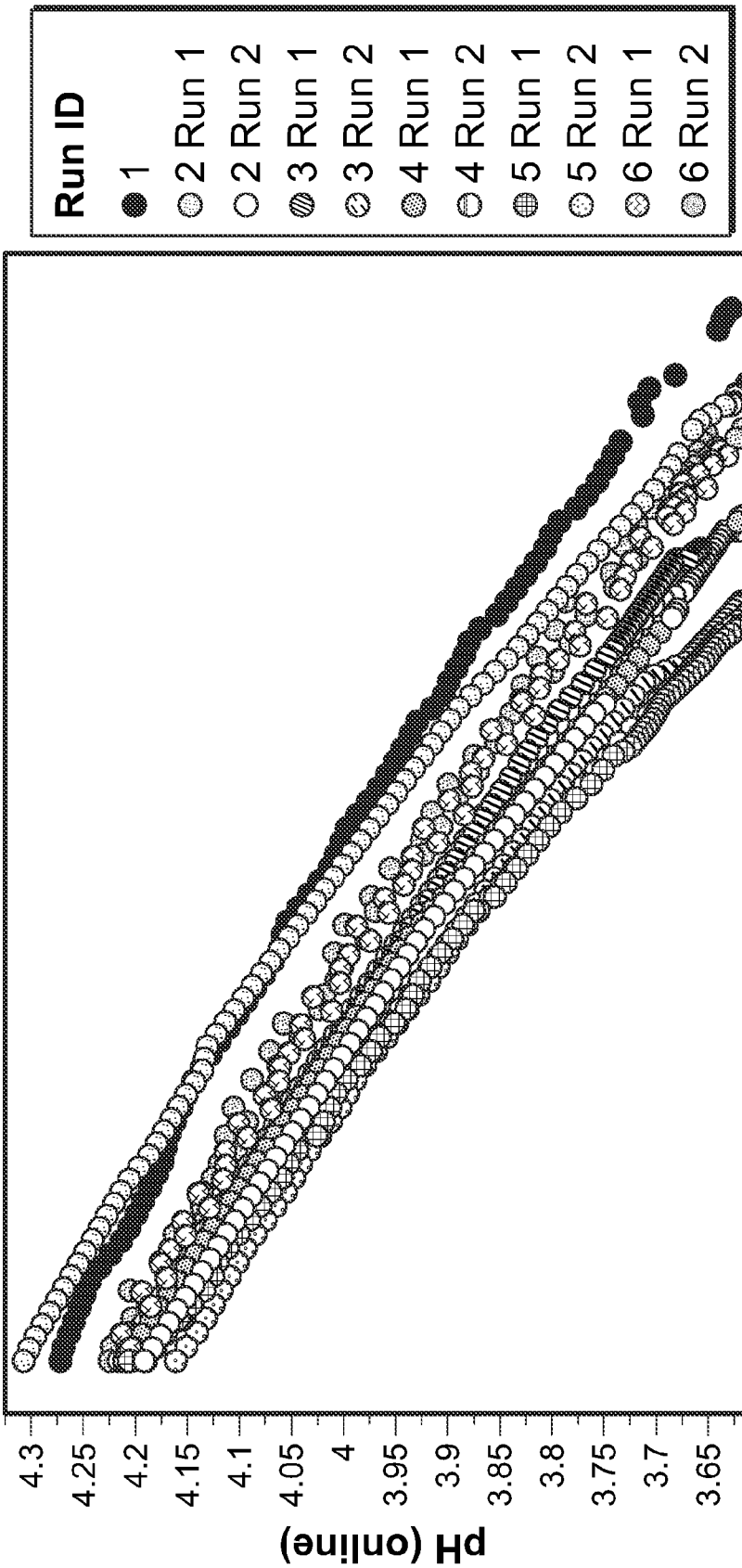

Run ID
1
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
6 Run 1
6 Run 2
pH (online)
4.3
4.25
4.2
4.15
4.1
4.05
4
3.95
3.9
3.85
3.8
3.75
3.7
3.65
3.6
0
1
2
3
4
5
6
7
8
9
10
Titrant Added (rot/kg)

FIG. 1

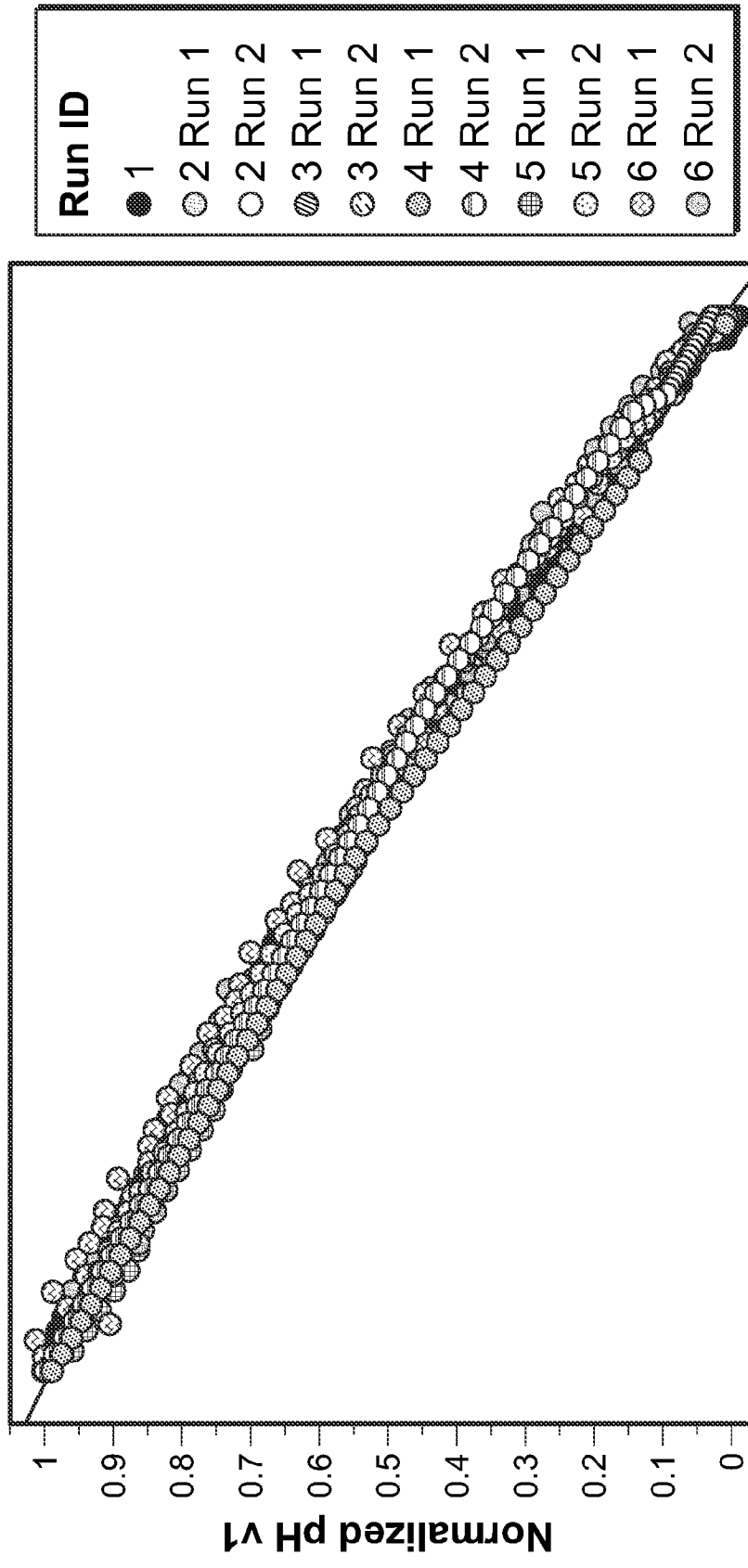
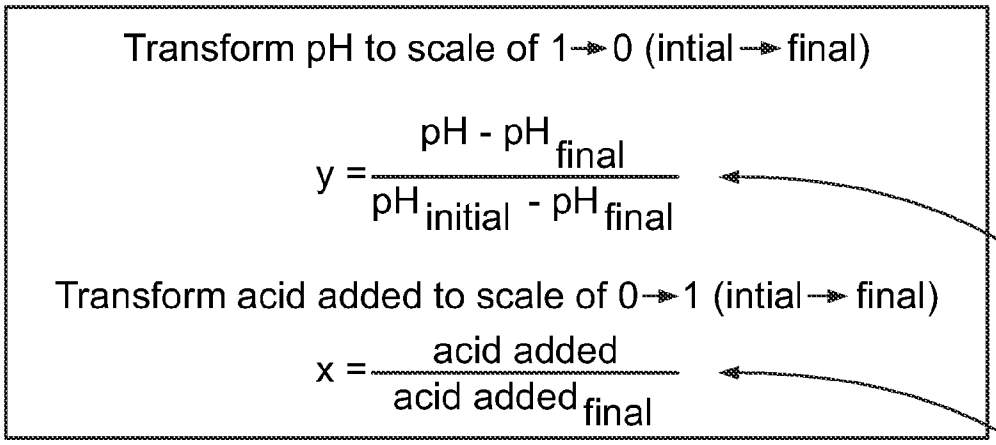

Run ID
1
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
6 Run 1
6 Run 2
Normalized pH v1
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Normalized Titrant Addition v1
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

FIG. 2




- RMSE of quadratic fit = 0.0175 normalized pH units
  - In pH units RMSE = $0.0175 * \left(\frac{4.2\text{-}3.6\ pH}{1}\right) = 0.011\ pH$

**How is the model used?**

1. Measure initial pH (autosample)
2. Add conservative amount of acid
3. Measure intermediate pH (autosample)
4. Calculate normalized intermediate pH
5. Calculate normalized acid added by solving polynomial fit
6. Calculate remaining acid to be added

FIG. 3

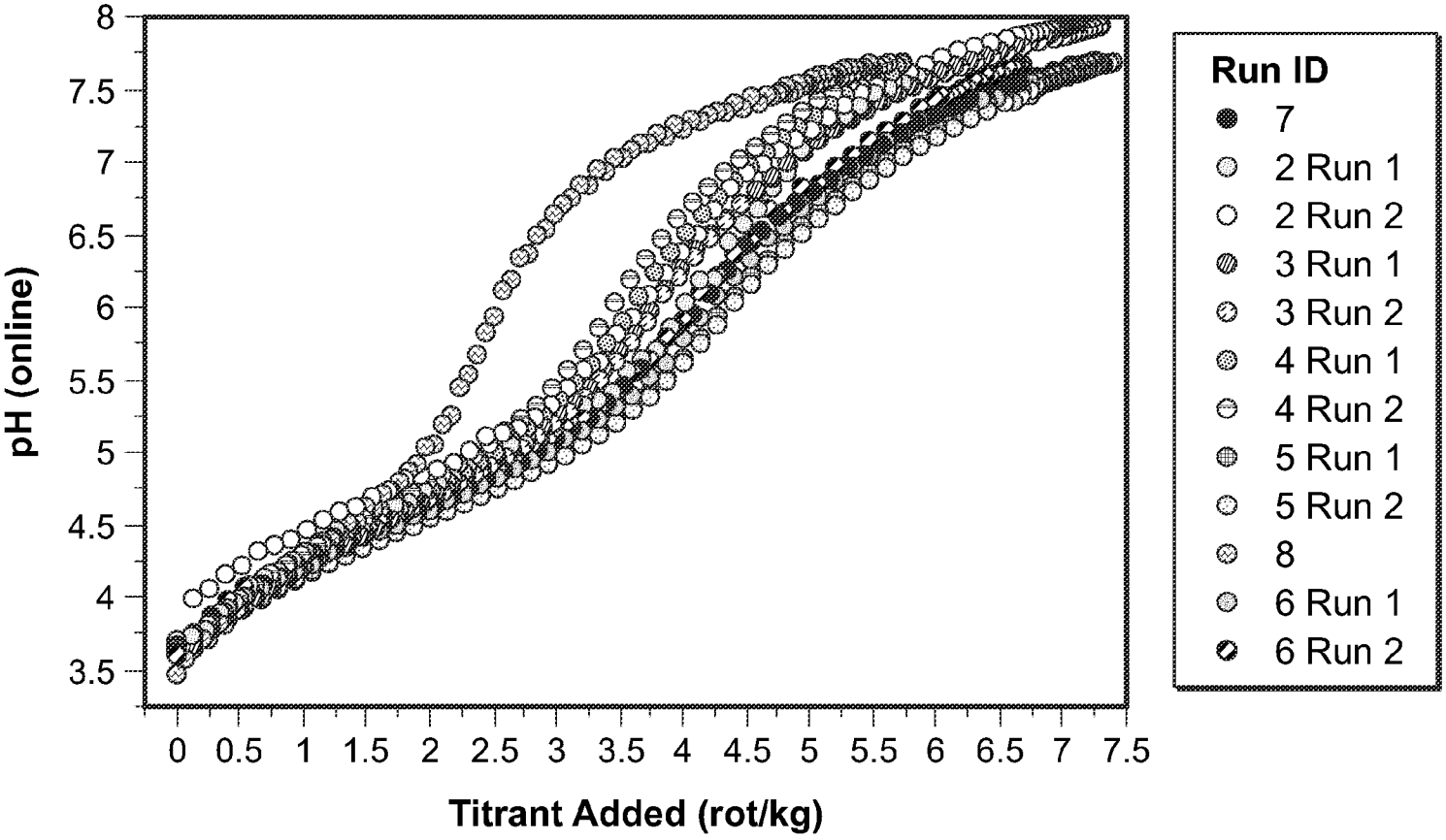

pH (online)
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5
Titrant Added (rot/kg)
Run ID
7
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
8
6 Run 1
6 Run 2

FIG. 4

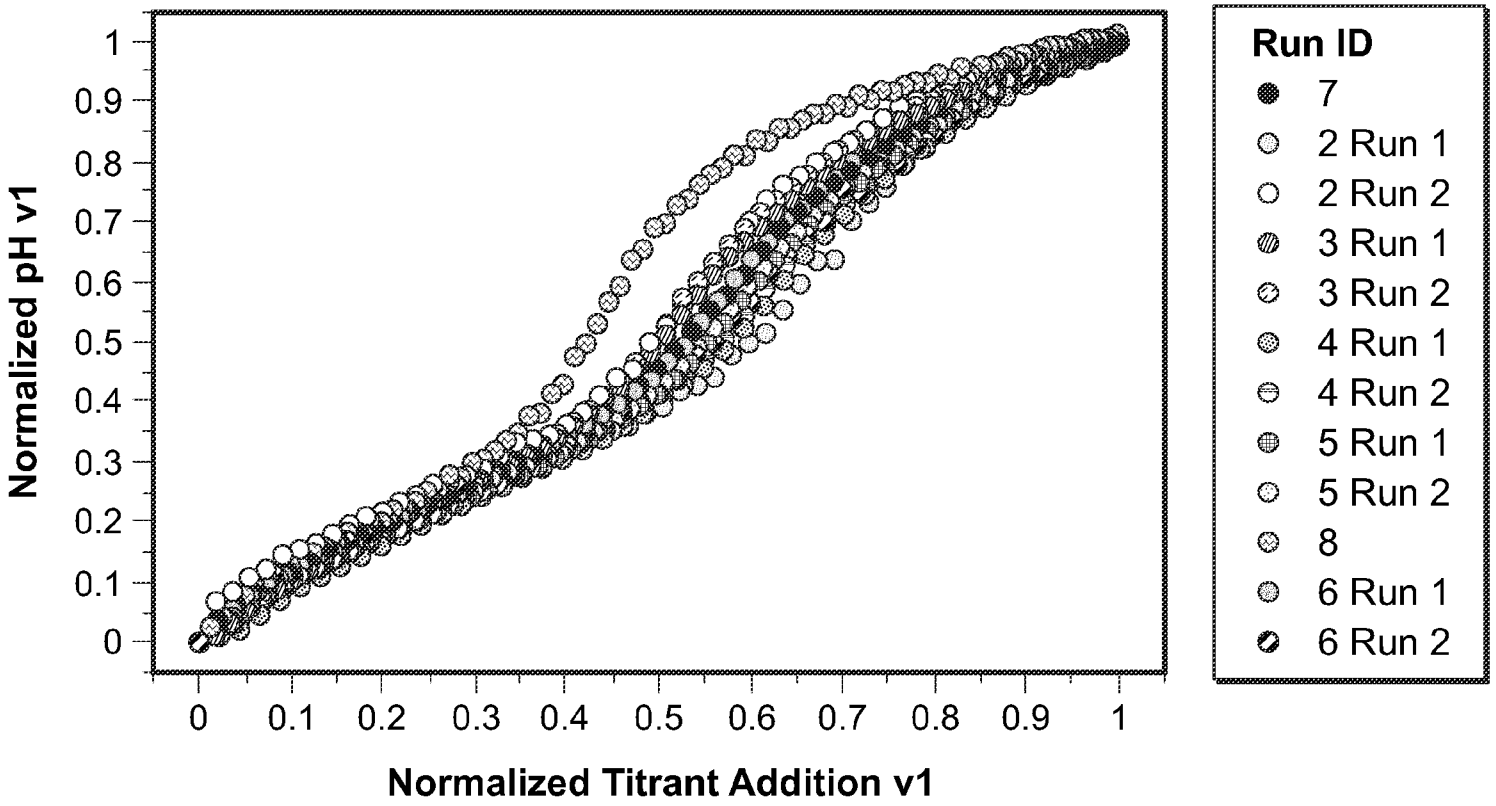

Normalized pH v1
Normalized Titrant Addition v1
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Run ID
7
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
8
6 Run 1
6 Run 2

FIG. 5

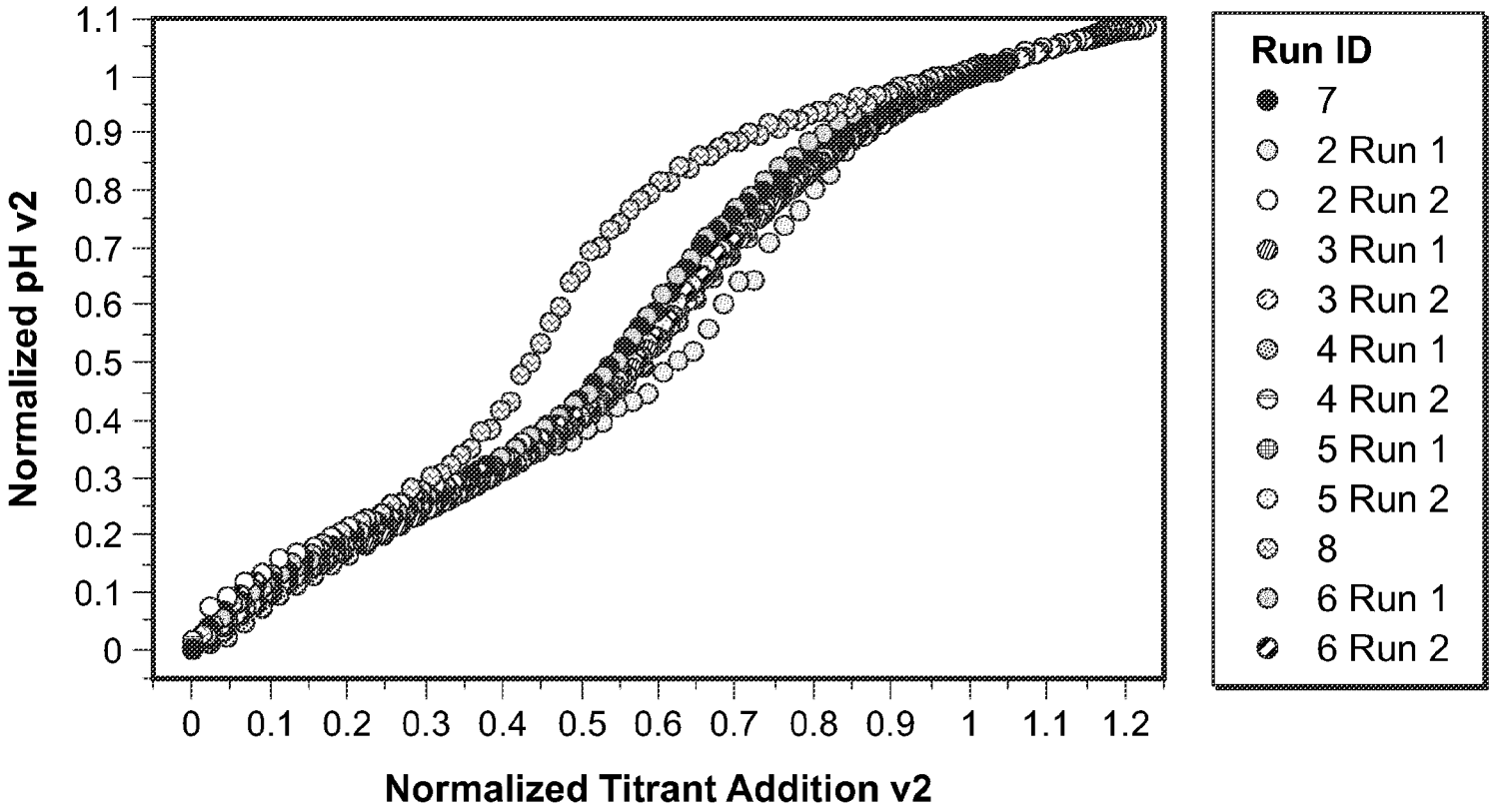

Normalized pH v2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 1.1 1.2
Normalized Titrant Addition v2
Run ID
7
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
8
6 Run 1
6 Run 2

FIG. 6

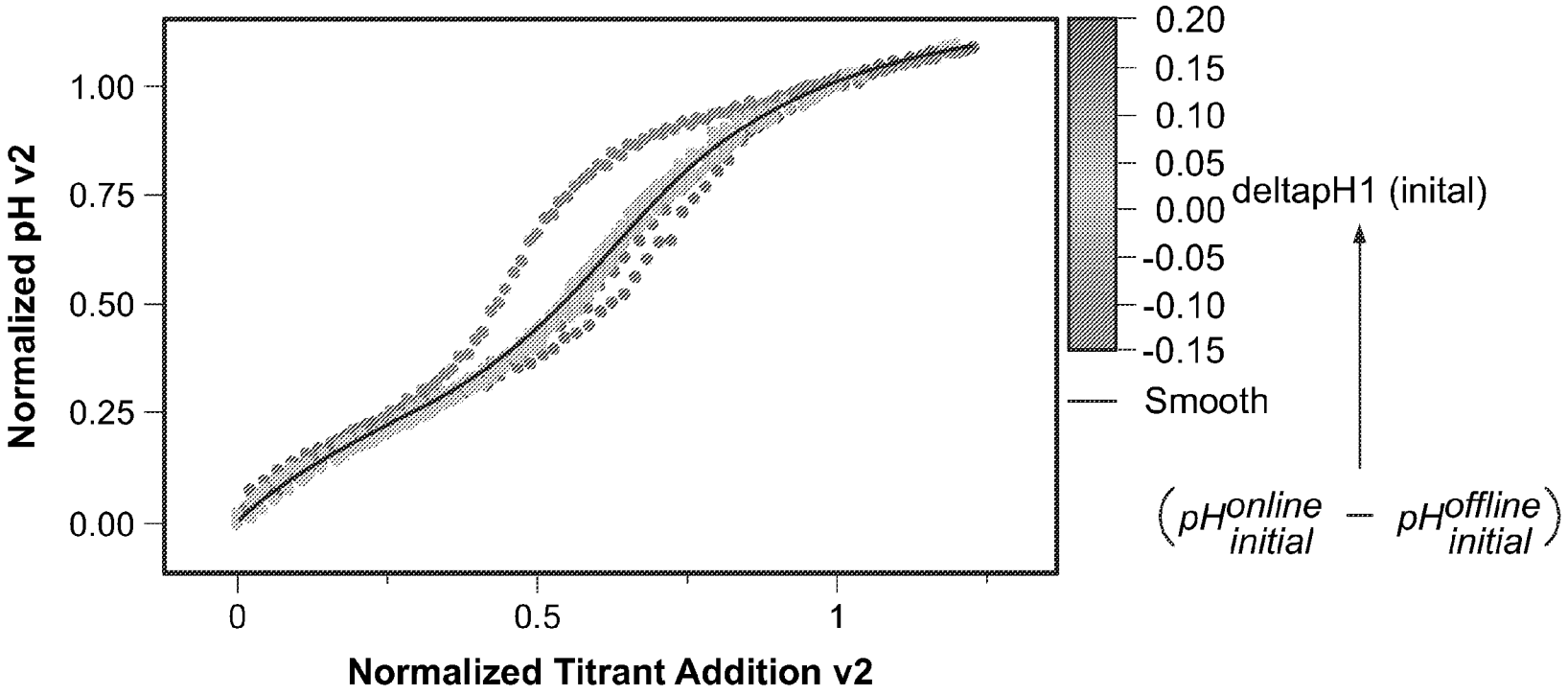

Normalized pH v2
1.00
0.75
0.50
0.25
0.00
0
0.5
1
Normalized Titrant Addition v2
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
deltapH1 (inital)
Smooth
$(pH^{online}_{initial} - pH^{offline}_{initial})$

FIG. 7

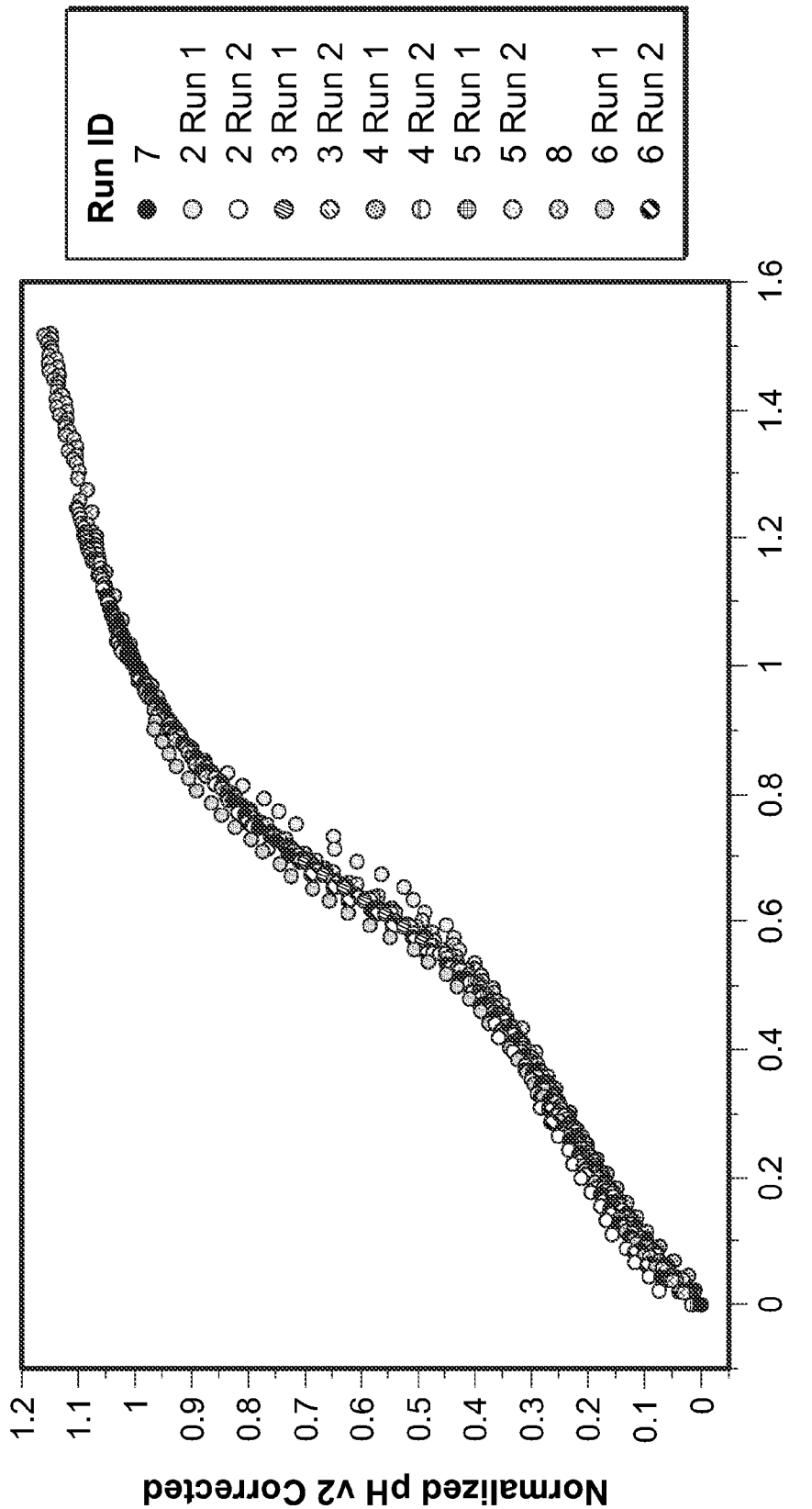

Run ID
7
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
8
6 Run 1
6 Run 2
Normalized pH v2 Corrected
Normalized Titrant Addition v2 Corrected
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6

FIG. 8

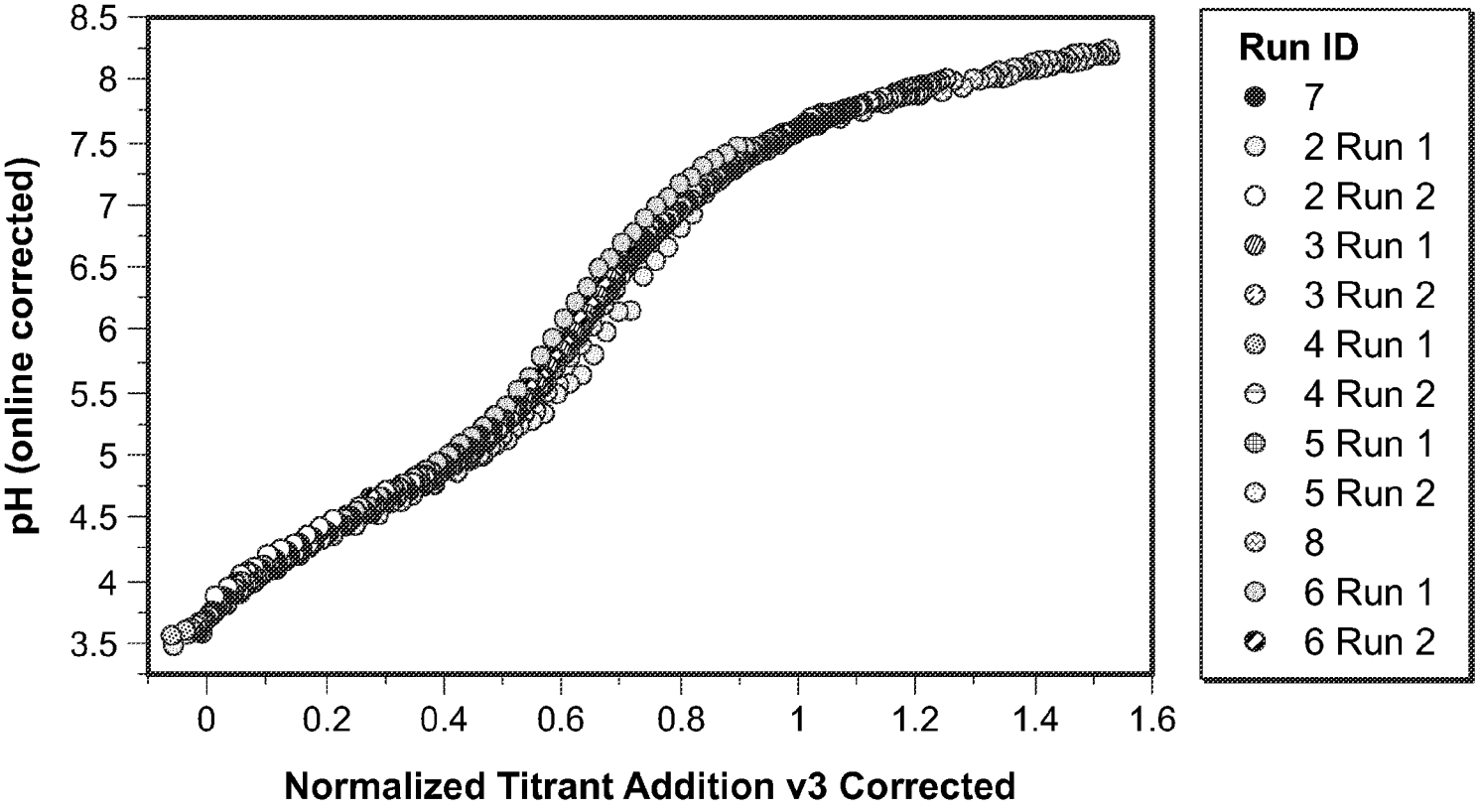

pH (online corrected)
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
Normalized Titrant Addition v3 Corrected
Run ID
7
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
8
6 Run 1
6 Run 2

FIG. 9

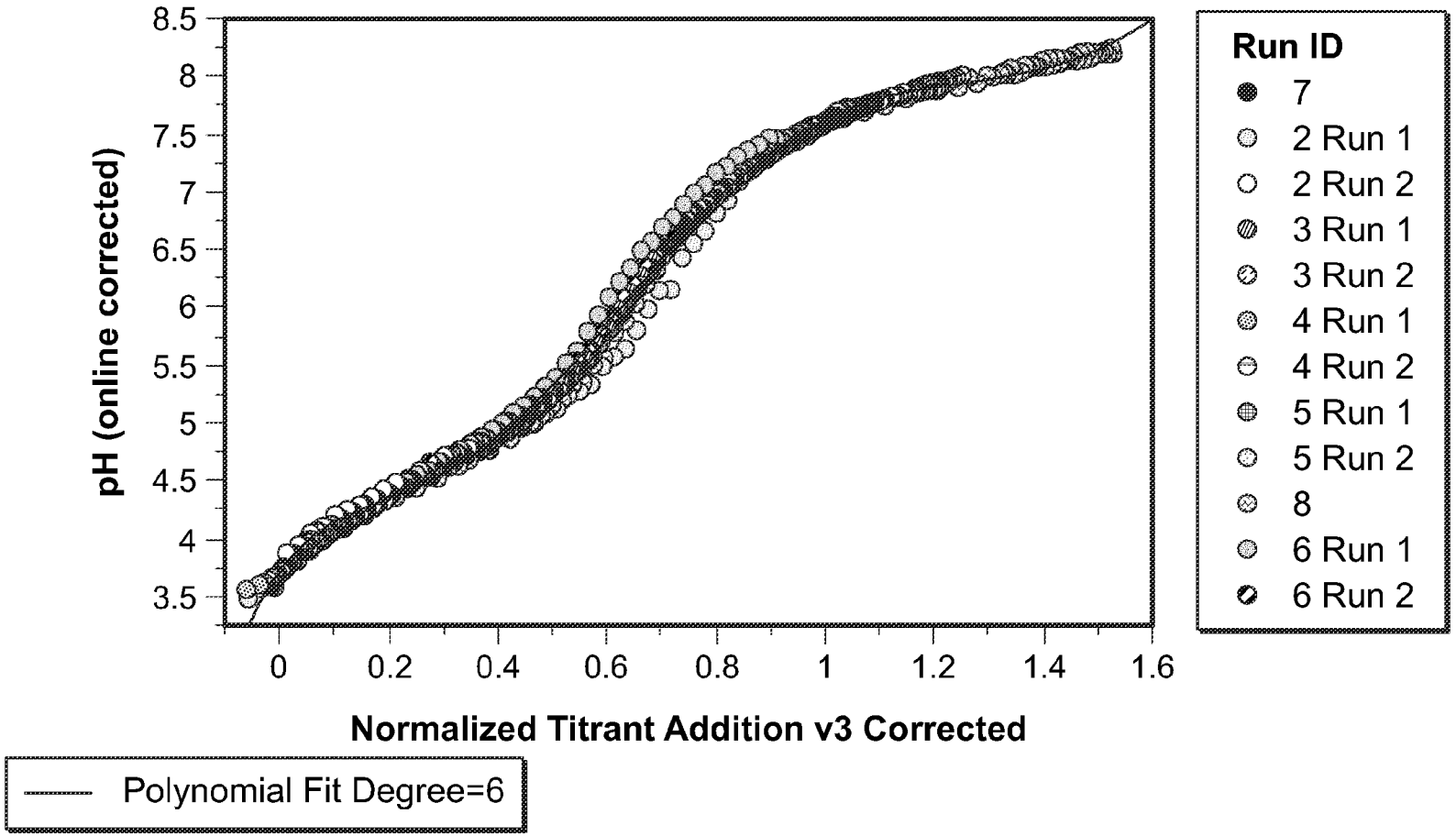

8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
pH (online corrected)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
Normalized Titrant Addition v3 Corrected
Run ID
7
2 Run 1
2 Run 2
3 Run 1
3 Run 2
4 Run 1
4 Run 2
5 Run 1
5 Run 2
8
6 Run 1
6 Run 2
Polynomial Fit Degree=6

FIG. 10

| Components | Signals |
|---|---|
| 2 x Watson Marlow 530 pumps | Speed Setpoint (AO)<br>Speed Feedback (AI)<br>On/Off (DO) |
| 1 x Watson Marlow 120 pump | Speed Setpoint (AO)<br>Speed Feedback (AI)<br>On/Off (DO) |
| 2 x Sonotec CO.55 ultrasonic flow meters | Autozero (DO)<br>Volume Pulse (DI) |
| 1 x Mettler M400 pH transmitter | pH (AI)<br>Temperature (AI)<br>mV (AI) |
| 1 x Mettler pH flow cell | N/A |
| 1 x imPULSE mixer control cable | Speed Setpoint (AO)<br>On/Off (DO) |
| 3 x Ethernet I/O modules | N/A |

FIG. 11

**Process Flow – Acid Adjustment**
Control Strategy for Slip-Stream Approach

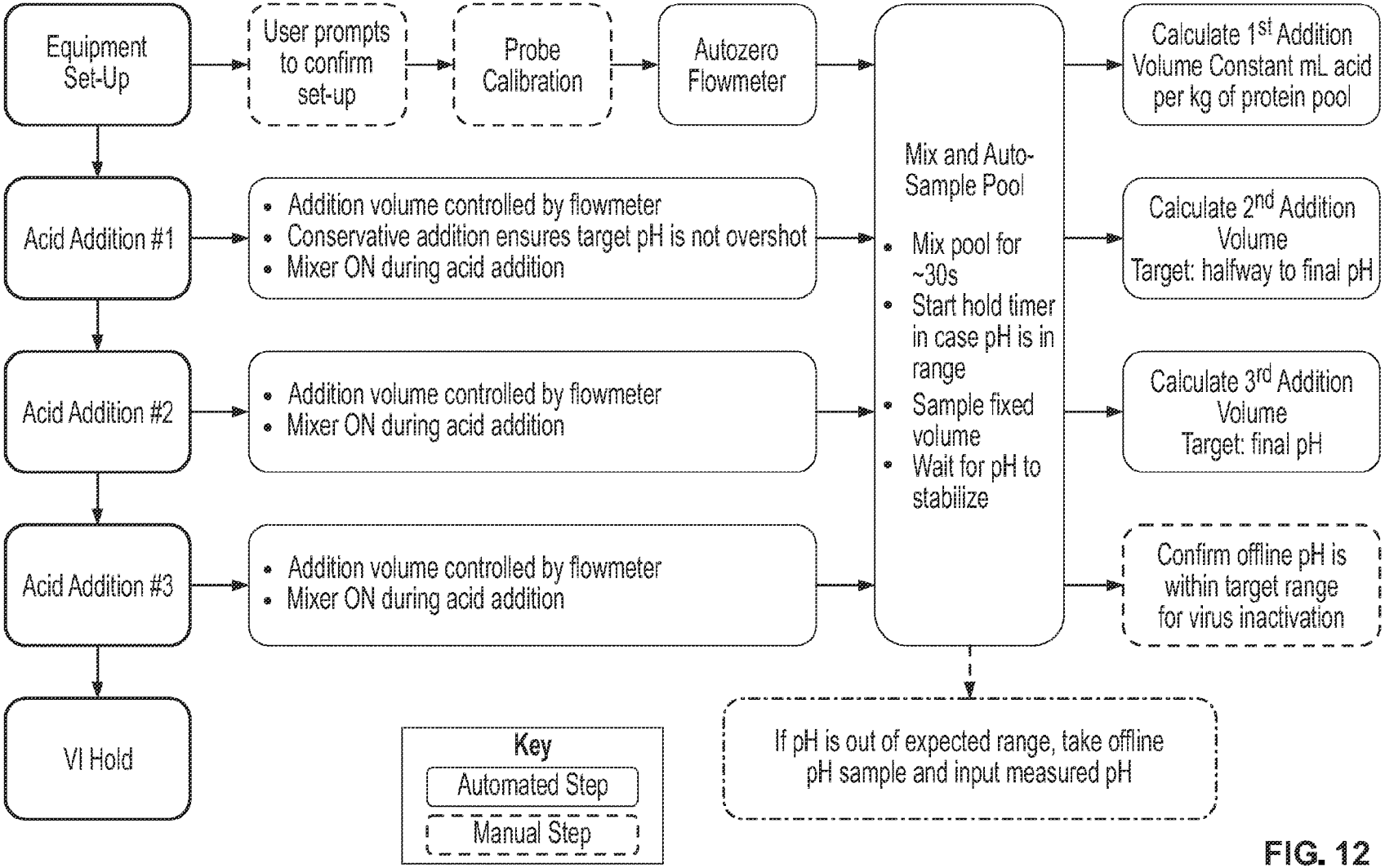



FIG. 12

**Process Flow – Base Adjustment**
Control Strategy for Slip-Stream Approach

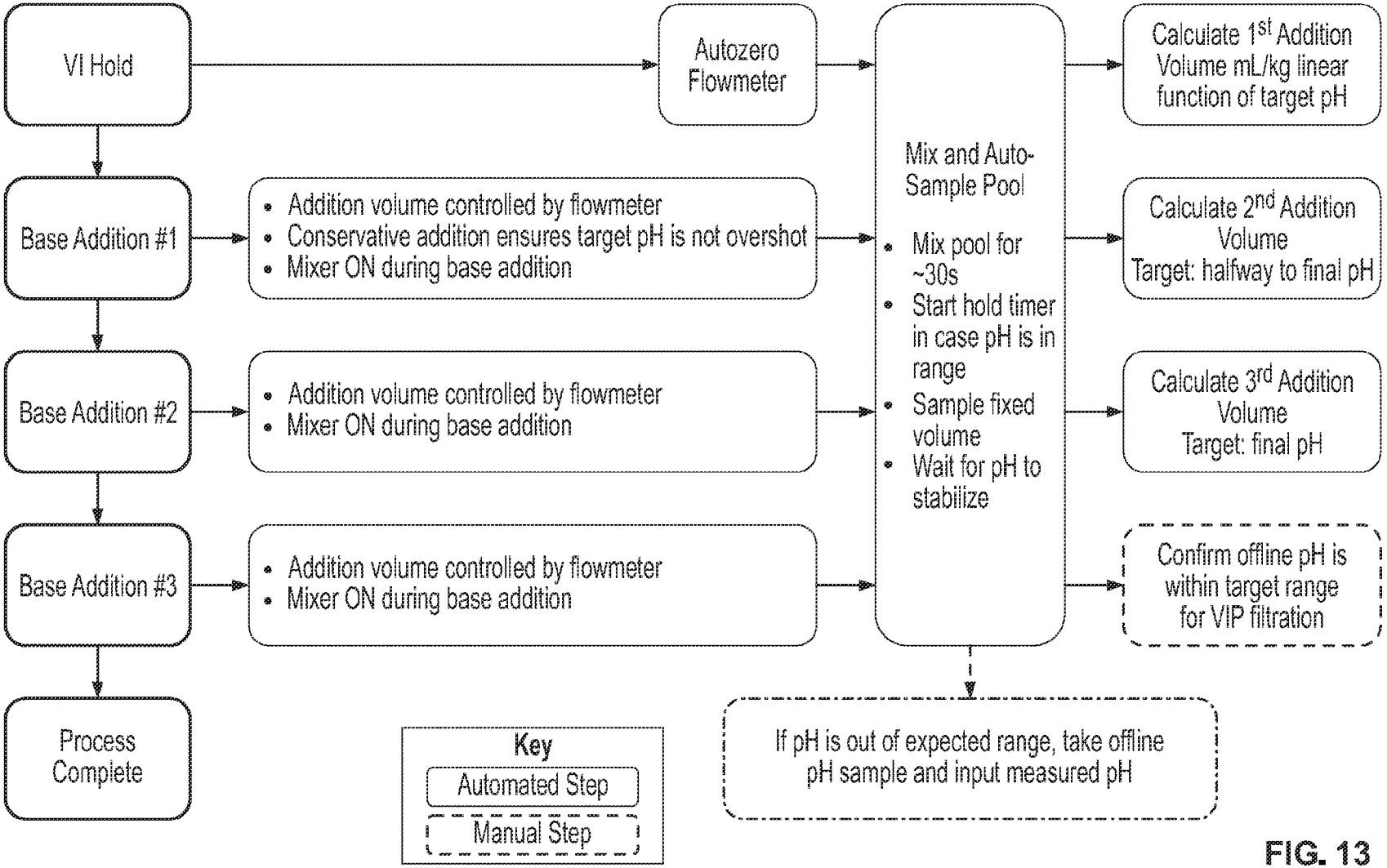



FIG. 13

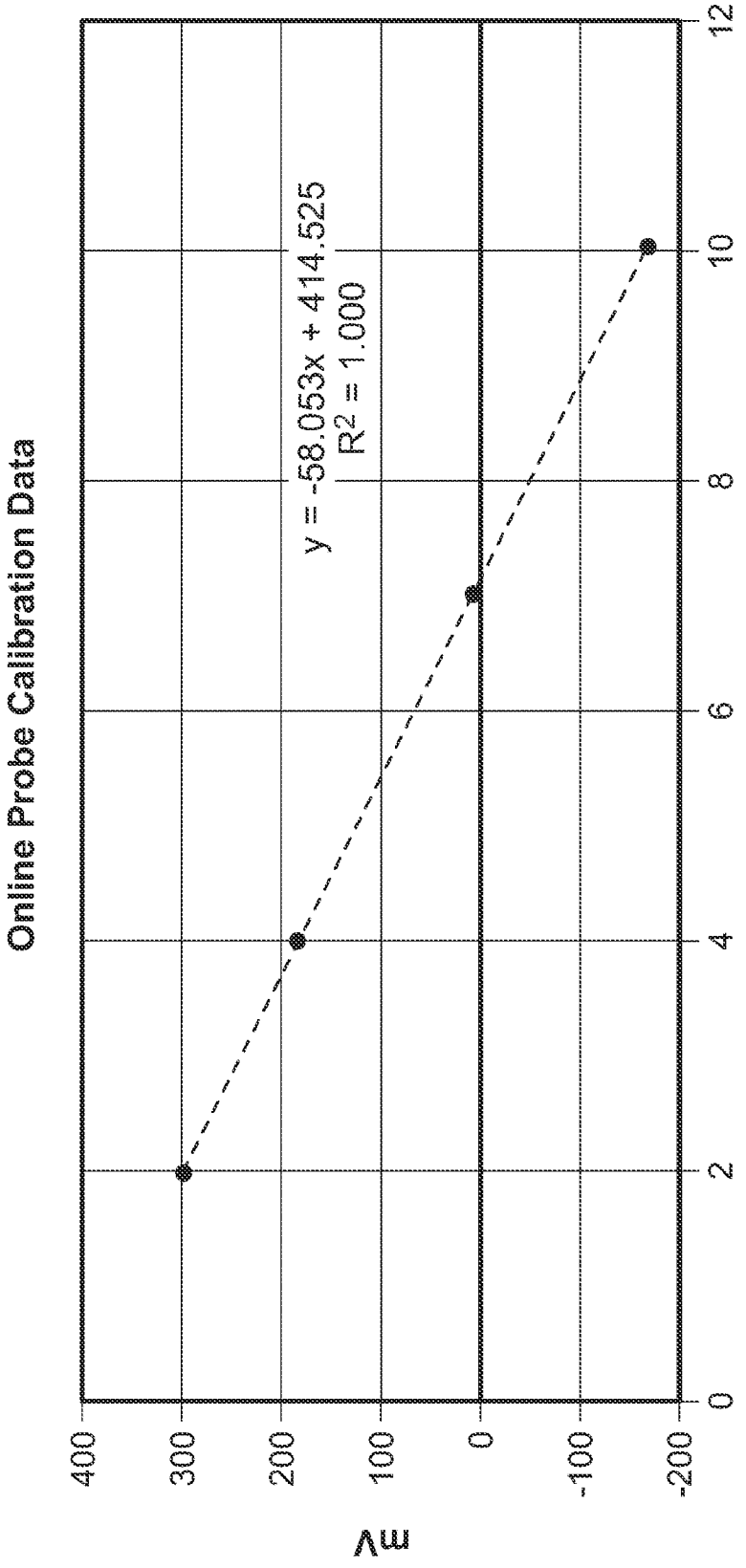

Online Probe Calibration Data
y = -58.053x + 414.525
R2 = 1.000
mV
pH
400
300
200
100
0
-100
-200
0
2
4
6
8
10
12

FIG. 14

| Process Step | Test Run #1 | | Test Run #2 | | Test Run #3 | | Test Run #4 | | Test Run #5 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ΔpH | Dosing Error (%) | ΔpH | Dosing Error (%) | ΔpH | Dosing Error (%) | ΔpH | Dosing Error (%) | ΔpH | Dosing Error (%) |
| Protein Pool | 0.05 | N/A | 0.05 | N/A | 0.00 | N/A | 0.00 | N/A | 0.04 | N/A |
| Acid Add #1 | 0.05 | 2.2 | 0.04 | 0.9 | 0.01 | 1.6 | 0.01 | 0.4 | 0.05 | 4.9 |
| Acid Add #2 | 0.05 | 4.0 | 0.06 | 0.9 | 0.01 | 1.1 | 0.00 | 0.3 | 0.05 | 5.0 |
| Acid Add #3 | 0.04 | 2.6 | 0.04 | 0.5 | 0.01 | 1.0 | 0.00 | 0.4 | 0.05 | 5.5 |
| Base Add #1 | 0.01 | 0.6 | 0.02 | 2.2 | 0.01 | 1.7 | 0.02 | 0.2 | 0.02 | -0.1 |
| Base Add #2 | 0.00 | 0.3 | 0.02 | 1.8 | 0.01 | 0.4 | 0.02 | -3.4 | 0.00 | -0.6 |
| Base Add #3 | 0.01 | 13.9 | 0.02 | 1.9 | 0.00 | 1.7 | 0.01 | -0.1 | 0.00 | 0.0 |

$$\Delta pH = \text{Slipstream pH} - \text{Offline pH}$$

$$\text{Dosing Error} = \frac{(\text{Volume Dosed} - \text{Target Volume})}{\text{Target Volume}} * 100\%$$

**FIG. 15**

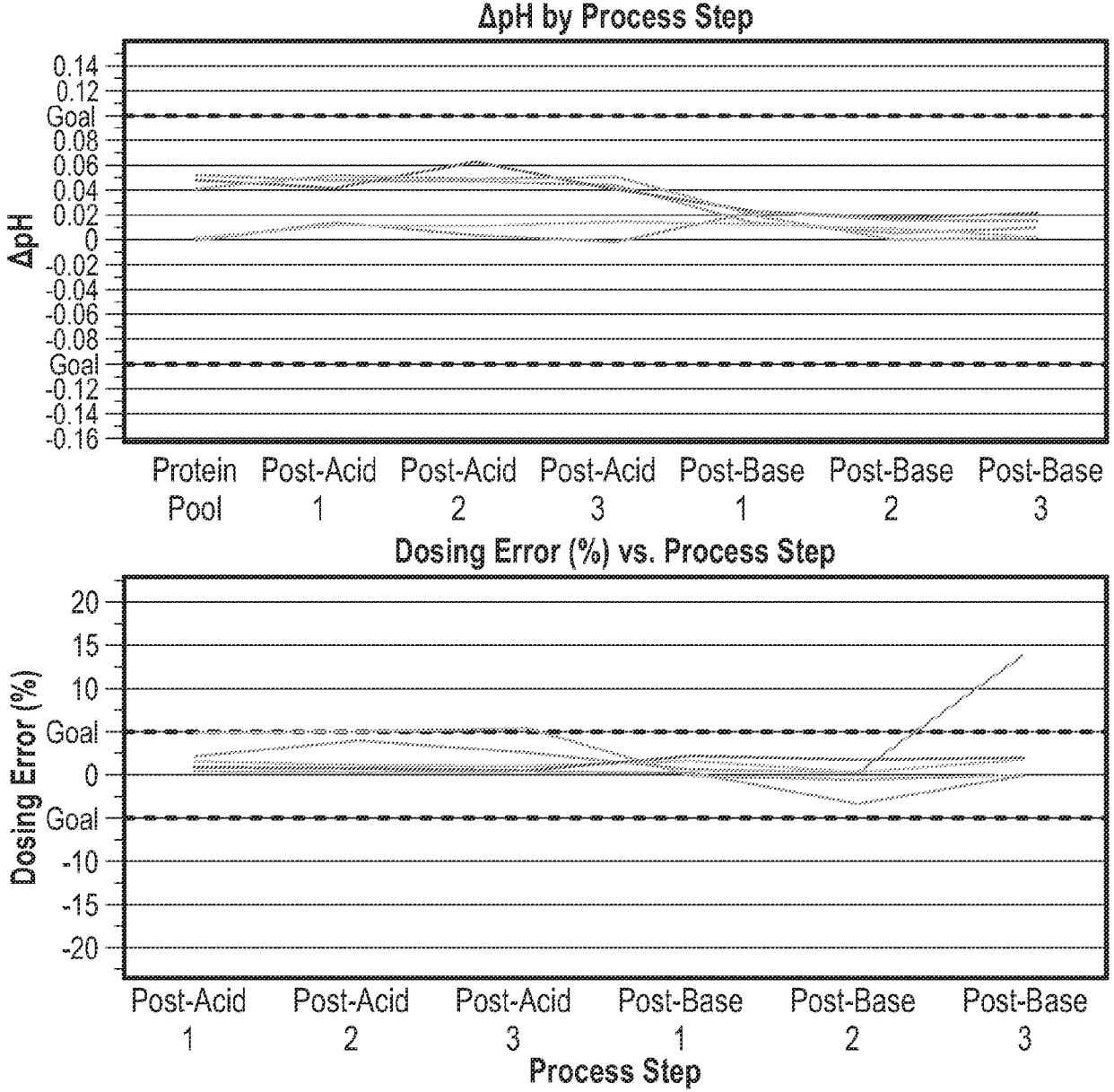

ΔpH by Process Step
ΔpH
0.14
0.12
Goal
0.08
0.06
0.04
0.02
0
-0.02
-0.04
-0.06
-0.08
Goal
-0.12
-0.14
-0.16
Protein Pool
Post-Acid 1
Post-Acid 2
Post-Acid 3
Post-Base 1
Post-Base 2
Post-Base 3
Dosing Error (%) vs. Process Step
Dosing Error (%)
20
15
10
Goal
0
Goal
-10
-15
-20
Post-Acid 1
Post-Acid 2
Post-Acid 3
Post-Base 1
Post-Base 2
Post-Base 3
Process Step

FIG. 16

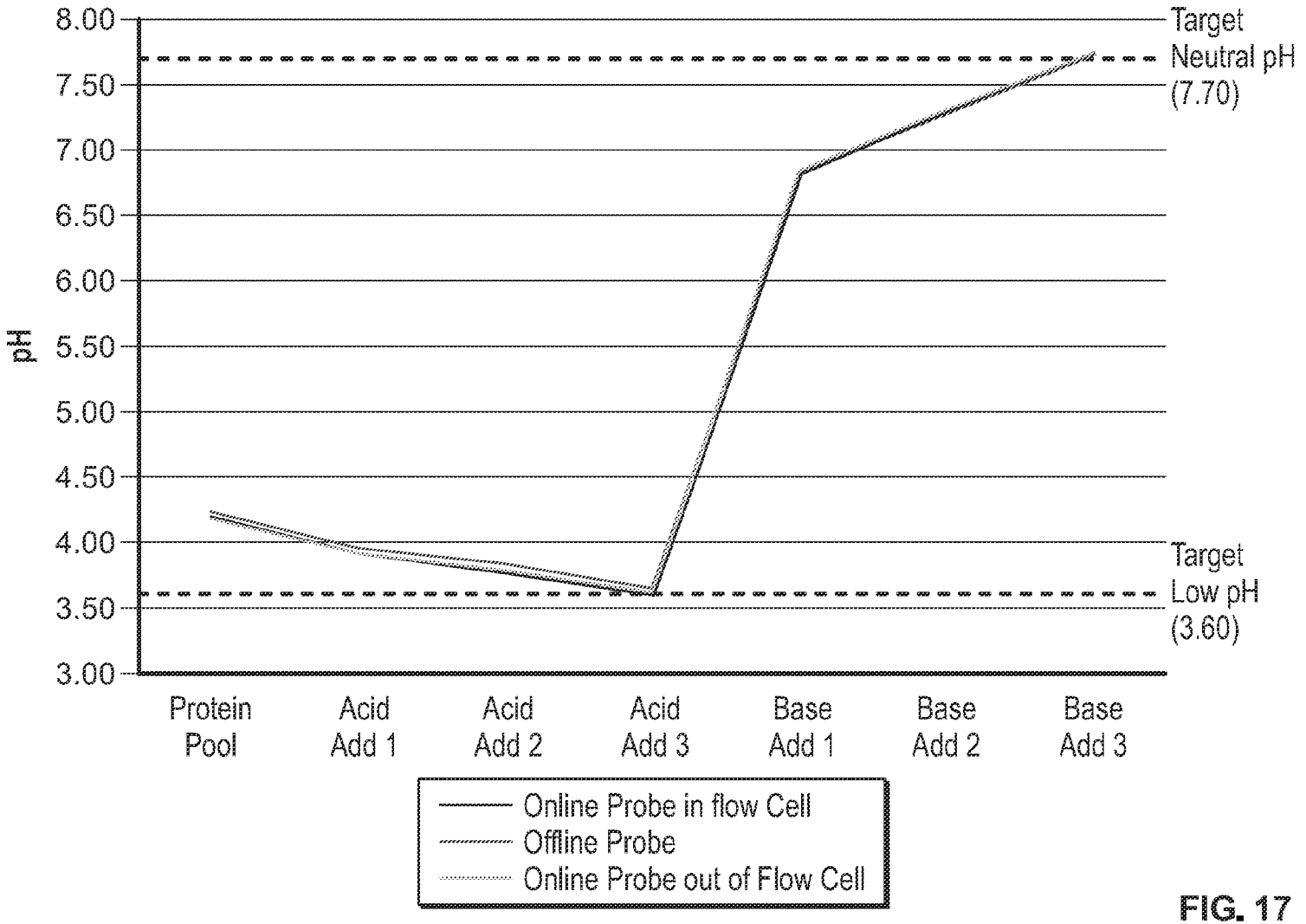

8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
pH
Target
Neutral pH
(7.70)
Target
Low pH
(3.60)
Protein Pool
Acid Add 1
Acid Add 2
Acid Add 3
Base Add 1
Base Add 2
Base Add 3
Online Probe in flow Cell
Offline Probe
Online Probe out of Flow Cell

FIG. 17

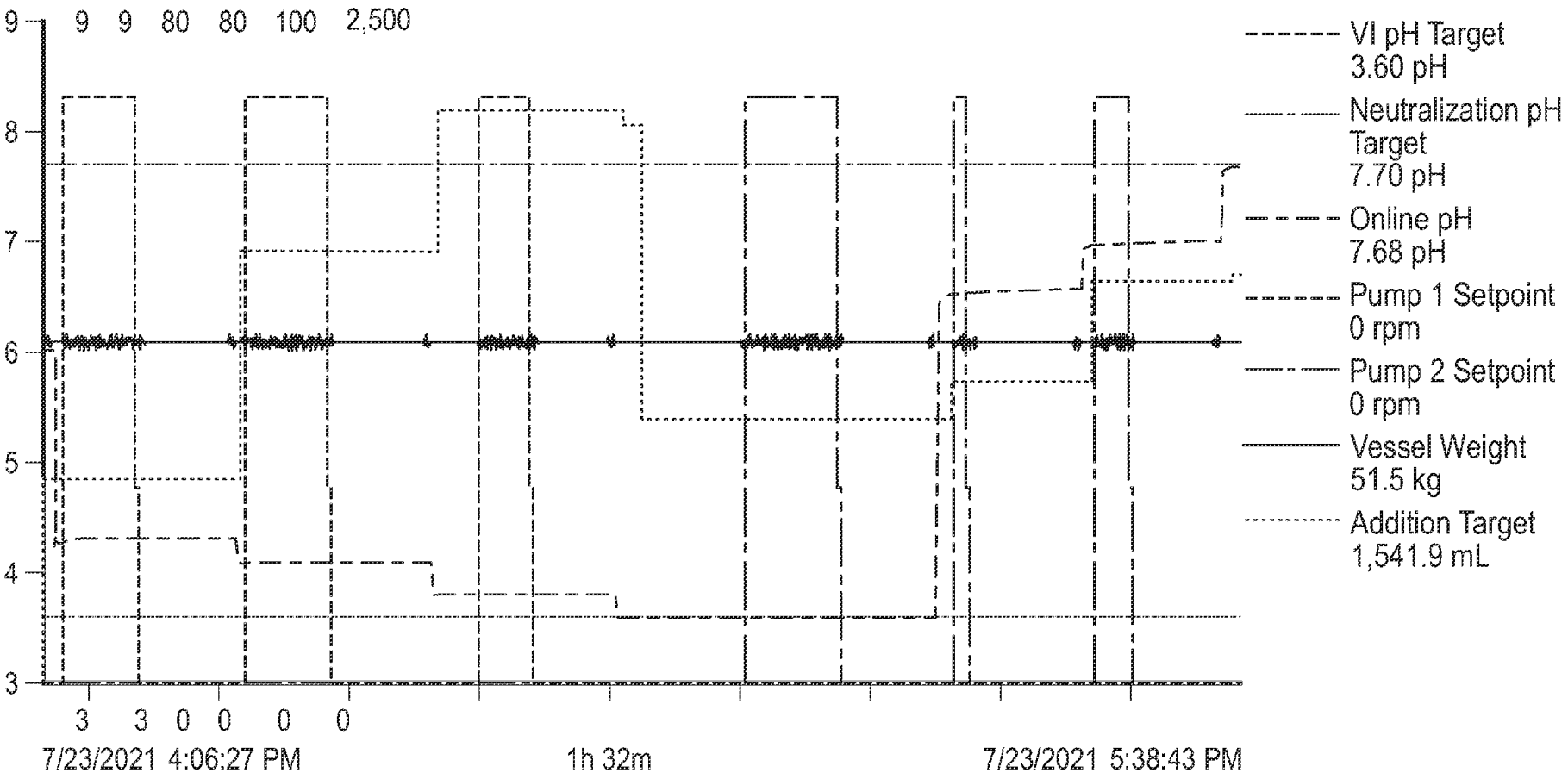

9 9 9 80 80 100 2,500
9
8
7
6
5
4
3
3 3 0 0 0 0
7/23/2021 4:06:27 PM
1h 32m
7/23/2021 5:38:43 PM
VI pH Target
3.60 pH
Neutralization pH
Target
7.70 pH
Online pH
7.68 pH
Pump 1 Setpoint
0 rpm
Pump 2 Setpoint
0 rpm
Vessel Weight
51.5 kg
Addition Target
1,541.9 mL

FIG. 18

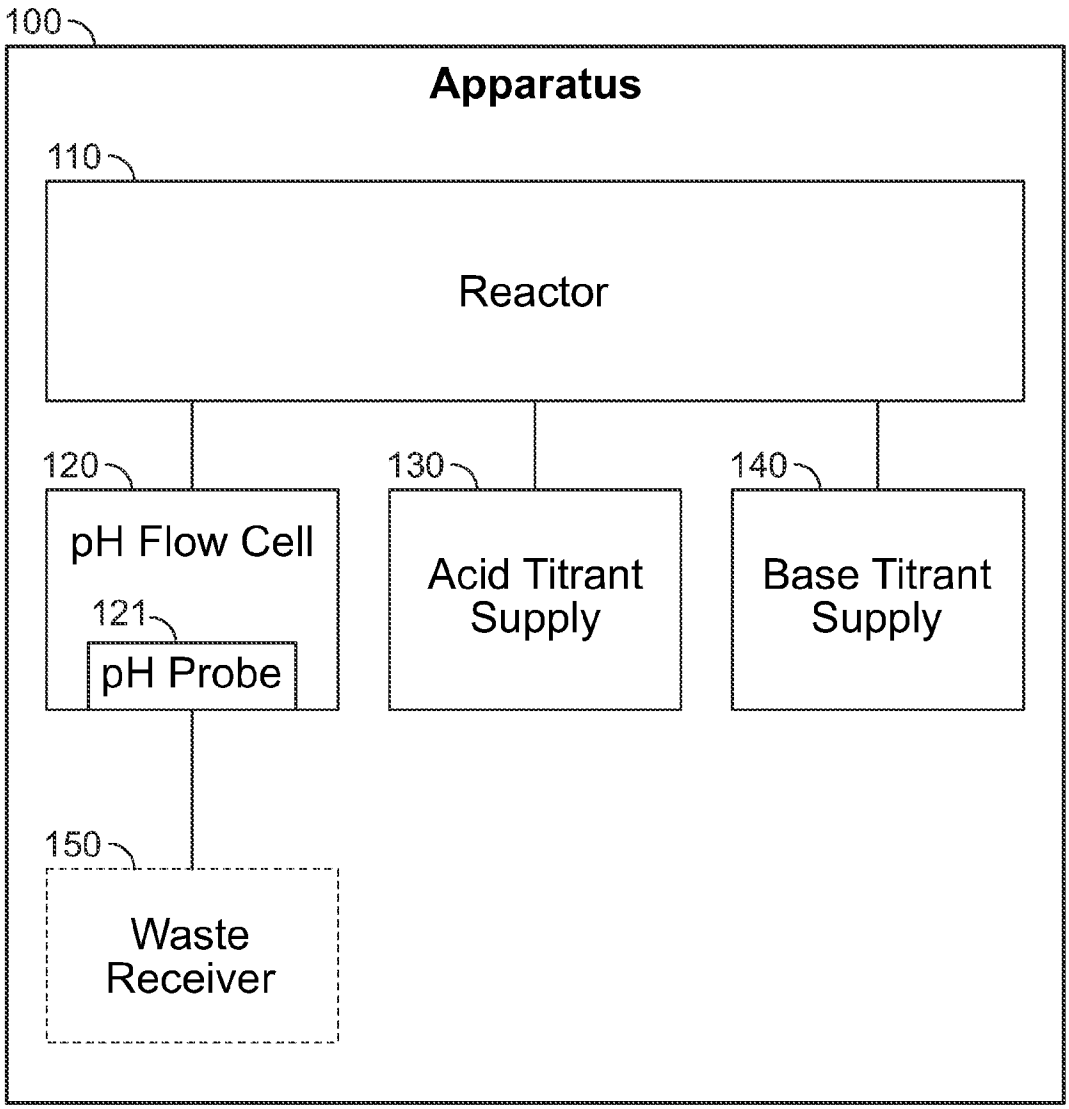

100
Apparatus
110
Reactor
120
pH Flow Cell
121
pH Probe
130
Acid Titrant Supply
140
Base Titrant Supply
150
Waste Receiver

FIG. 19

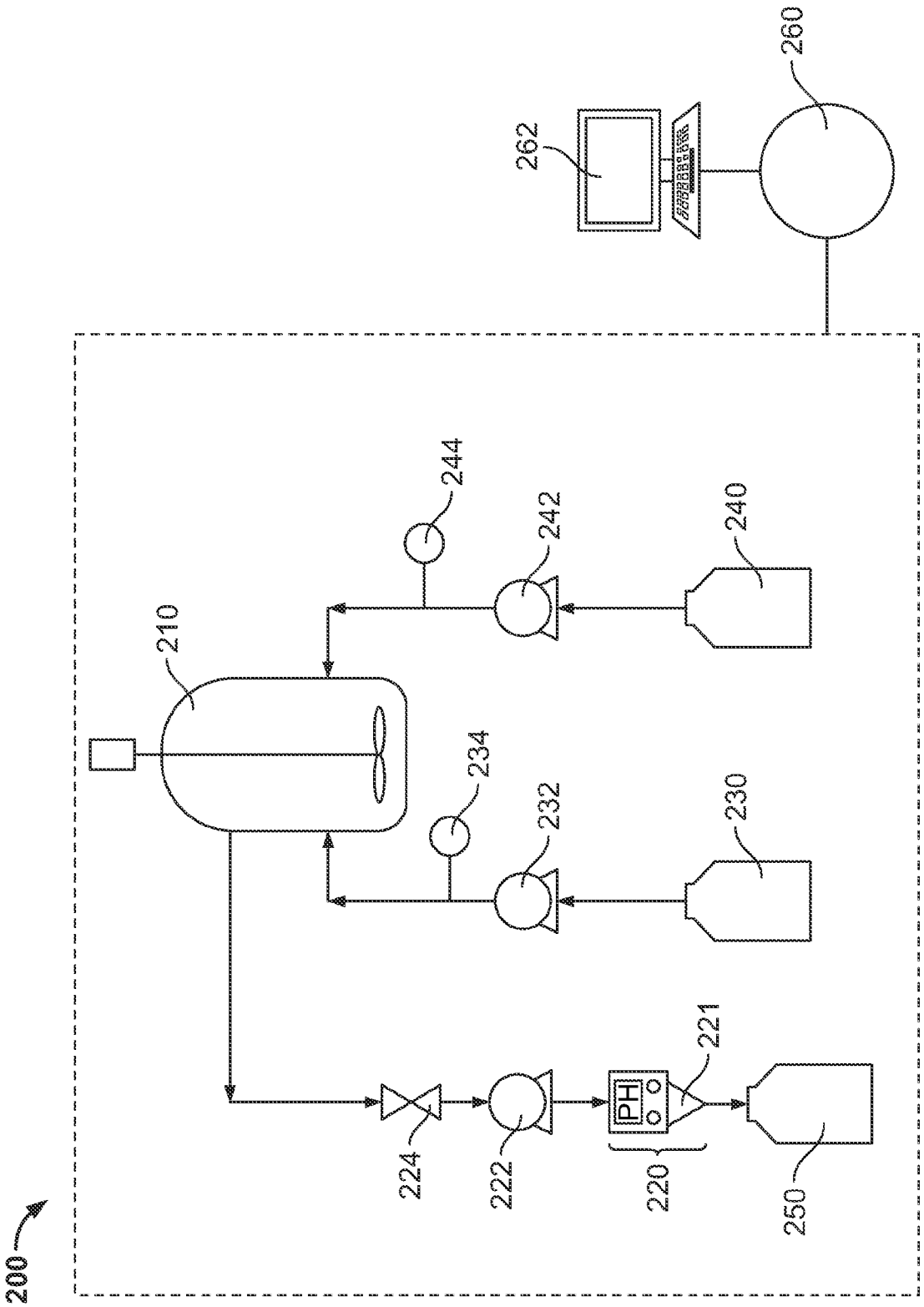



FIG. 20

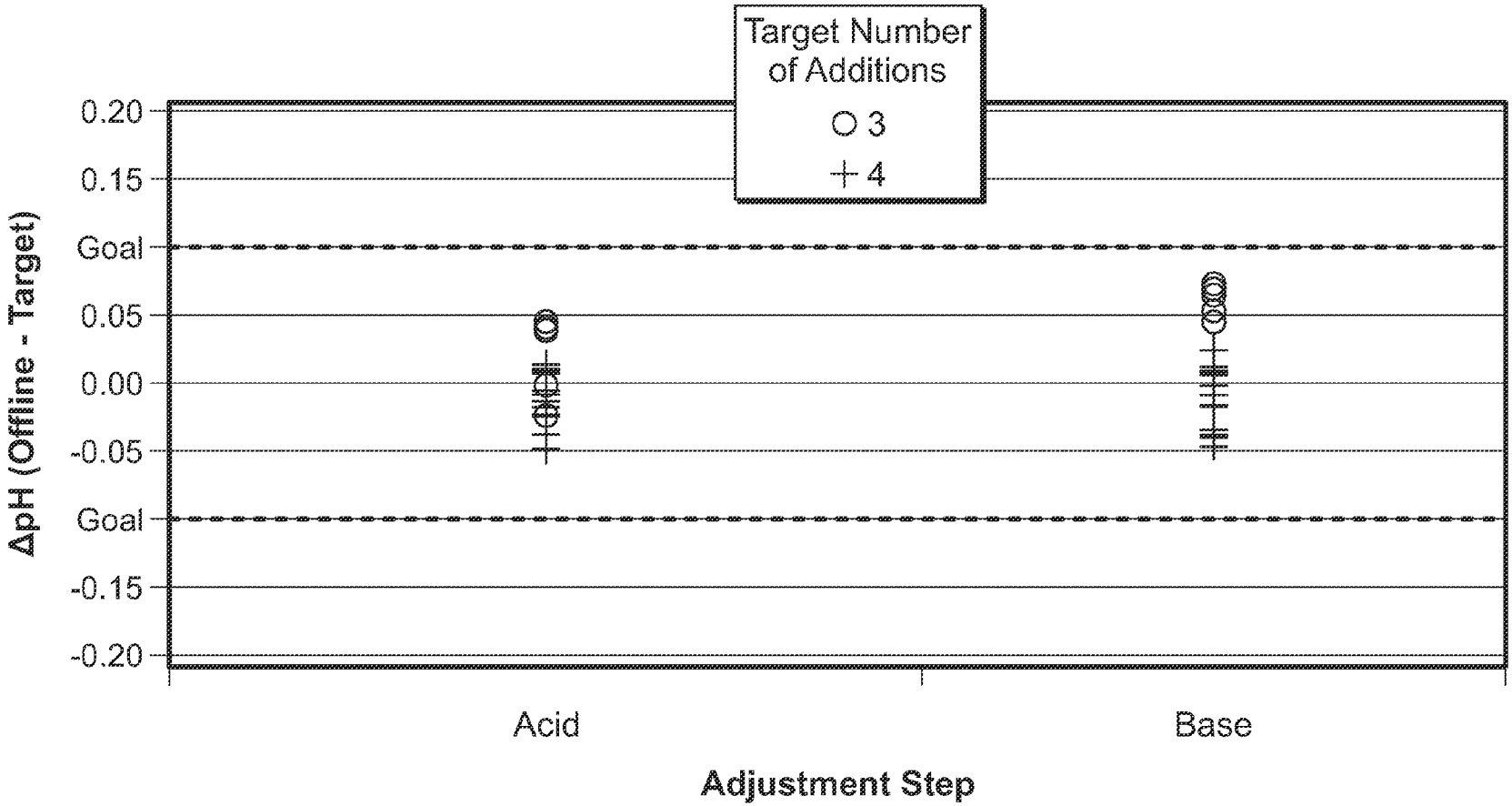

Target Number of Additions
3
4
0.20
0.15
Goal
0.05
0.00
-0.05
Goal
-0.15
-0.20
ΔpH (Offline - Target)
Acid
Base
Adjustment Step

FIG. 21

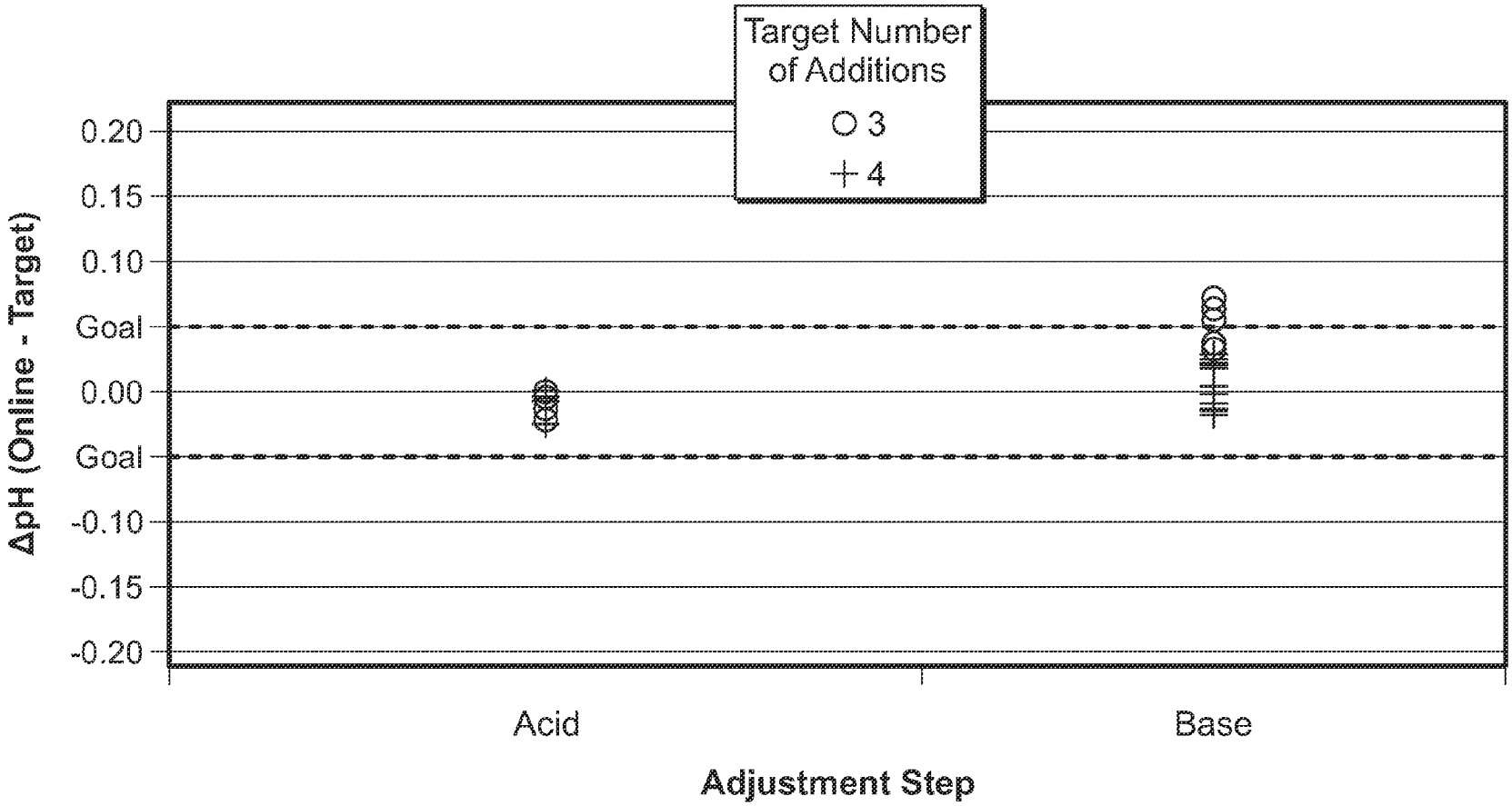

Target Number of Additions
3
4
0.20
0.15
0.10
Goal
0.00
Goal
-0.10
-0.15
-0.20
ΔpH (Online - Target)
Acid
Base
Adjustment Step

FIG. 22

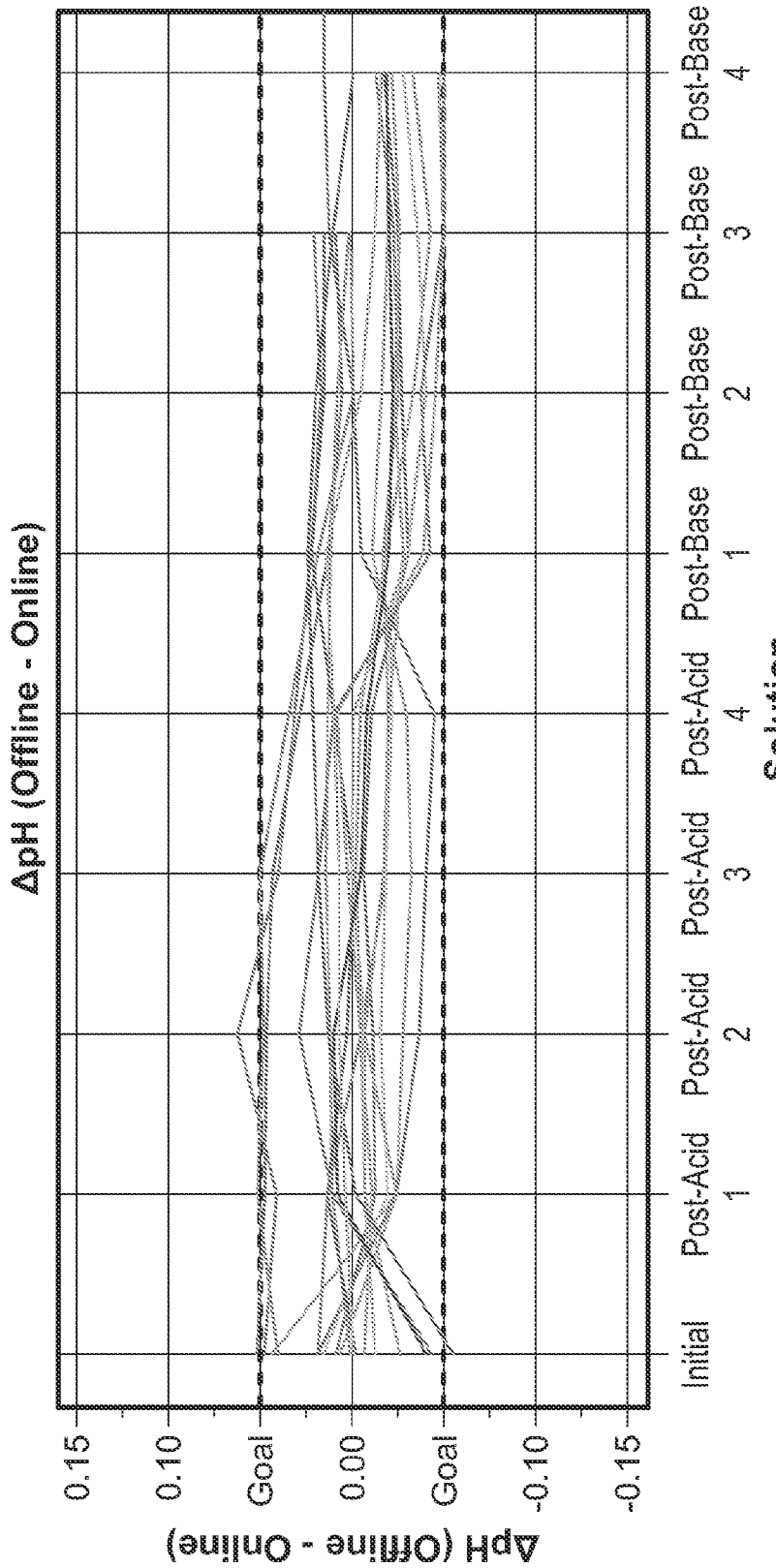

ΔpH (Offline - Online)
ΔpH (Offline - Online)
0.15
0.10
Goal
0.00
Goal
-0.10
-0.15
Initial
Post-Acid 1
Post-Acid 2
Post-Acid 3
Post-Acid 4
Post-Base 1
Post-Base 2
Post-Base 3
Post-Base 4
Solution

FIG. 23

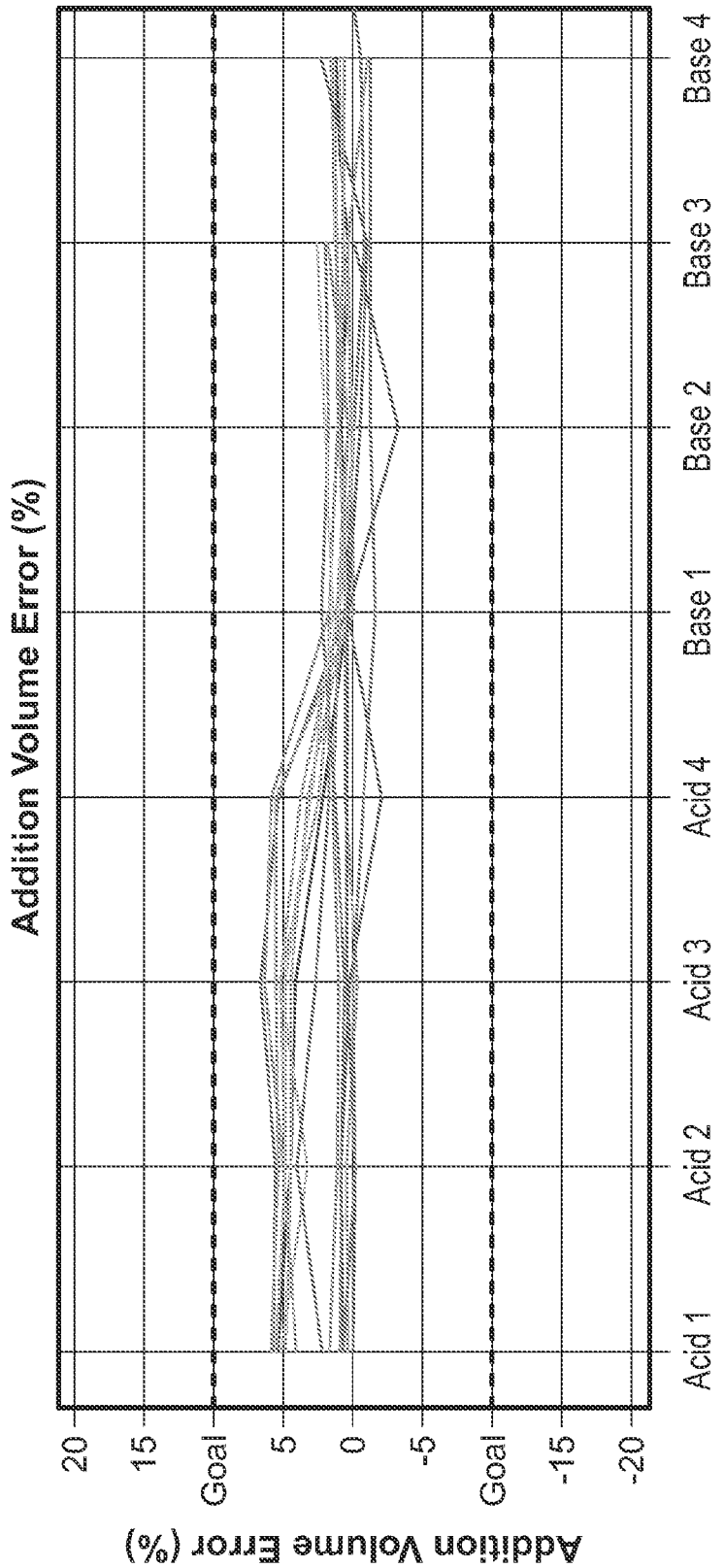

Addition Volume Error (%)
Addition Volume Error (%)
20
15
Goal
5
0
-5
Goal
-15
-20
Acid 1
Acid 2
Acid 3
Acid 4
Base 1
Base 2
Base 3
Base 4
Addition

FIG. 24