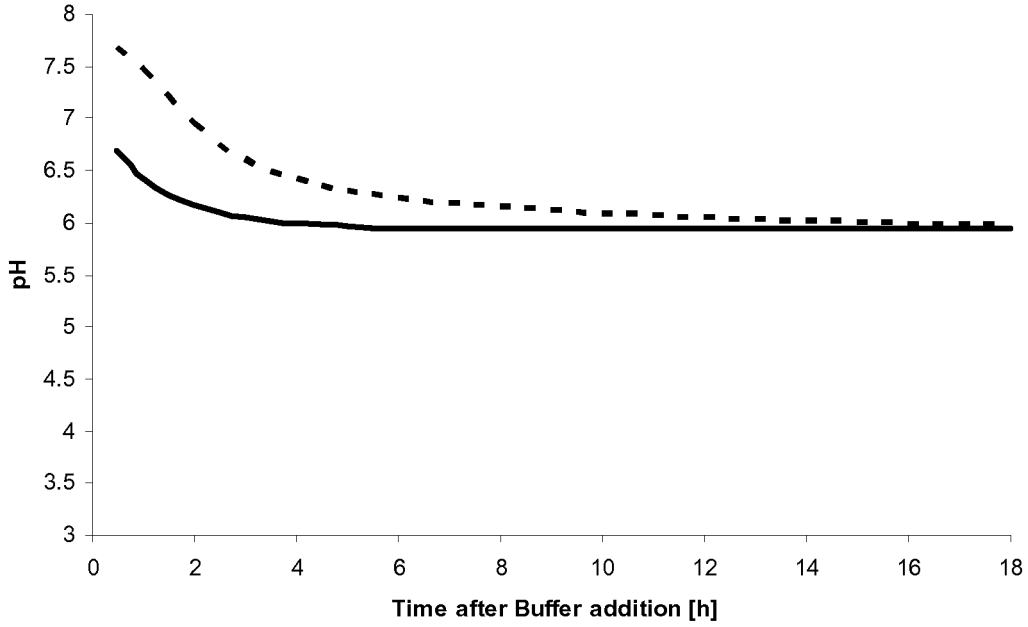

8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
pH
0
2
4
6
8
10
12
14
16
18
Time after Buffer addition [h]

Figure 1

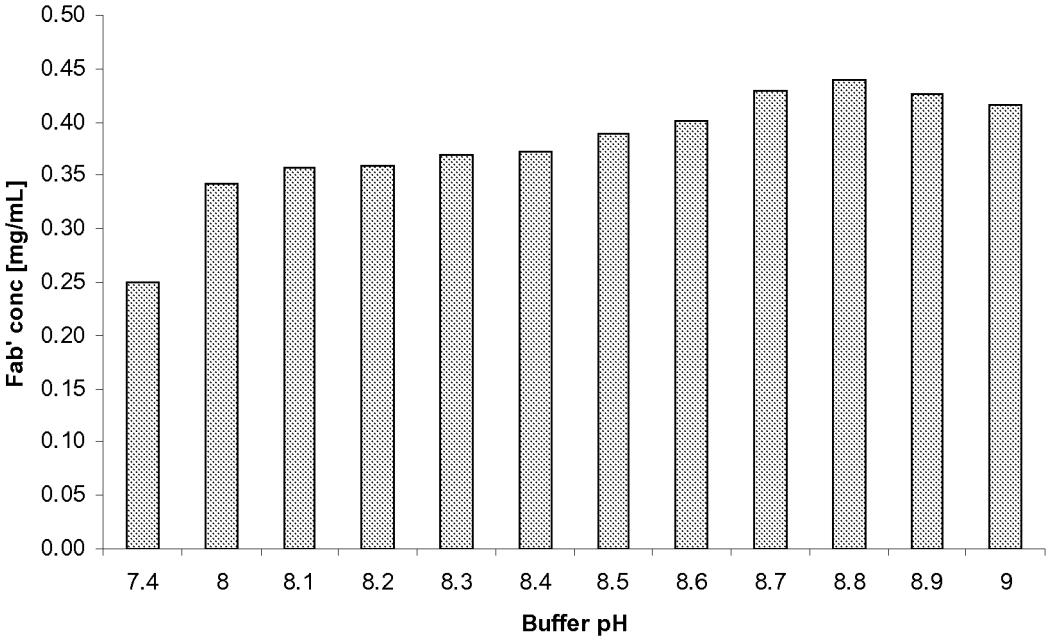


Figure 2a

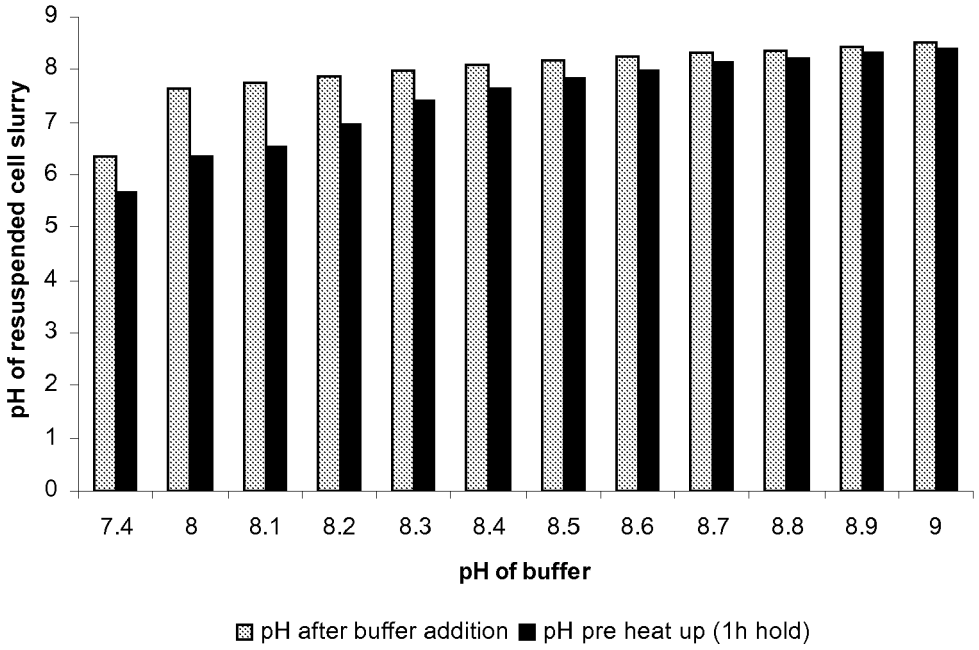


Figure 2b

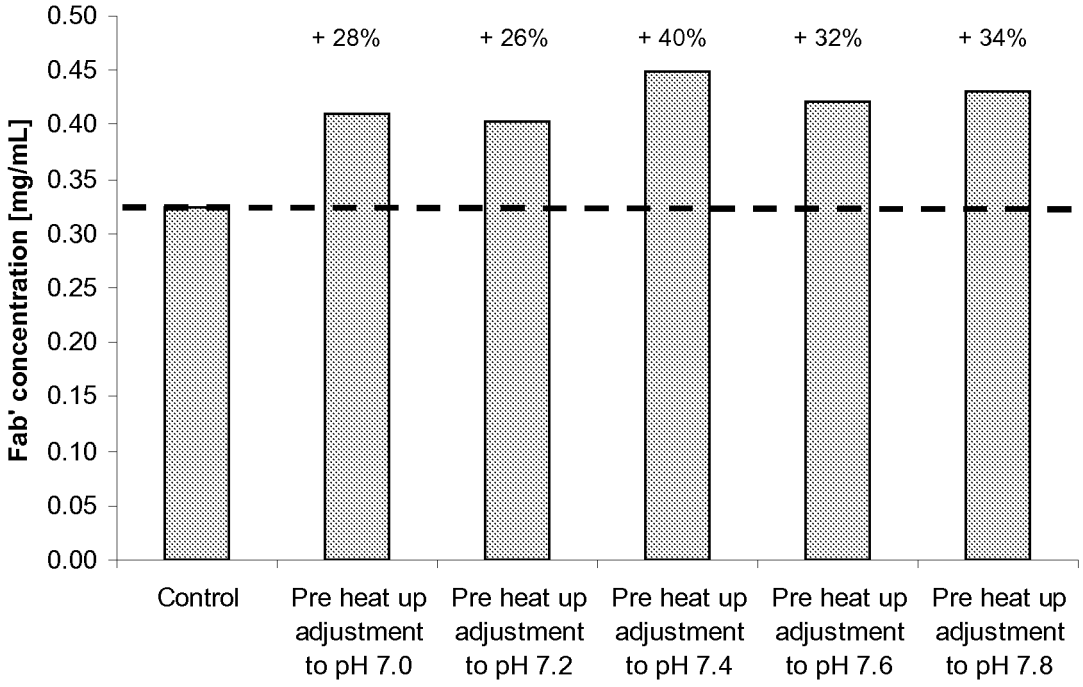

0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Fab' concentration [mg/mL]
+ 28%
+ 26%
+ 40%
+ 32%
+ 34%
Control
Pre heat up adjustment to pH 7.0
Pre heat up adjustment to pH 7.2
Pre heat up adjustment to pH 7.4
Pre heat up adjustment to pH 7.6
Pre heat up adjustment to pH 7.8

Figure 3a

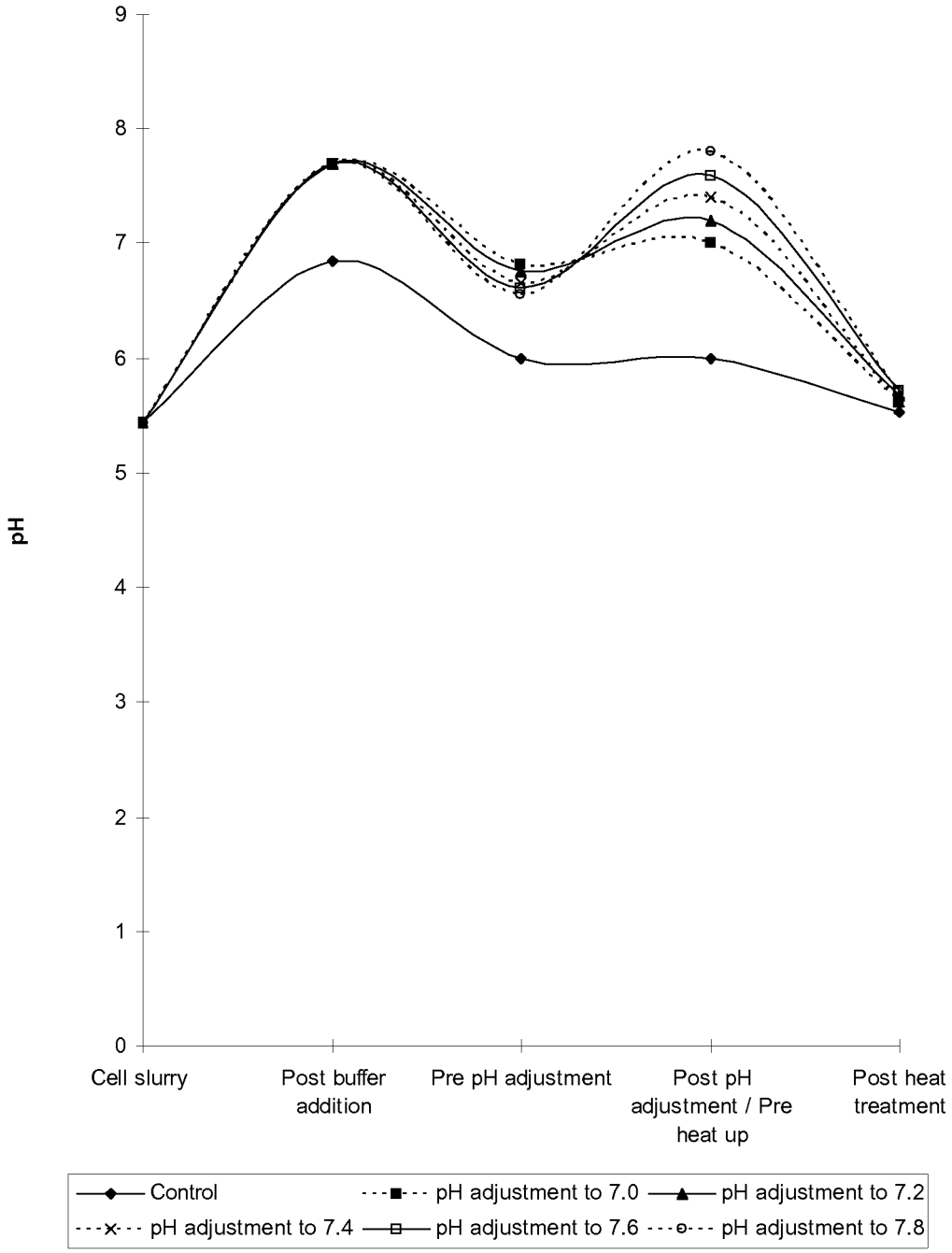

9
8
7
6
5
4
3
2
1
0
pH
Cell slurry
Post buffer addition
Pre pH adjustment
Post pH adjustment / Pre heat up
Post heat treatment
Control
pH adjustment to 7.0
pH adjustment to 7.2
pH adjustment to 7.4
pH adjustment to 7.6
pH adjustment to 7.8

Figure 3b

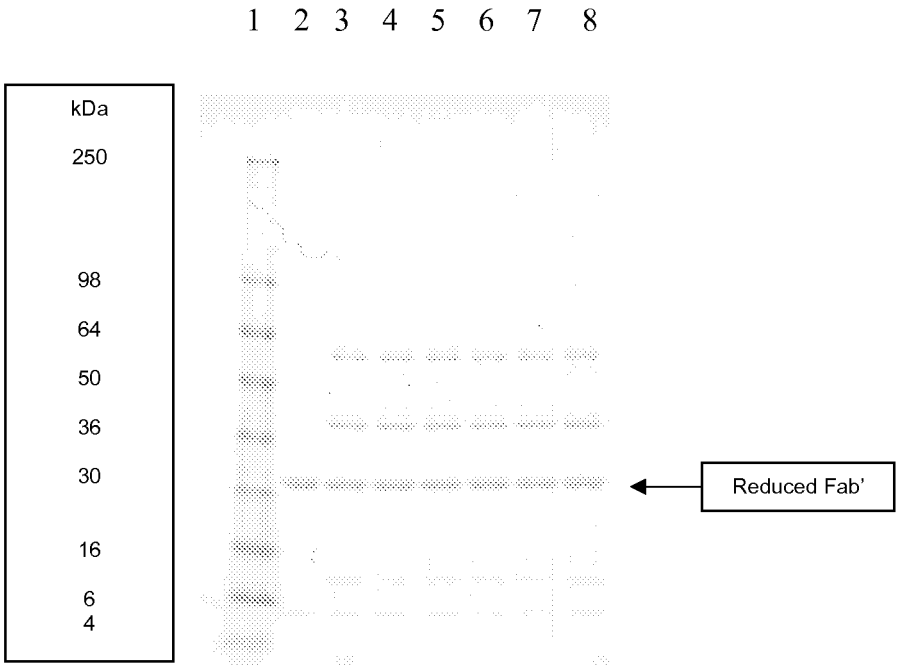


Figure 4

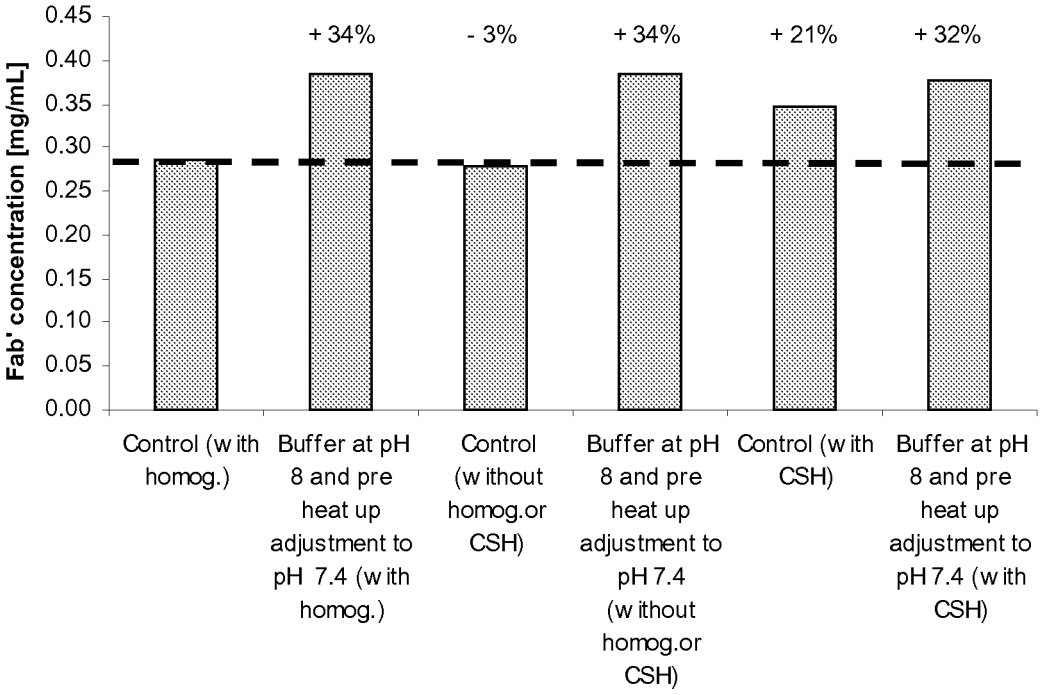

0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Fab' concentration [mg/mL]
+ 34%
- 3%
+ 34%
+ 21%
+ 32%
Control (with homog.)
Buffer at pH 8 and pre heat up adjustment to pH 7.4 (with homog.)
Control (without homog.or CSH)
Buffer at pH 8 and pre heat up adjustment to pH 7.4 (without homog.or CSH)
Control (with CSH)
Buffer at pH 8 and pre heat up adjustment to pH 7.4 (with CSH)

Figure 5

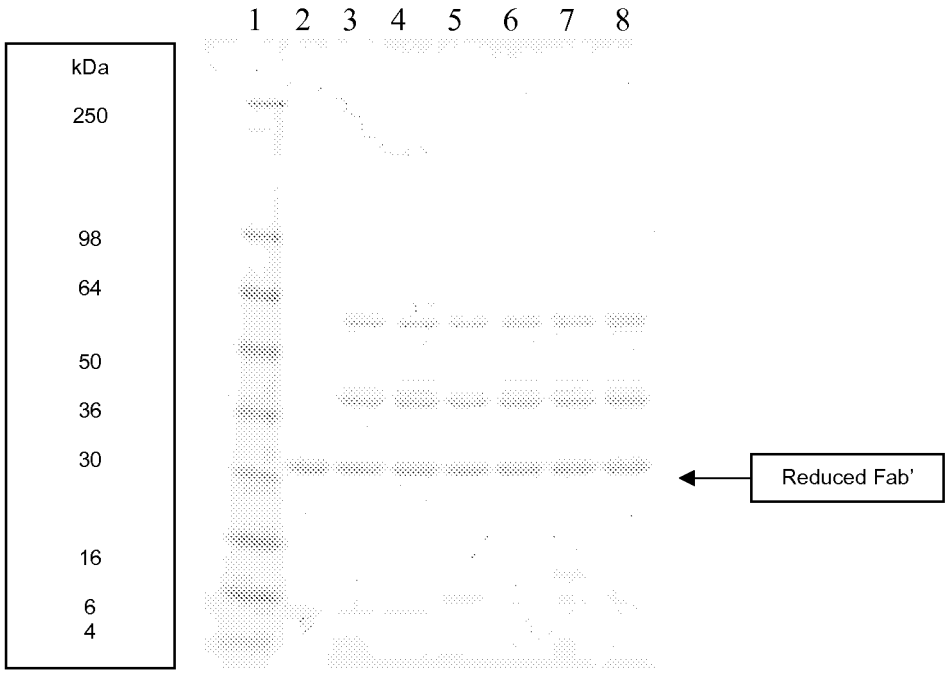
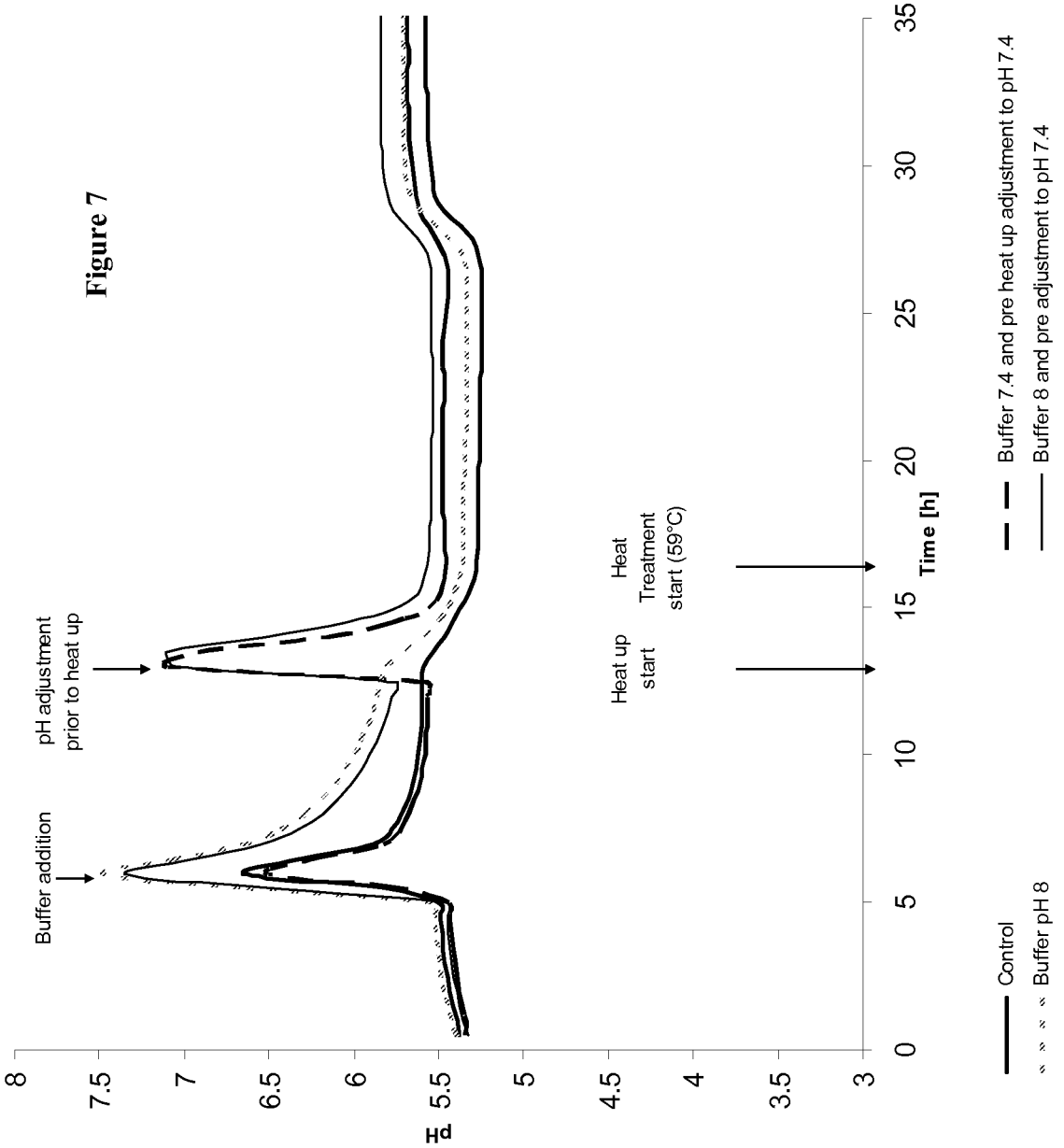


Figure 6

Figure 7


Buffer addition
pH adjustment prior to heat up
Heat up start
Heat Treatment start (59°C)
pH
Time [h]
Control
Buffer pH 8
Buffer 7.4 and pre heat up adjustment to pH 7.4
Buffer 8 and pre adjustment to pH 7.4

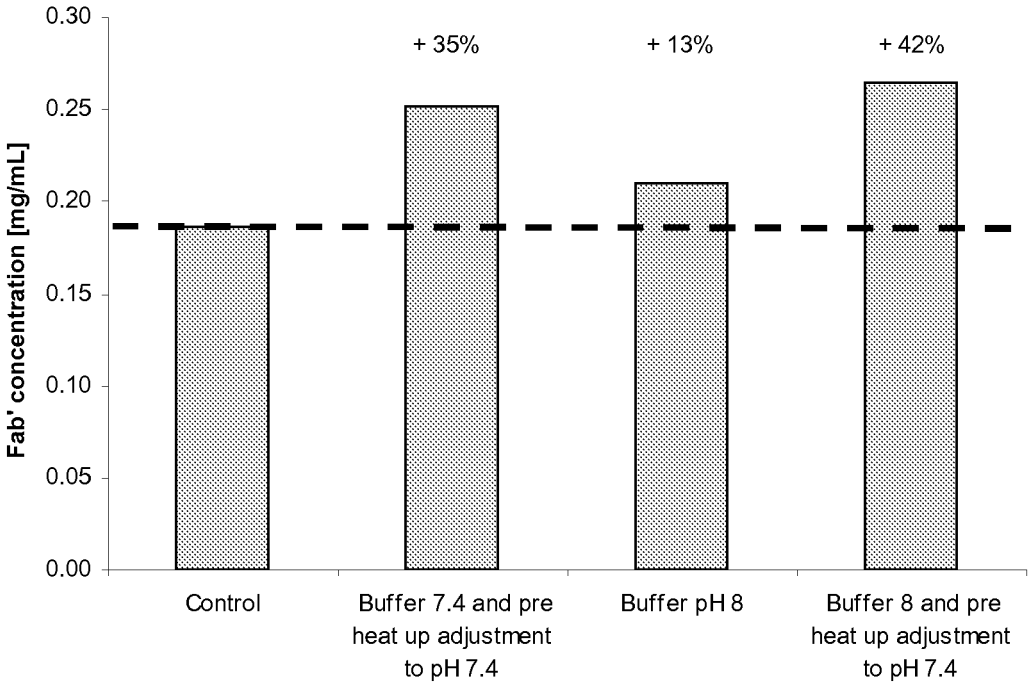

0.30
0.25
0.20
0.15
0.10
0.05
0.00
Fab' concentration [mg/mL]
+ 35%
+ 13%
+ 42%
Control
Buffer 7.4 and pre heat up adjustment to pH 7.4
Buffer pH 8
Buffer 8 and pre heat up adjustment to pH 7.4

Figure 8

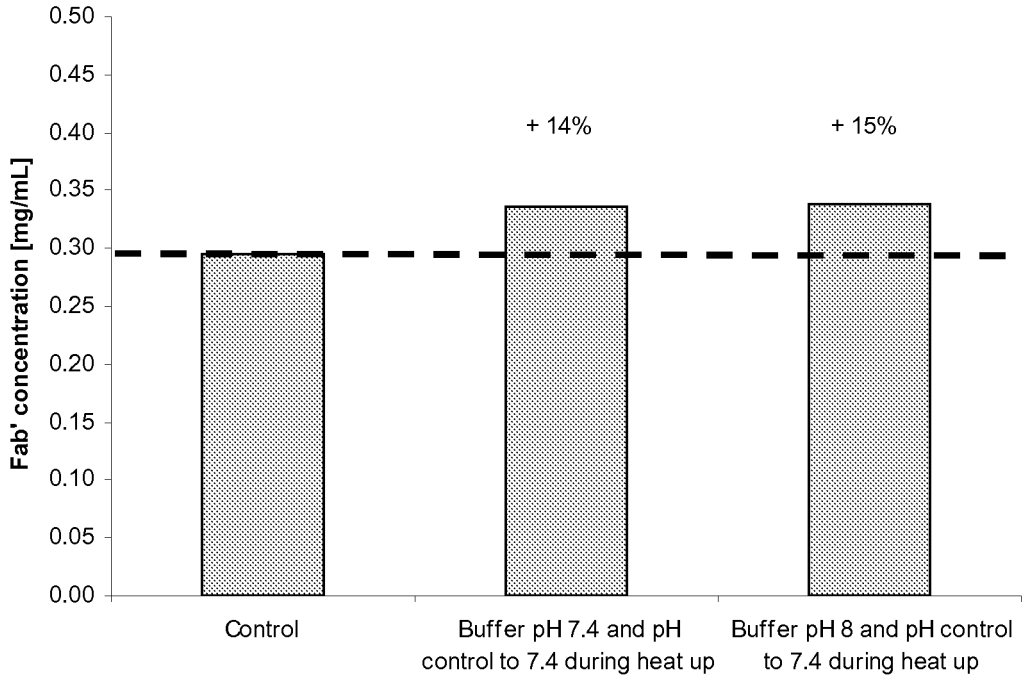

0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Fab' concentration [mg/mL]
+ 14%
+ 15%
Control
Buffer pH 7.4 and pH control to 7.4 during heat up
Buffer pH 8 and pH control to 7.4 during heat up

Figure 9

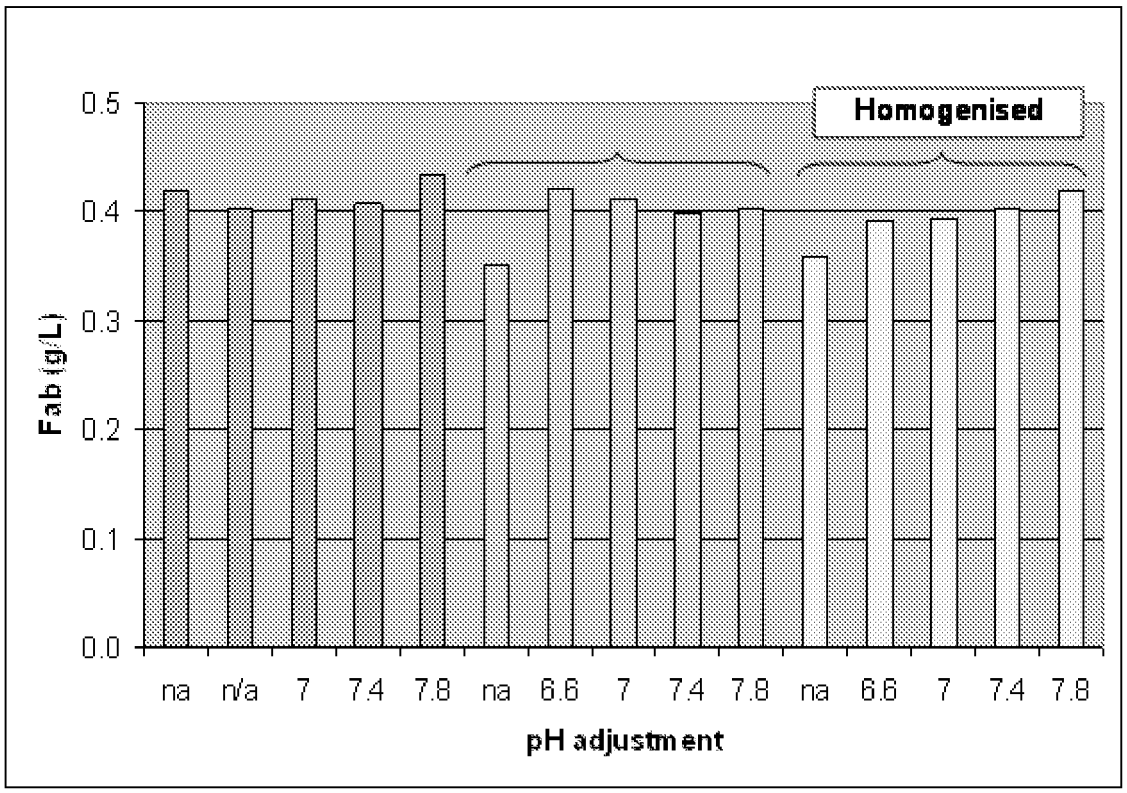


Figure 10

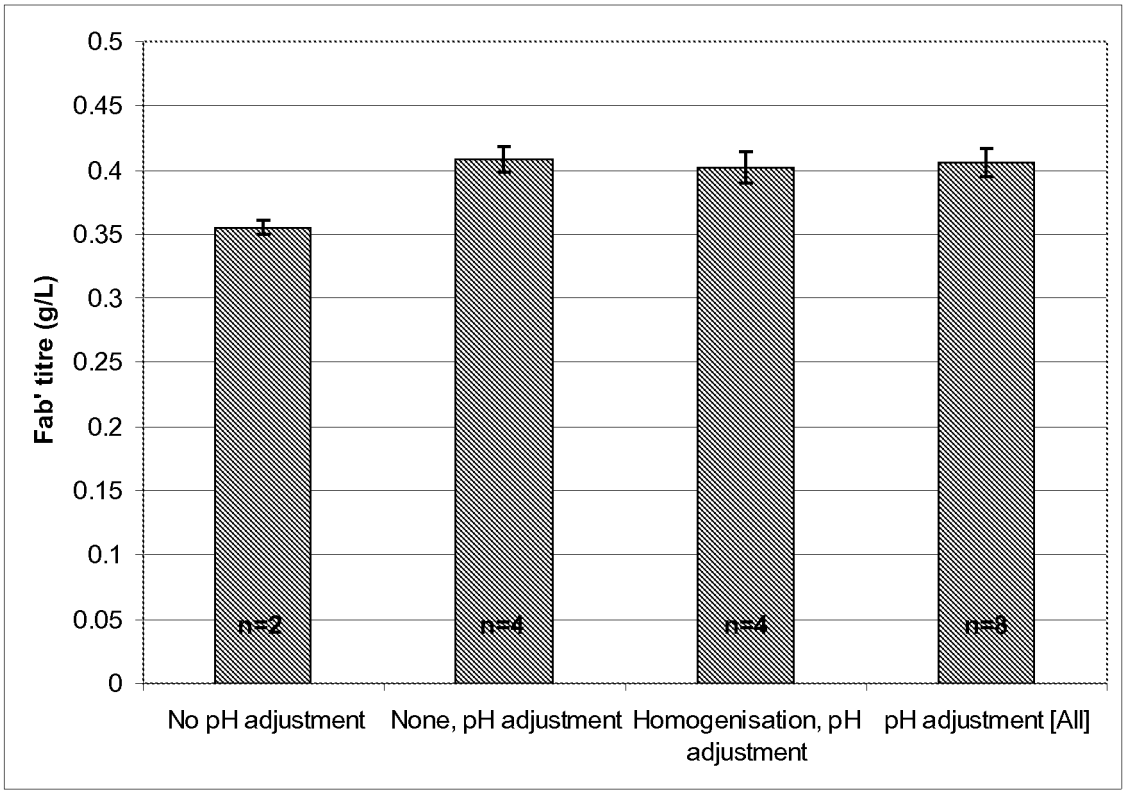


Figure 11