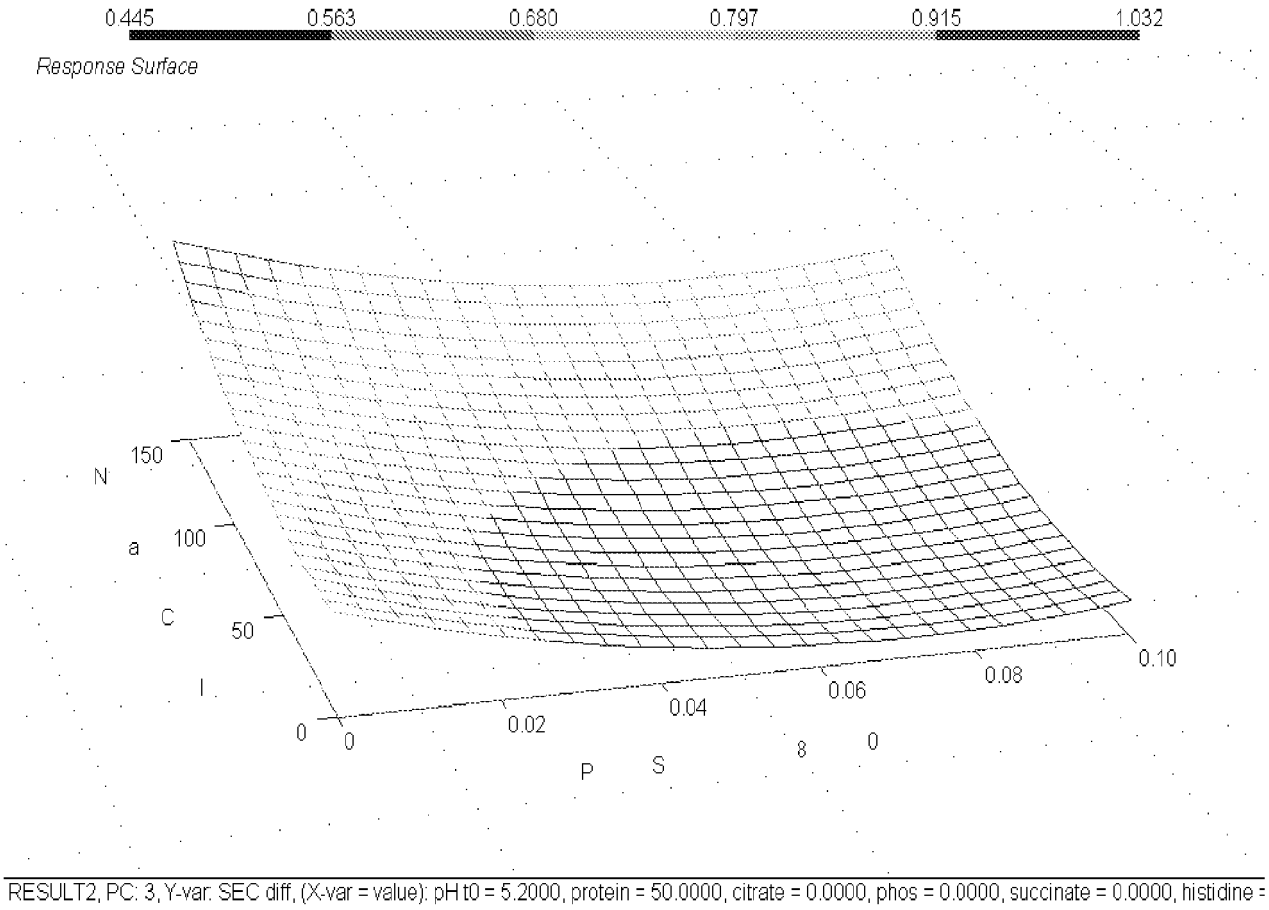
Effect of Gly and Arg according to the PLS model A using the difference in monomer content at t1 as the endpoint. The pH is fixed at 5.2 and the protein concentration at 50 mg.ml



RESULT2, PC: 3, Y-var: SEC diff, (X-var = value): pH t0 = 5.2000, protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, histidine =

FIGURE 16

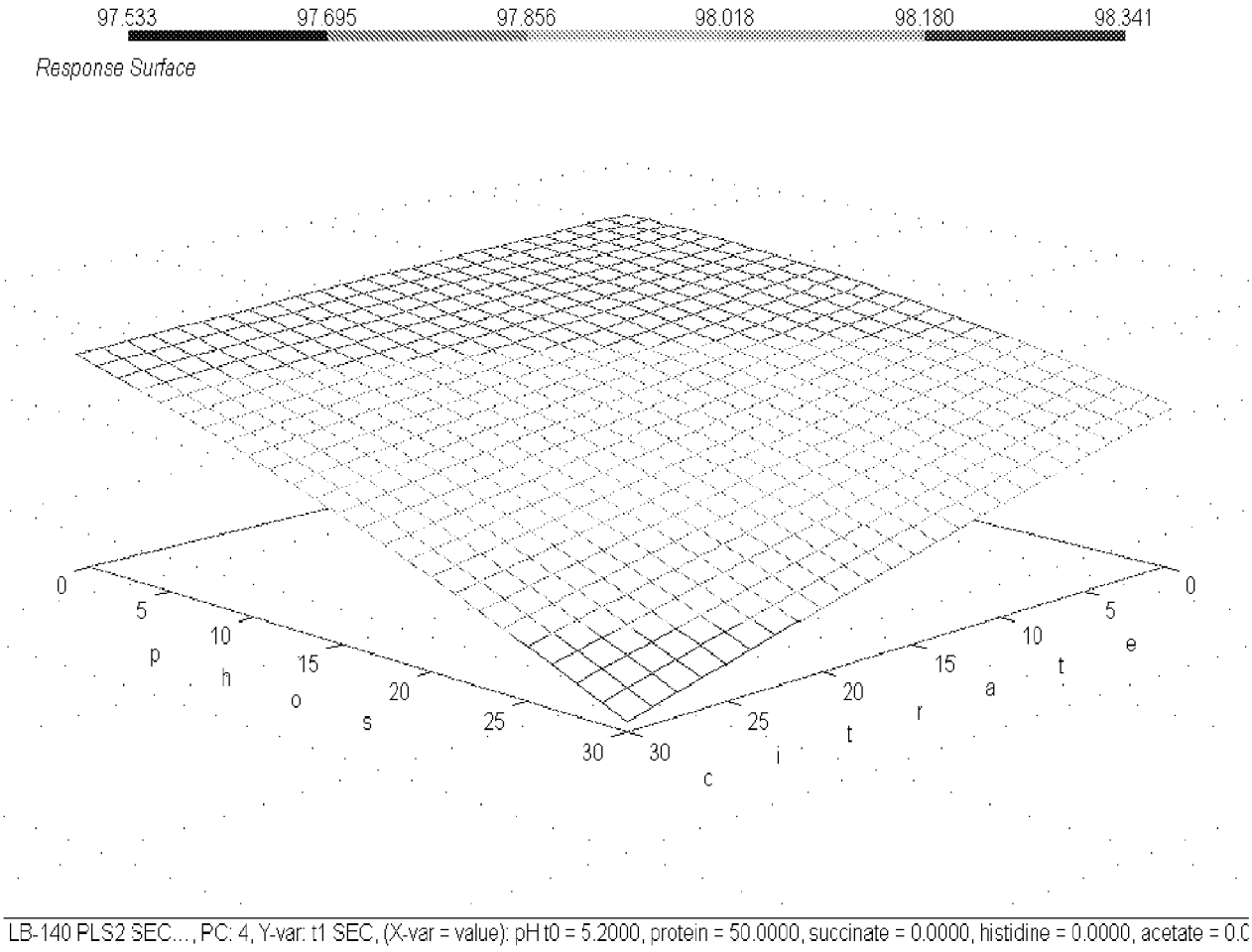
Effect of NaCl and polysorbate 80 (PS 80) according to PLS model A using the difference in monomer content at t1 as the endpoint. The pH is fixed at 5.2 and the protein concentration is fixed at 50 mg/ml.



RESULT2, PC: 3, Y-var: SEC diff, (X-var = value): pH t0 = 5.2000, protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, histidine =

FIGURE 17

Effect of citrate and phosphate according to the PLS model B using the monomer contents at t1 and t2 as the endpoints. The pH is fixed at 5.2 and the protein concentration is fixed at 50 mg/ml.



LB-140 PLS2 SEC..., PC: 4, Y-var: t1 SEC, (X-var = value): pH t0 = 5.2000, protein = 50.0000, succinate = 0.0000, histidine = 0.0000, acetate = 0.0

FIGURE 18

Effect of pH and His according to PLS model B using the monomer contents at t1 abd t2 as the enpoints. The protein concentration is set at 50 mg.ml

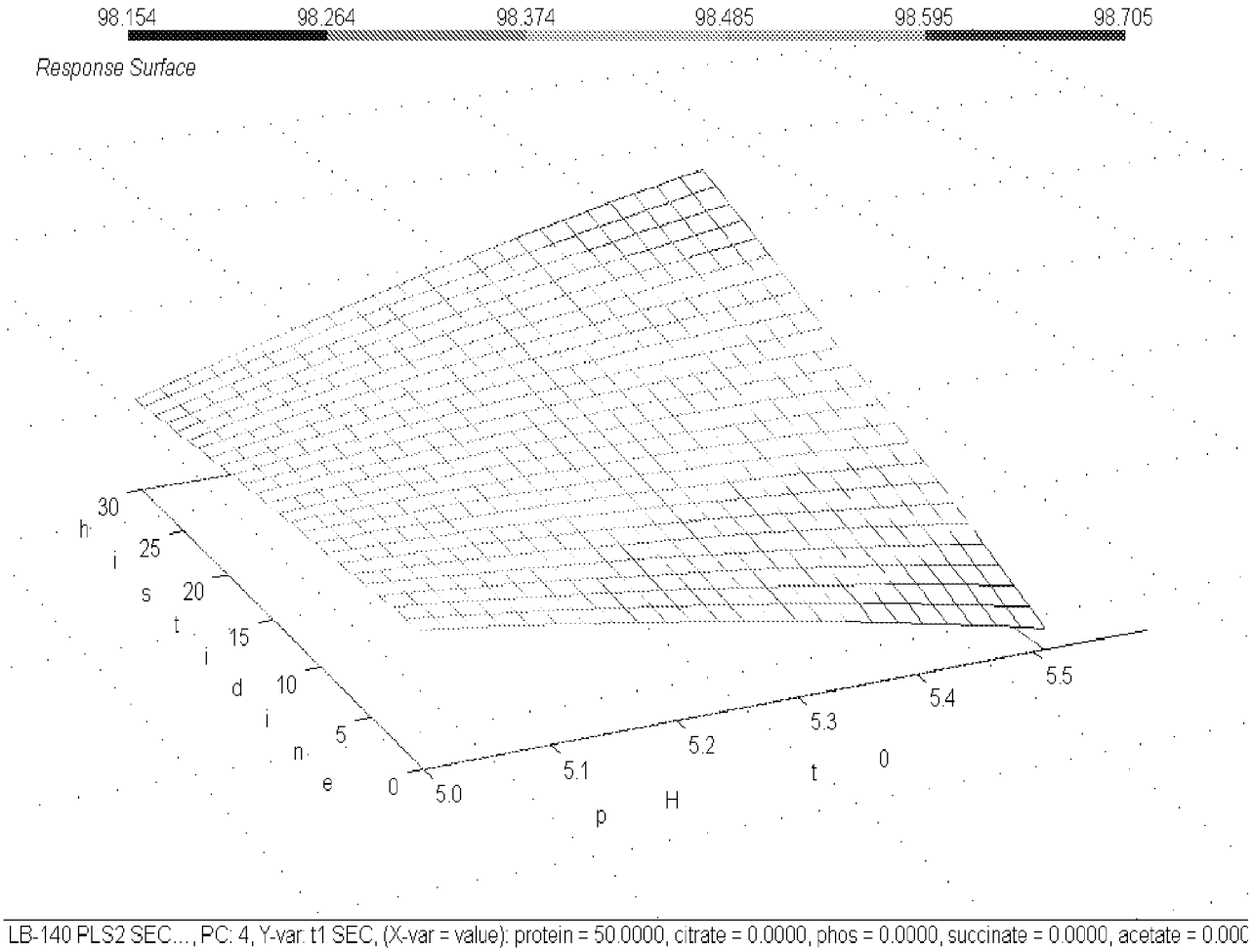
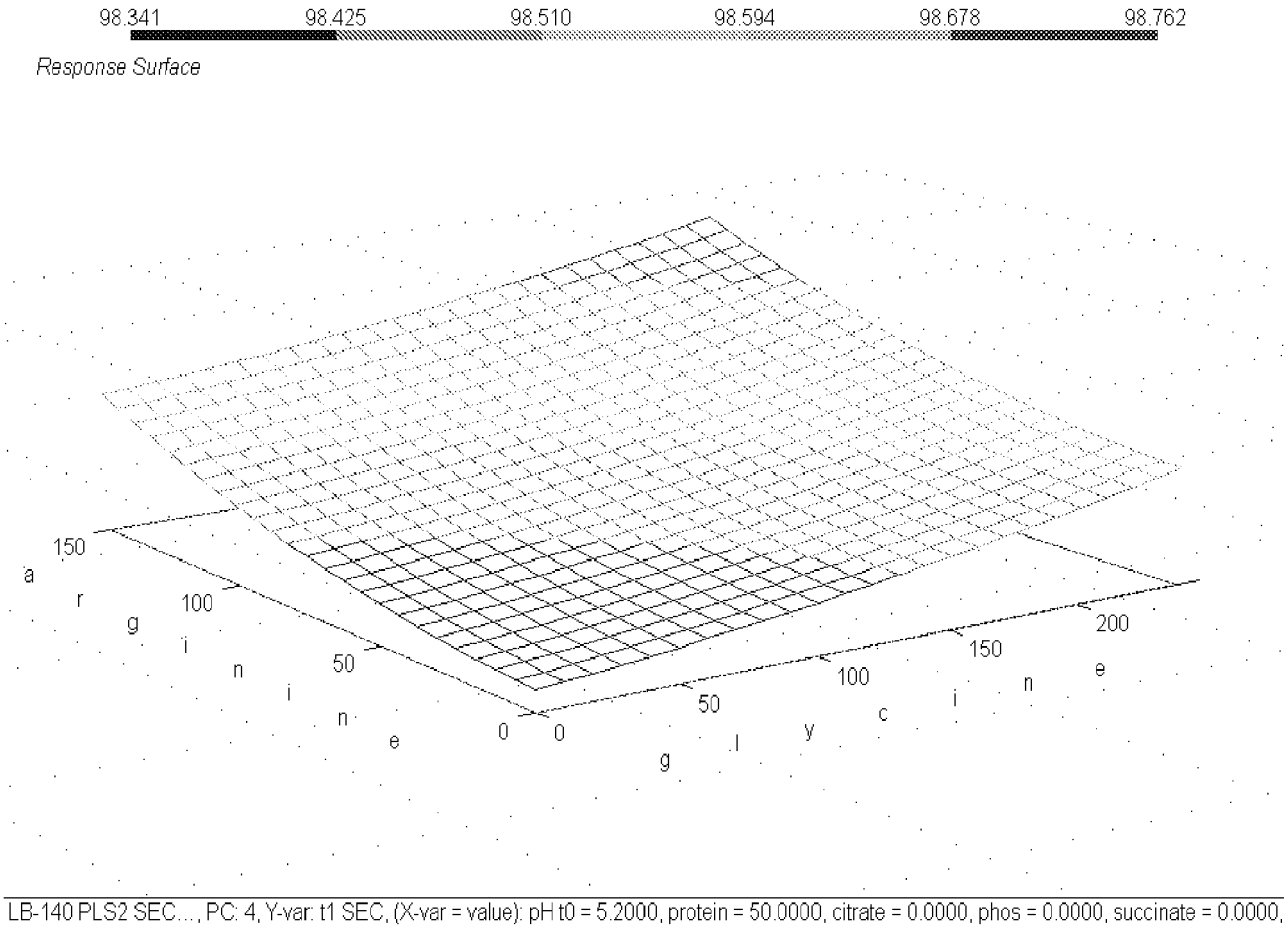


FIGURE 19

Effect of Arg and Gly according to PLS model B using the monomer contents at t1 and t2 as the endpoints. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml



LB-140 PLS2 SEC..., PC: 4, Y-var: t1 SEC, (X-var = value): pH t0 = 5.2000, protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000,

FIGURE 20

Effect of PS 80 and mannitol according to PLS model B using the monomer contents at t1 and t2 as the endpoints. The pH is fixed at 5.2 and the protein concentration is fixed at 50 mg/ml.

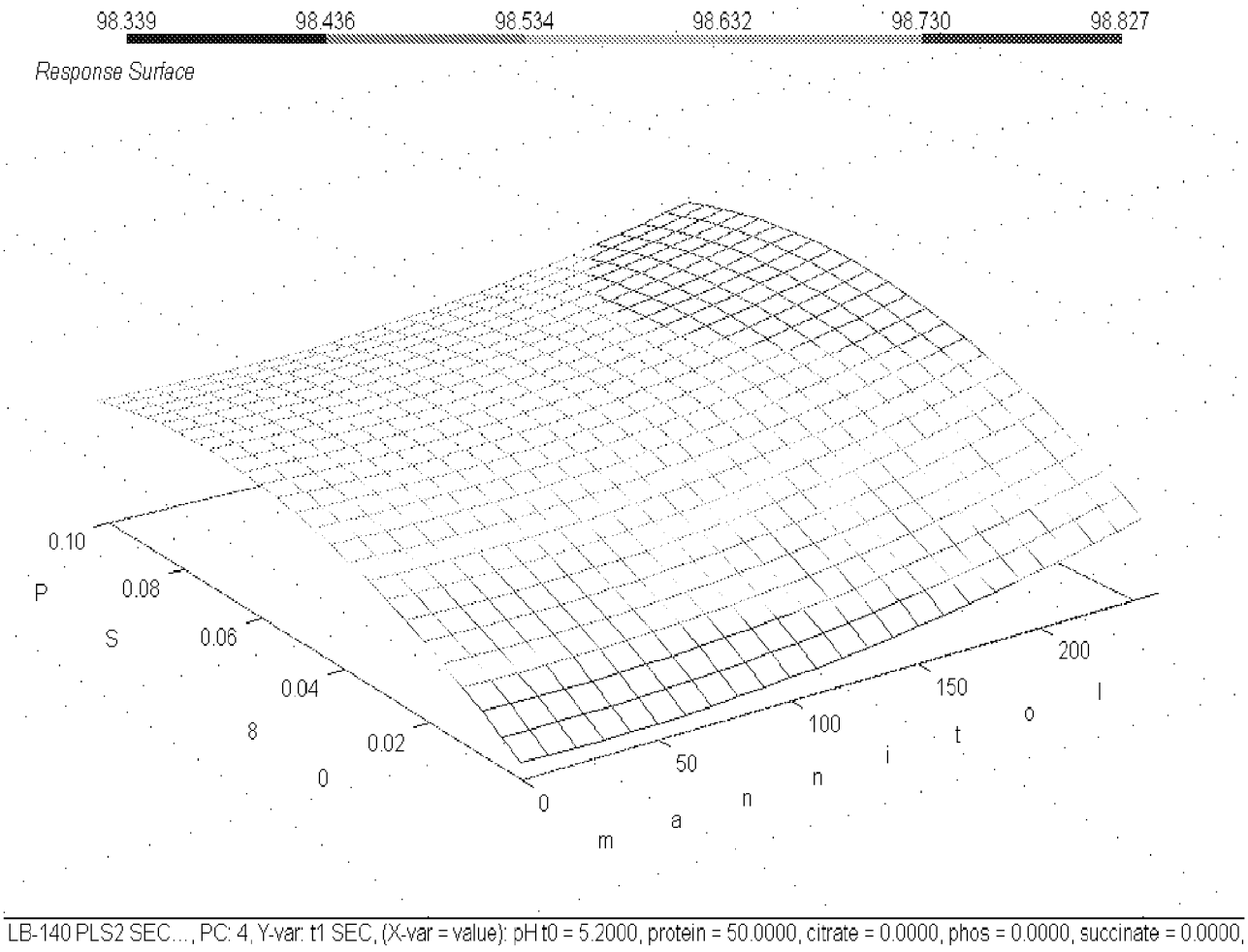
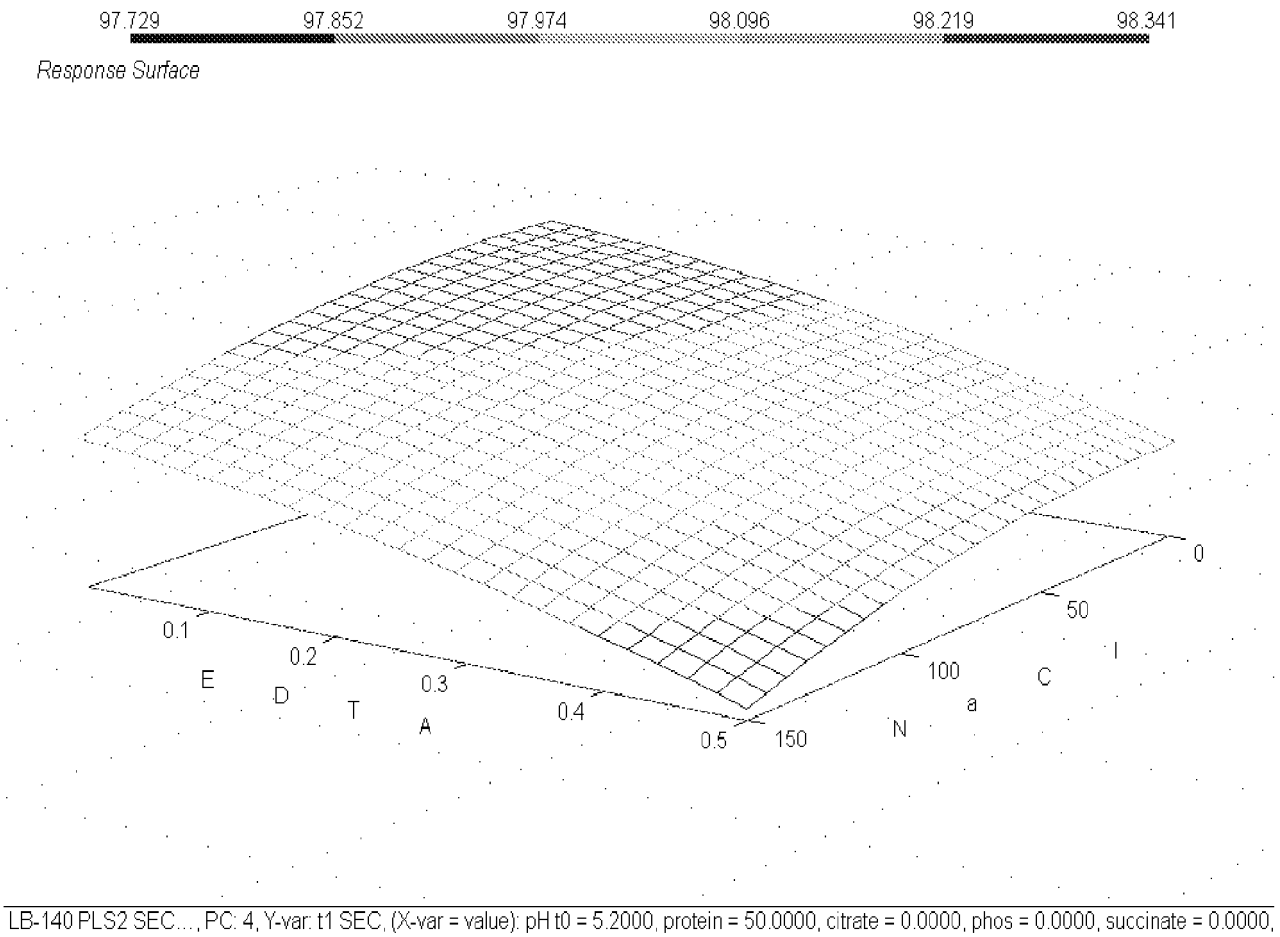


FIGURE 21

Effect of EDTA and NaCl according to the PLS model B using the monomer contents at t1 and t2 as the endpoints. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml.



LB-140 PLS2 SEC..., PC: 4, Y-var: t1 SEC, (X-var = value): pH t0 = 5.2000, protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000,

FIGURE 22

Effect of succinate and His according to the PLS model B using the monomer contents at t1 and t2 as the endpoints. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml.

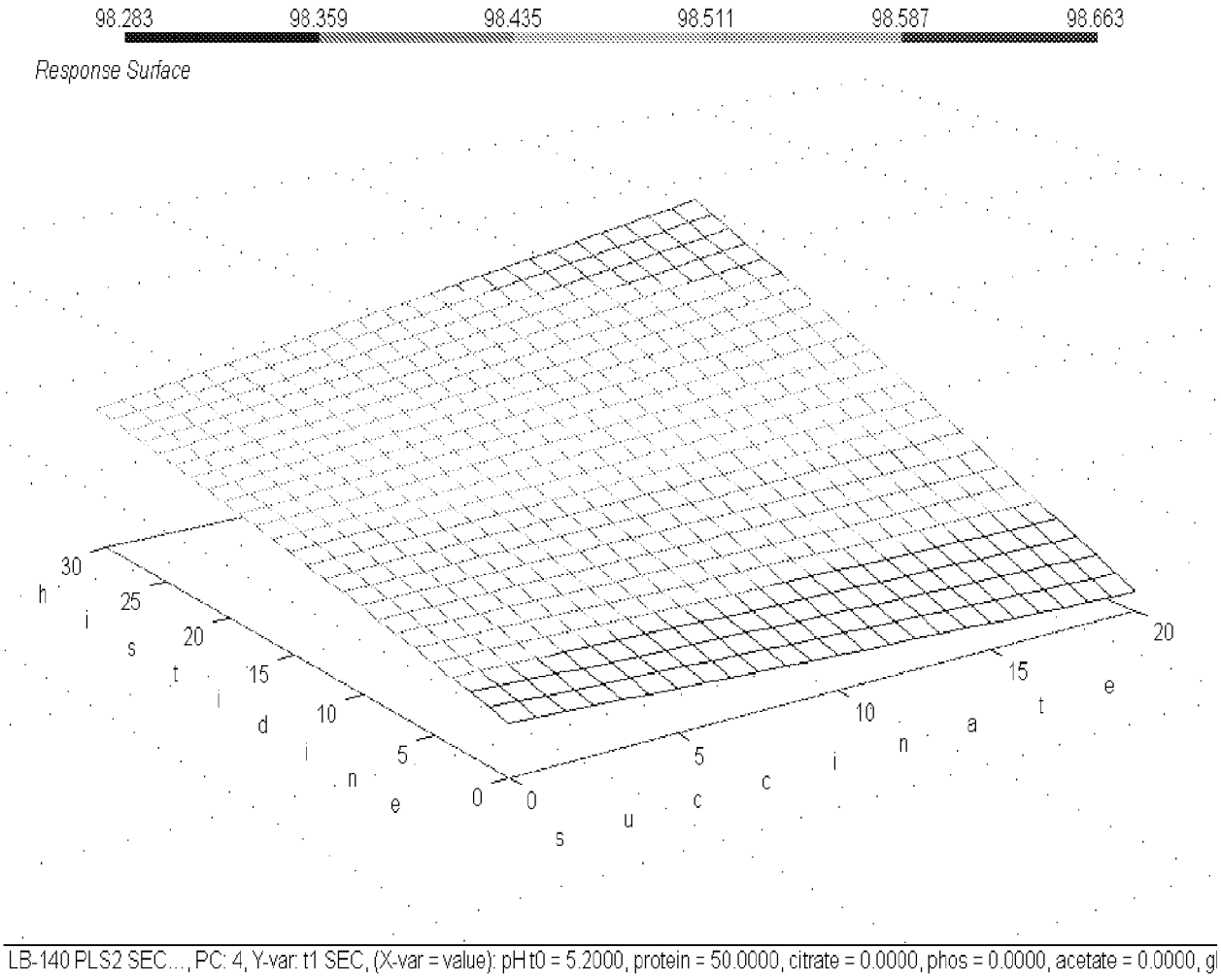
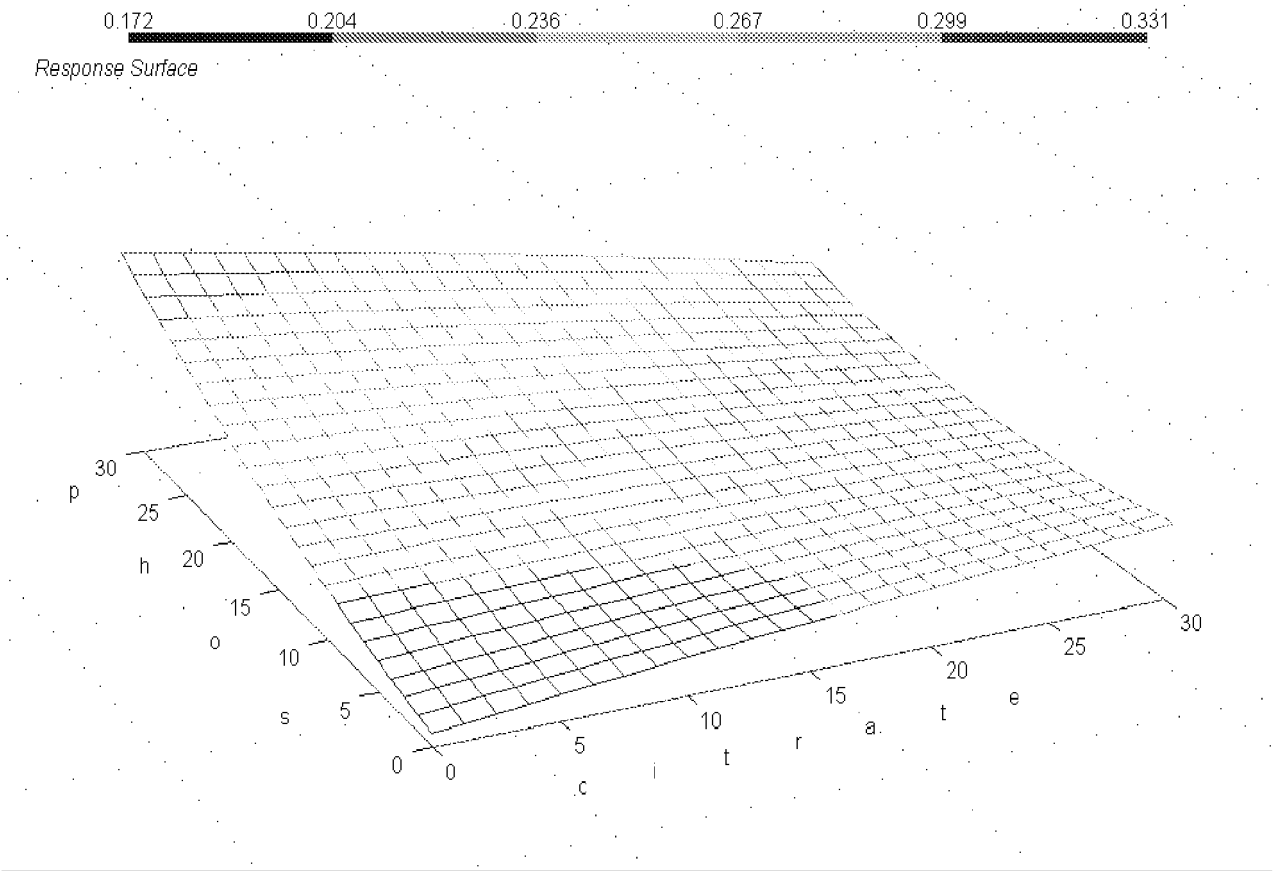


Figure 23

Effect of phosphate and citrate according to PLS model C using the difference in purity at t1 by RP HPLC as the endpoint. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml.



RESULT14, PC: 2, Y-var: t1 RP diff, (X-var = value): pH t0 = 5.2000, protein = 50.0000, succinate = 0.0000, histidine = 0.0000, acetate = 0.0000, gly

Figure 24

Effect of pH and His according to PLS model C using the difference in purity at t1 by RP HPLC as the endpoint. The protein concentration is fixed at 50 mg/ml.

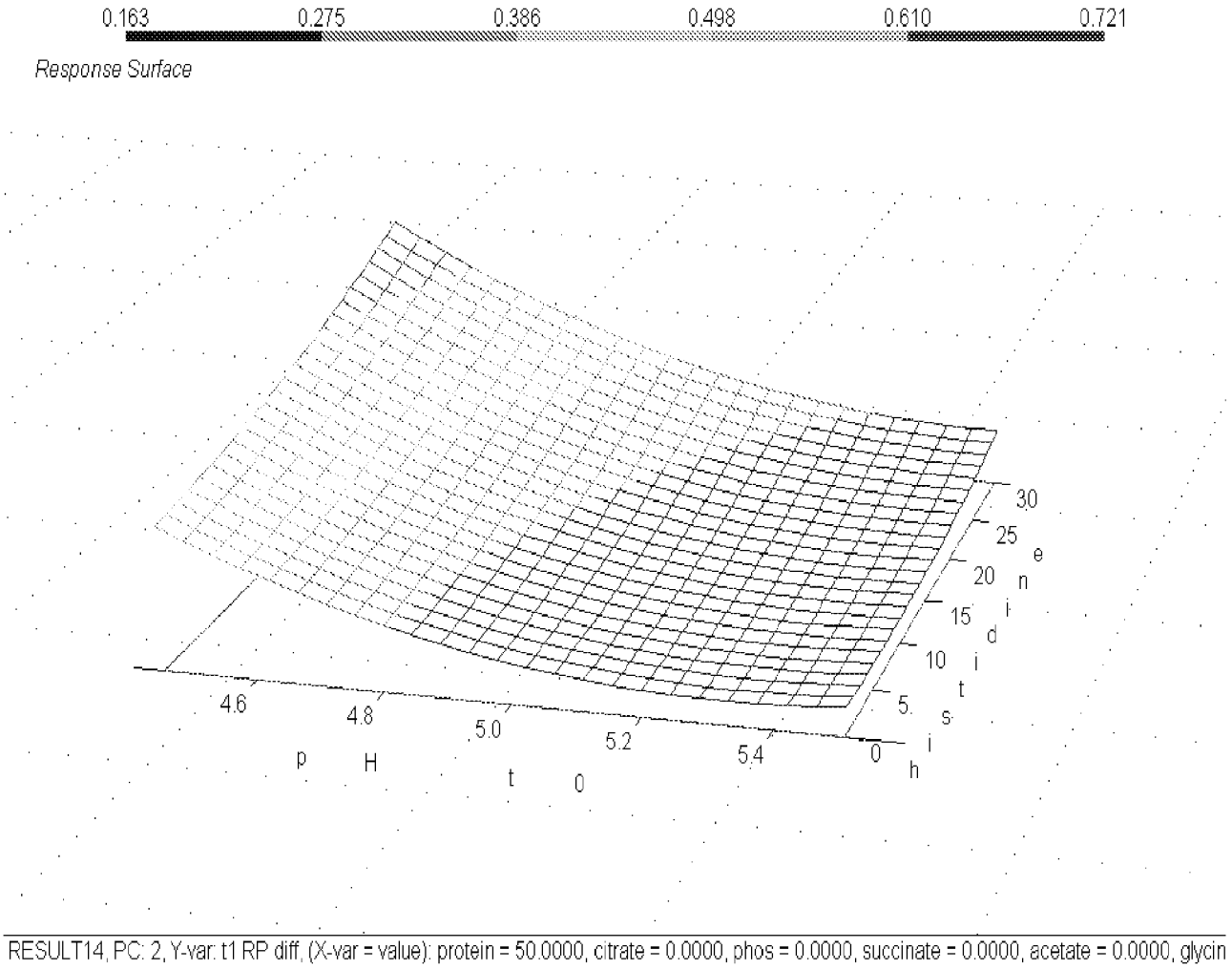


Figure 25

Effect of Arg and Gly according to PLS model C using the difference in purity at t1 by RP HPLC as the endpoint. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml.

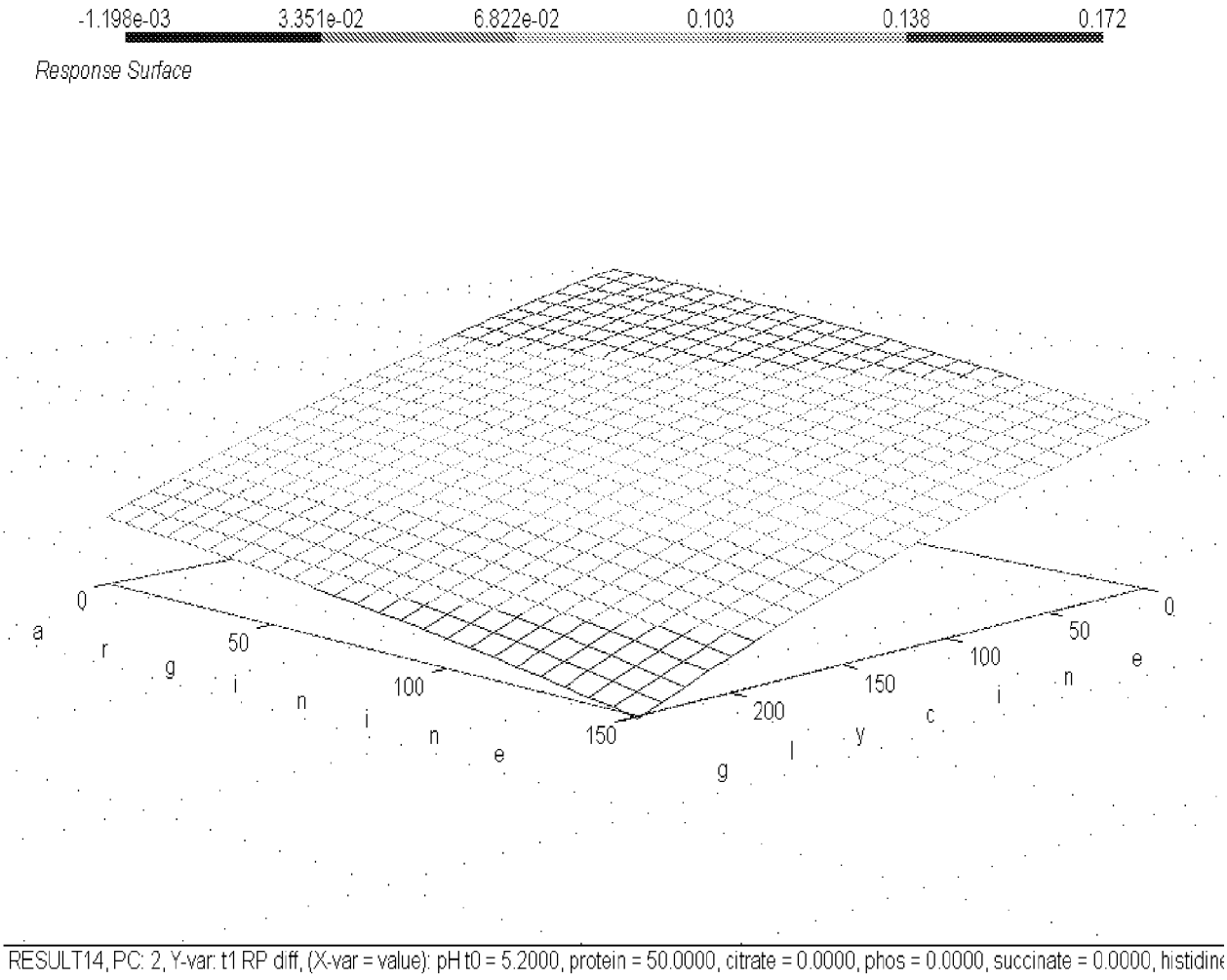
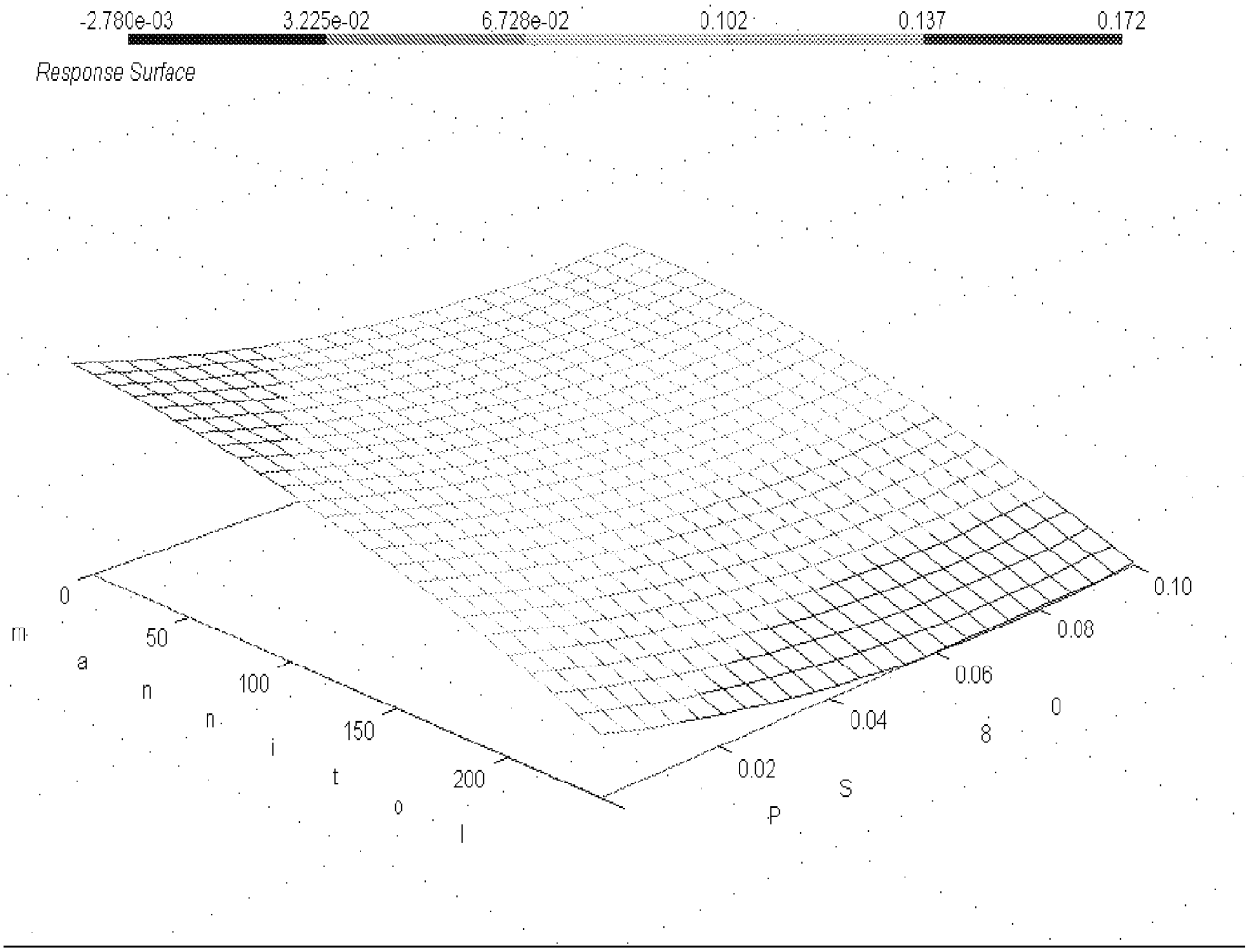


FIGURE 26

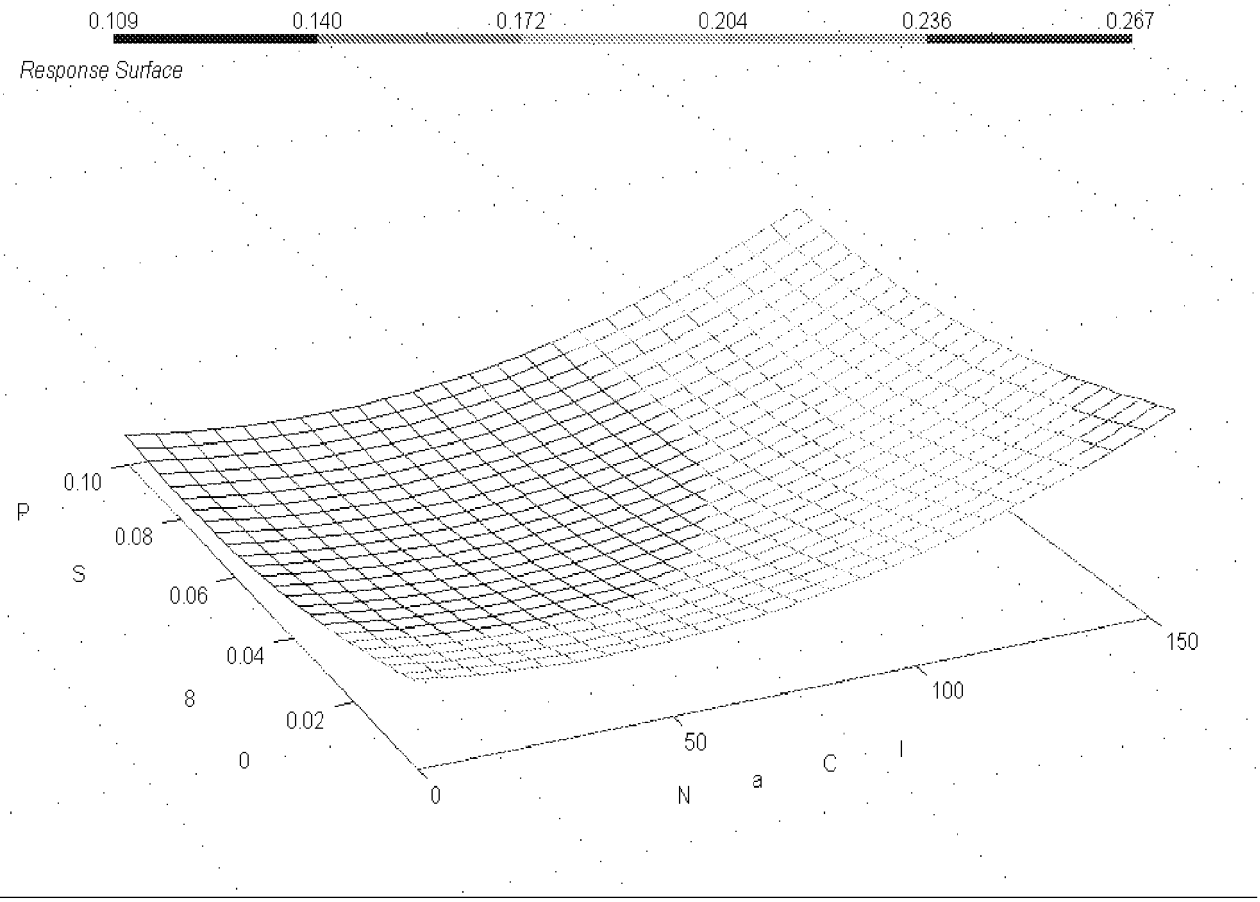
Effect of mannitol and PS 80 according to PLS model C using the difference in purity at t1 by RP HPLC as the endpoint. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml.



RESULT14, PC: 2, Y-var: t1 RP diff, (X-var = value): pH t0 = 5.2000, protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, histidine

FIGURE 27

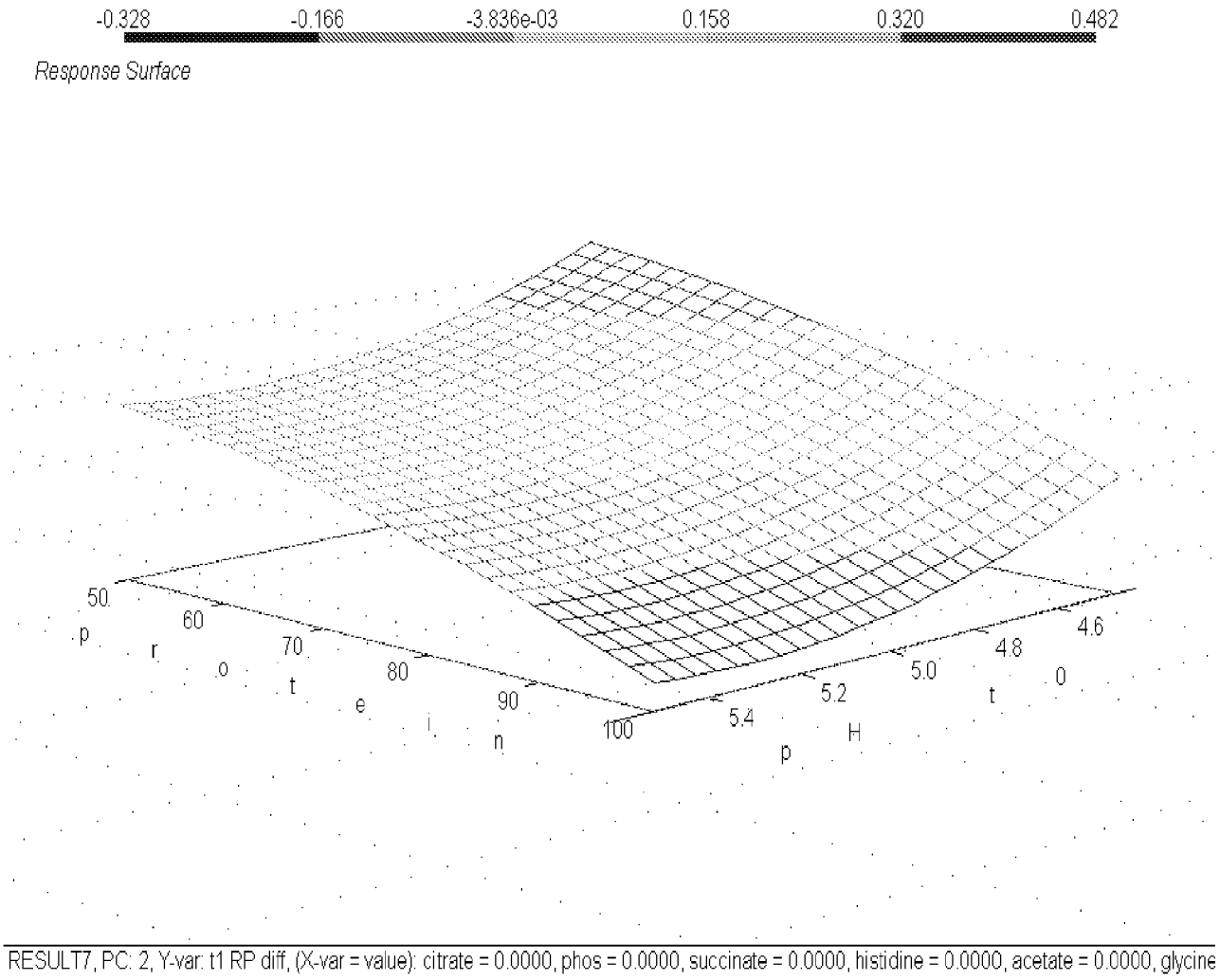
Effect of PS 80 and NaCl according to PLS model C using the difference in purity at t1 by RP HPLC as the endpoint. The pH is fixed at 5.2 and the protein concentration is set at 50 mg/ml.



RESULT14, PC: 2, Y-var: t1 RP diff, (X-var = value): pH t0 = 5.2000, protein = 50.0000, citrate = 0.0000, phos = 0.0000, succinate = 0.0000, histidine

FIGURE 28

Effect of pH and protein concentration according to PLS model C using the difference in purity at t1 by RP HPLC as the endpoint.



RESULT7, PC: 2, Y-var: t1 RP diff, (X-var = value): citrate = 0.0000, phos = 0.0000, succinate = 0.0000, histidine = 0.0000, acetate = 0.0000, glycine