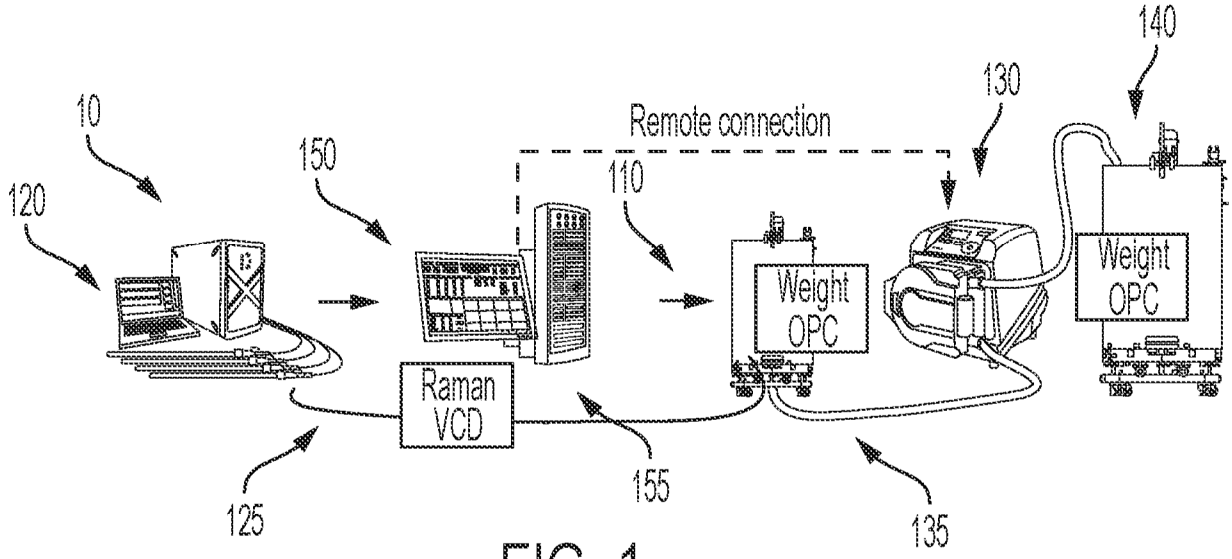
10
120
150
Remote connection
110
130
140
Weight OPC
Weight OPC
Raman VCD
125
155
135

FIG. 1

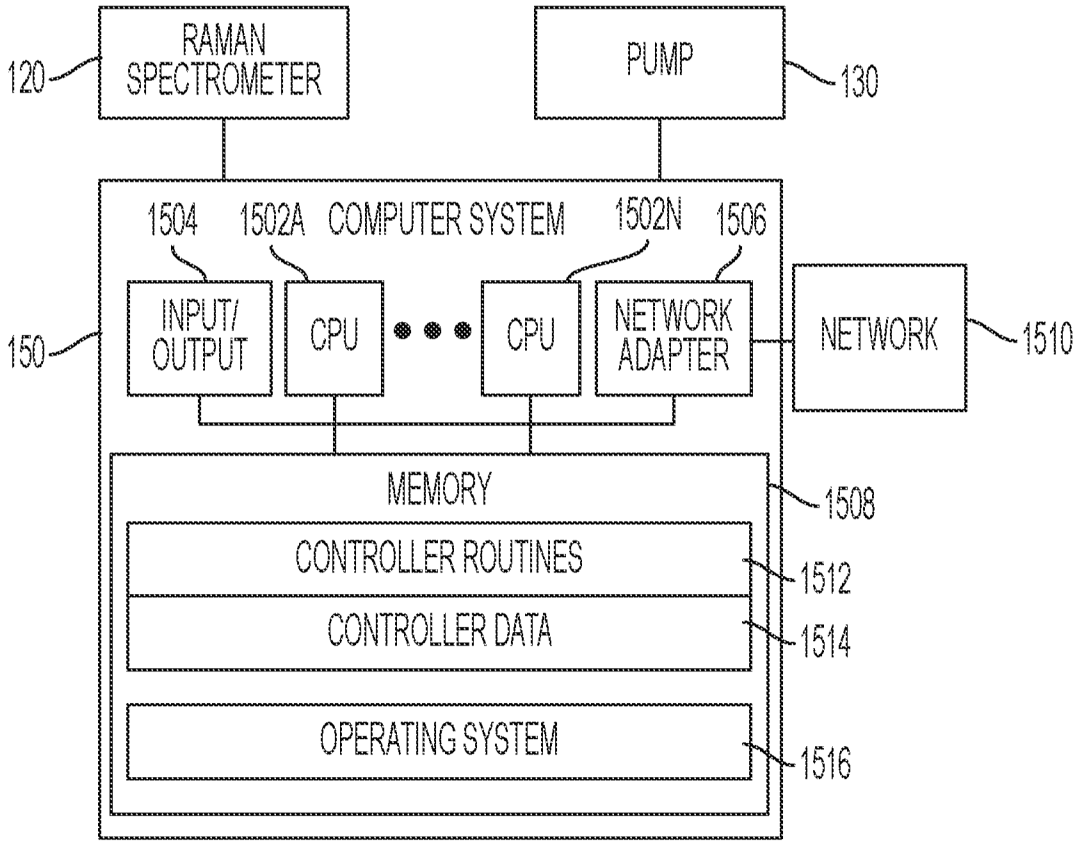
120
RAMAN SPECTROMETER
PUMP
130
1504
1502A
COMPUTER SYSTEM
1502N
1506
150
INPUT/ OUTPUT
CPU
CPU
NETWORK ADAPTER
NETWORK
1510
MEMORY
1508
CONTROLLER ROUTINES
1512
CONTROLLER DATA
1514
OPERATING SYSTEM
1516

FIG. 2

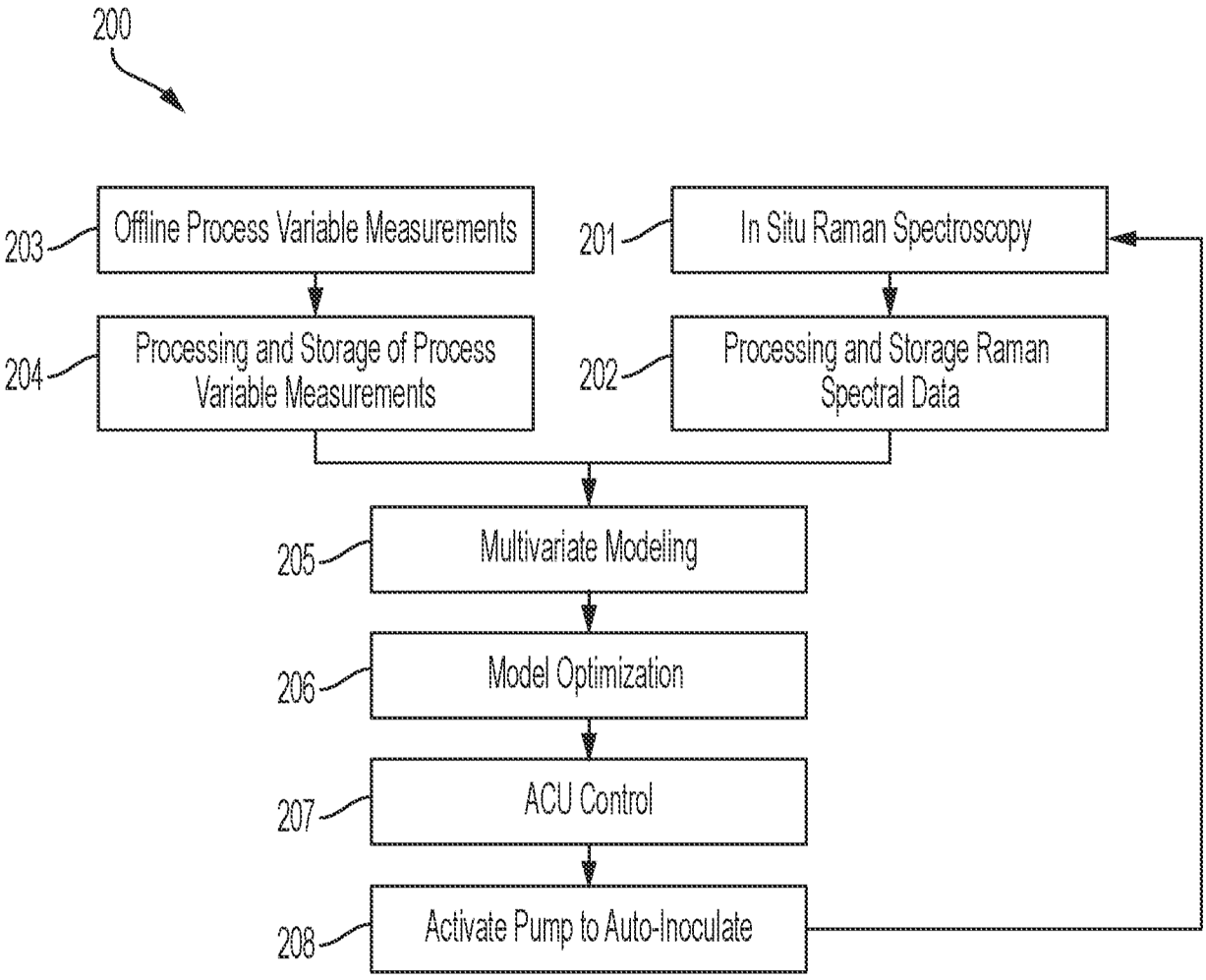
200
203
Offline Process Variable Measurements
201
In Situ Raman Spectroscopy
204
Processing and Storage of Process Variable Measurements
202
Processing and Storage Raman Spectral Data
205
Multivariate Modeling
206
Model Optimization
207
ACU Control
208
Activate Pump to Auto-Inoculate

FIG. 3

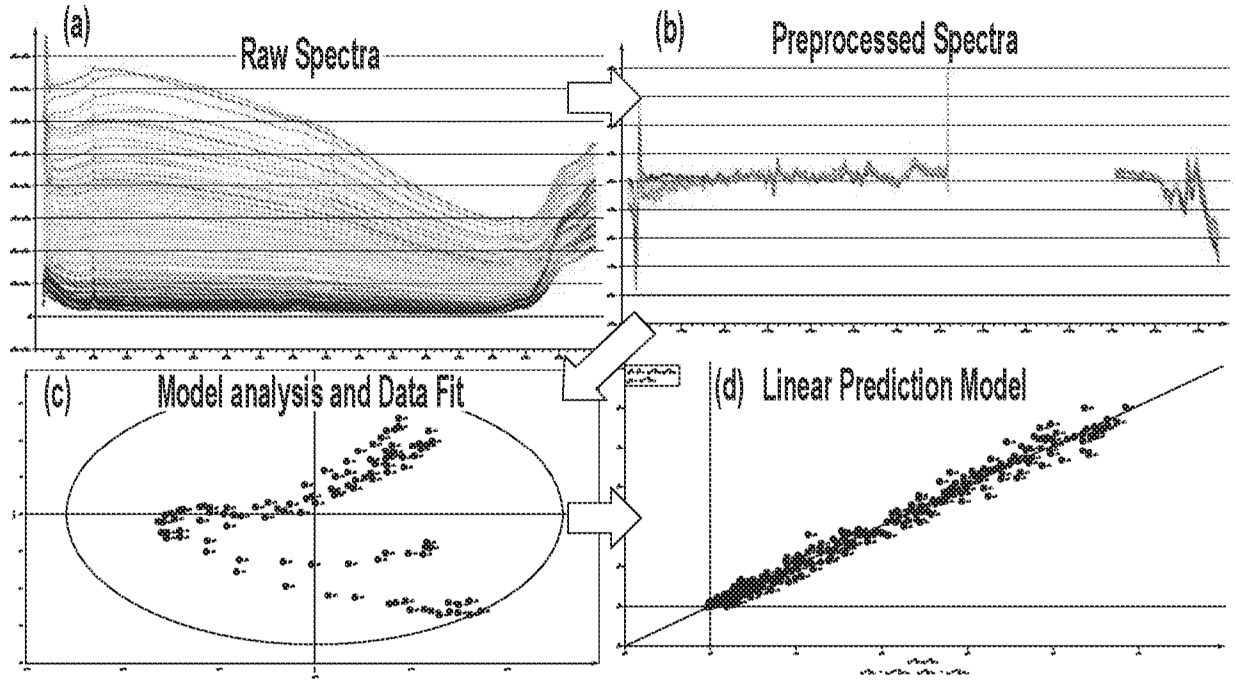
(a)
Raw Spectra
(b)
Preprocessed Spectra
(c)
Model analysis and Data Fit
(d) Linear Prediction Model

FIG. 4

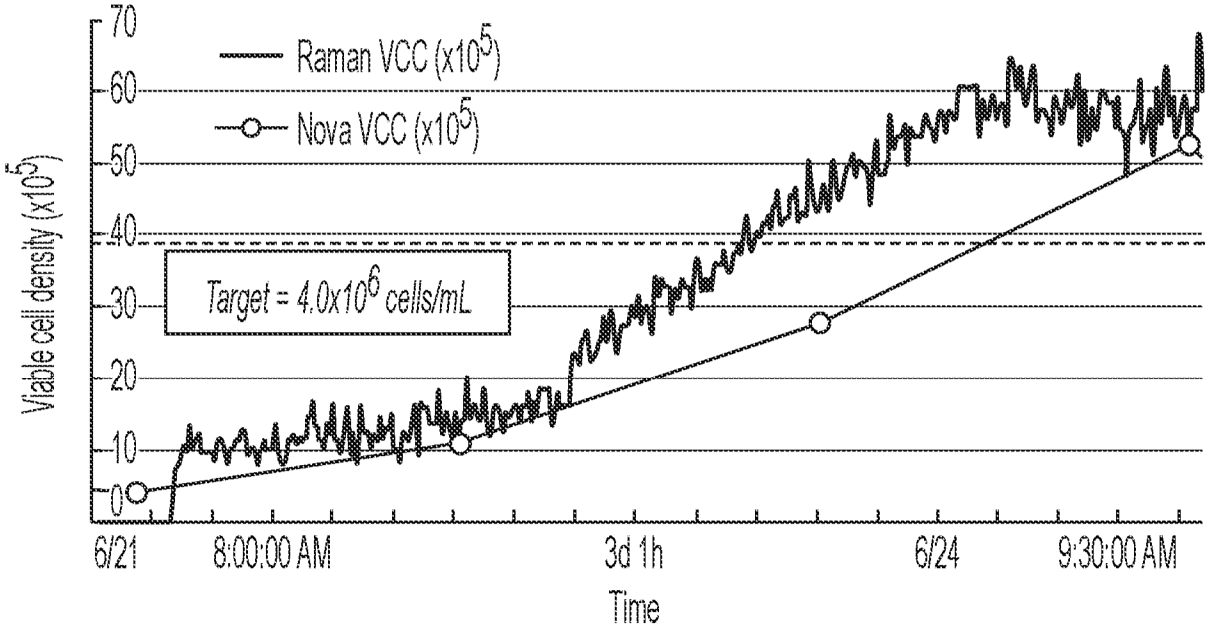
Raman VCC (x10^5)
Nova VCC (x10^5)
Target = 4.0x10^6 cells/mL
Viable cell density (x10^5)
70
60
50
40
30
20
10
0
6/21
8:00:00 AM
3d 1h
6/24
9:30:00 AM
Time

FIG. 5

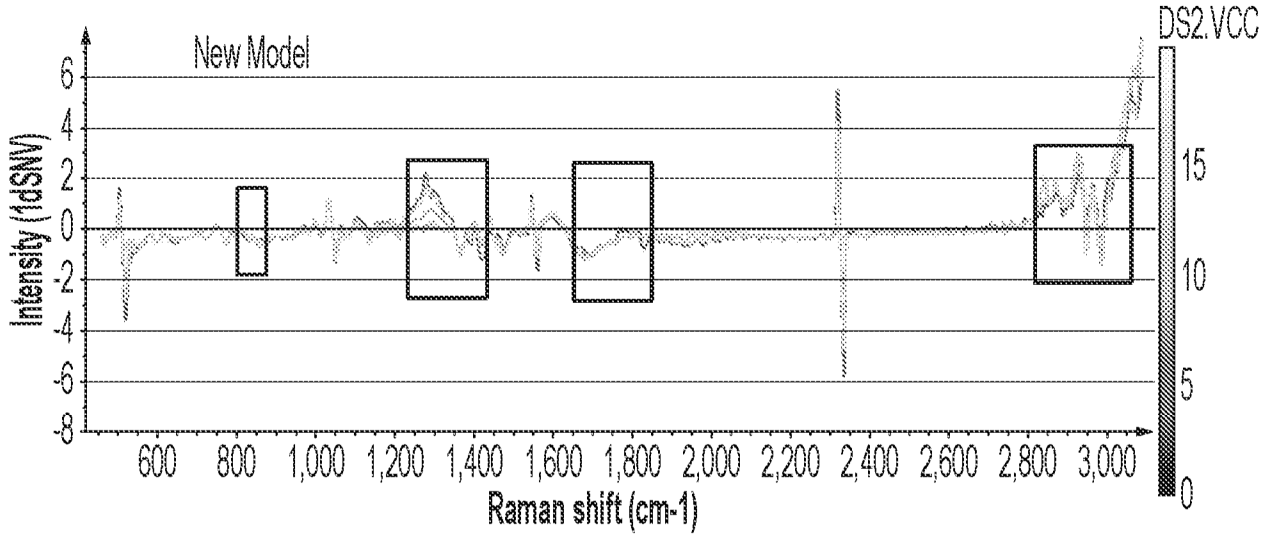
New Model
DS2.VCC
Intensity (1dSNV)
6
4
2
0
-2
-4
-6
-8
600
800
1,000
1,200
1,400
1,600
1,800
2,000
2,200
2,400
2,600
2,800
3,000
Raman shift (cm-1)
15
10
5
0

FIG. 6

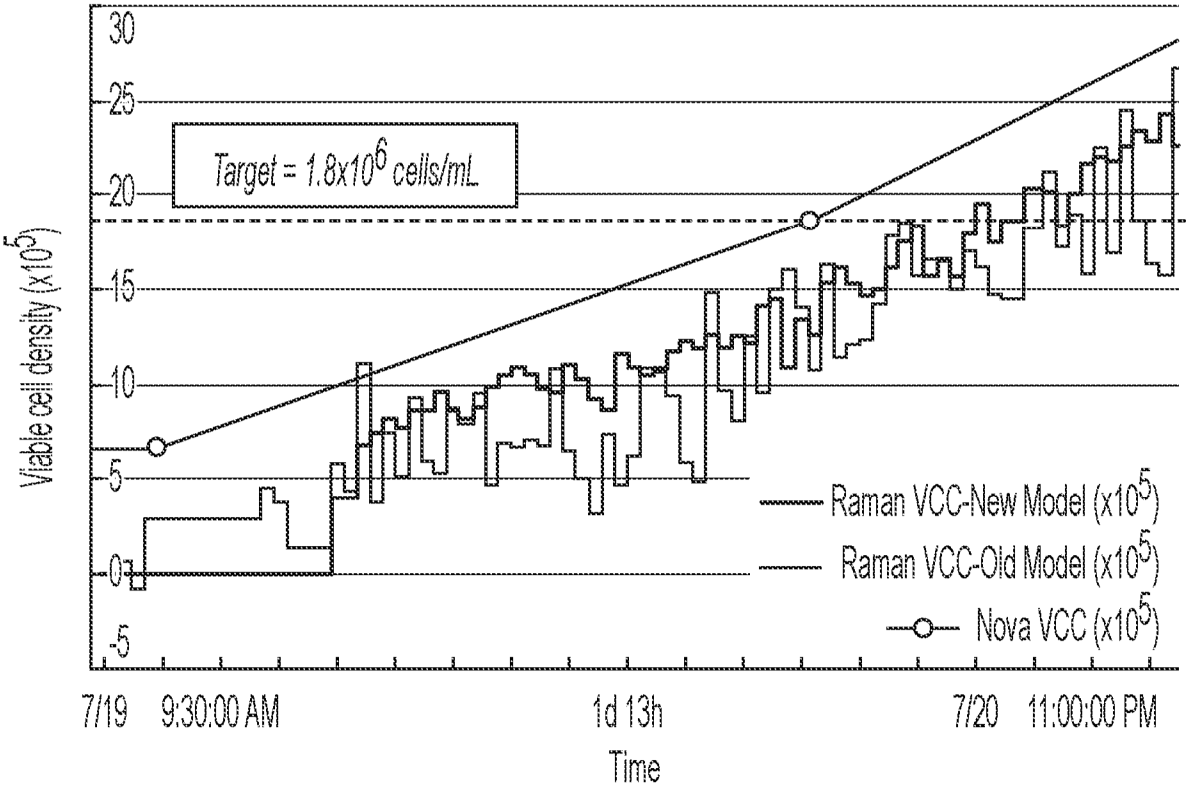
Target = 1.8x10^6 cells/mL
Viable cell density (x10^5)
30
25
20
15
10
5
0
-5
Raman VCC-New Model (x10^5)
Raman VCC-Old Model (x10^5)
Nova VCC (x10^5)
7/19 9:30:00 AM
1d 13h
7/20 11:00:00 PM
Time

FIG. 7

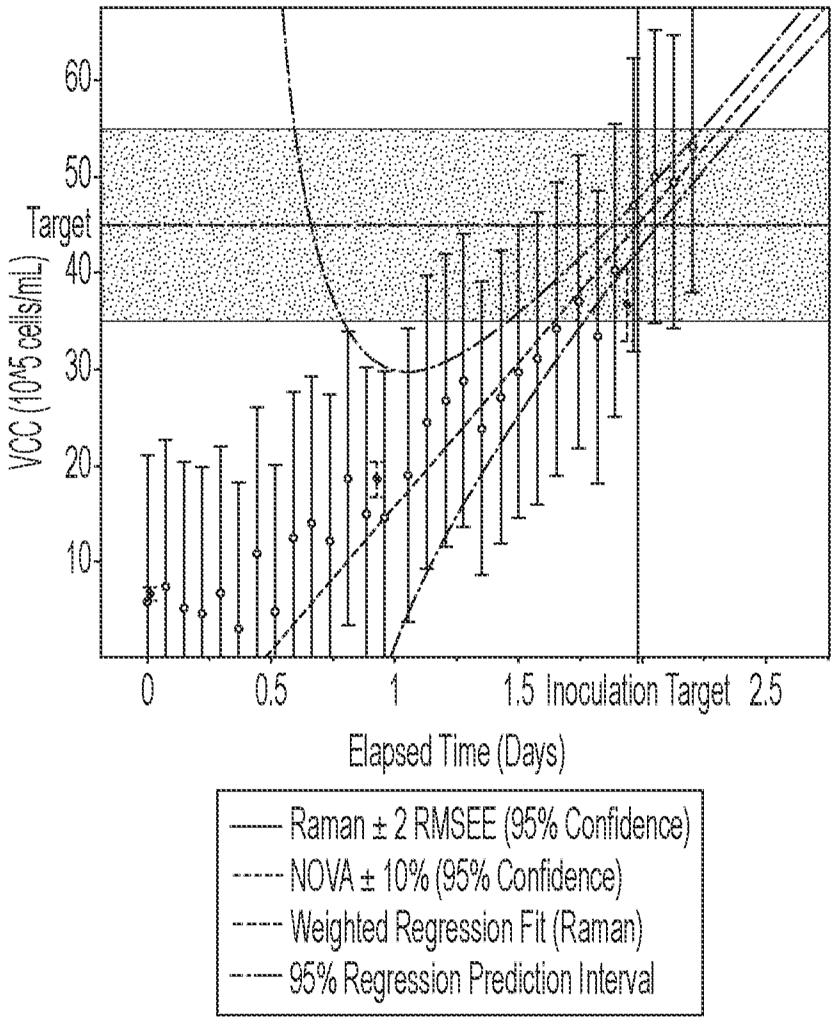
60
50
Target
40
30
20
10
VCC (10^5 cells/mL)
0
0.5
1
1.5 Inoculation Target
2.5
Elapsed Time (Days)
Raman ± 2 RMSEE (95% Confidence)
NOVA ± 10% (95% Confidence)
Weighted Regression Fit (Raman)
95% Regression Prediction Interval

FIG. 8