

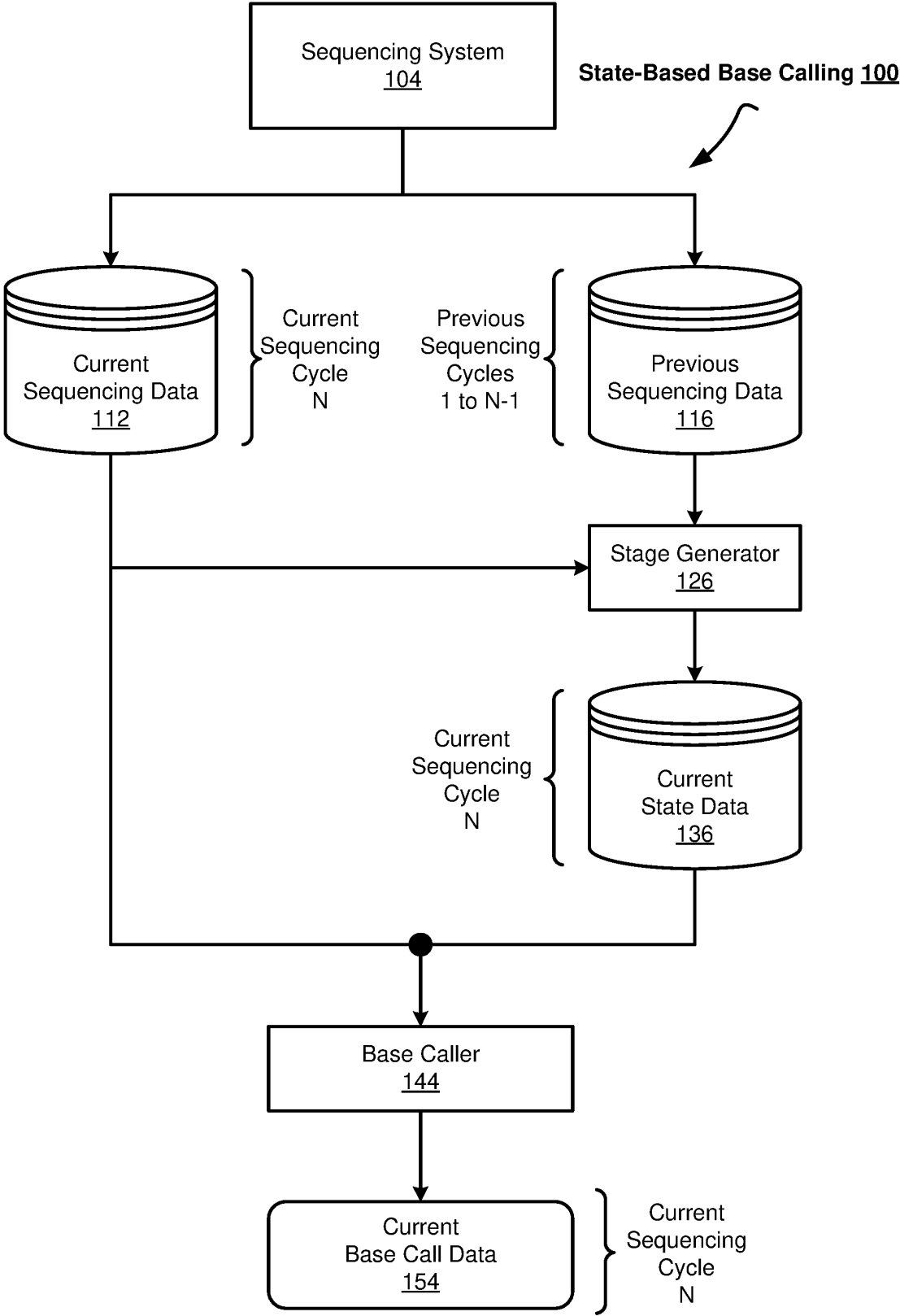
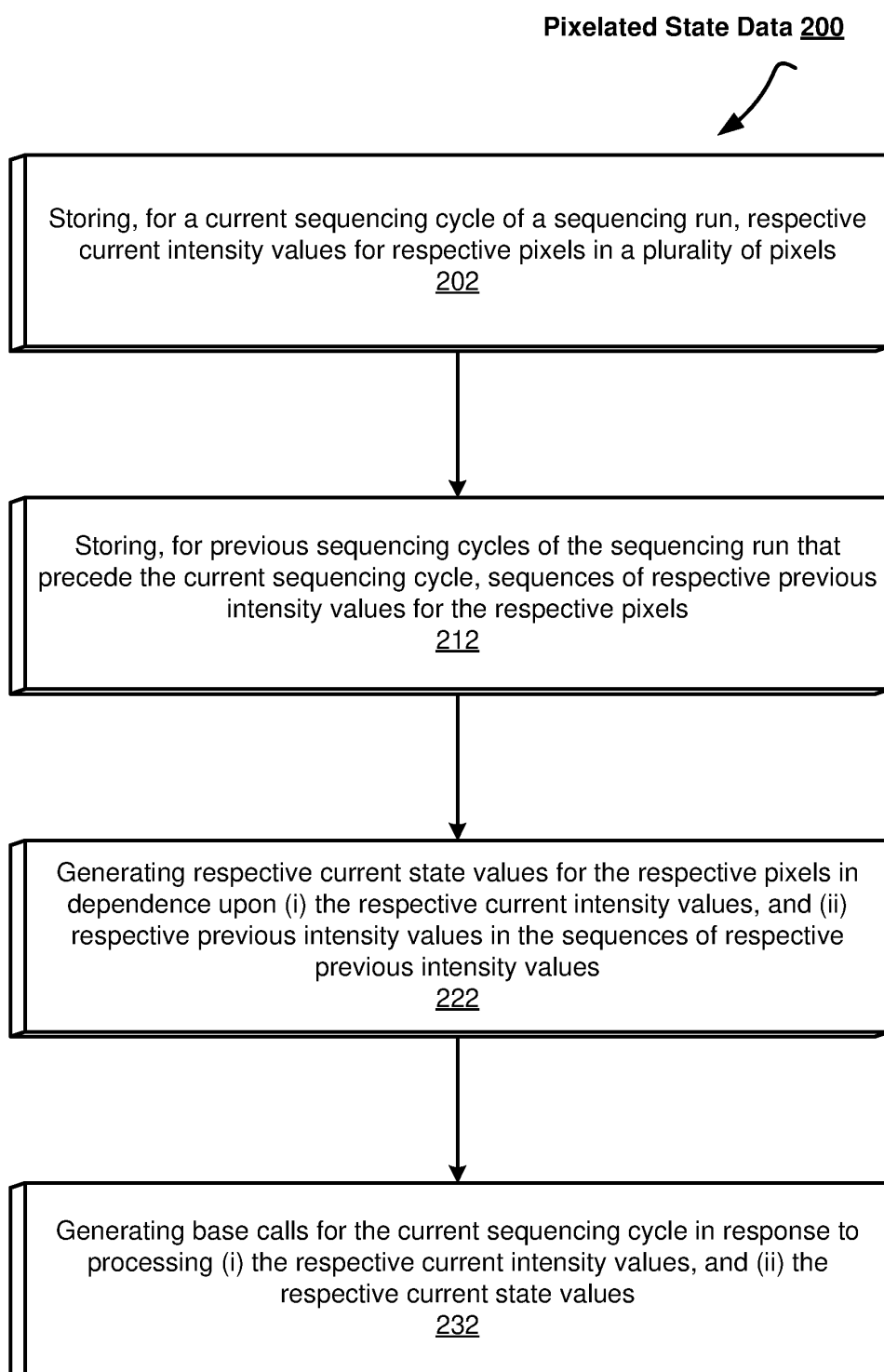
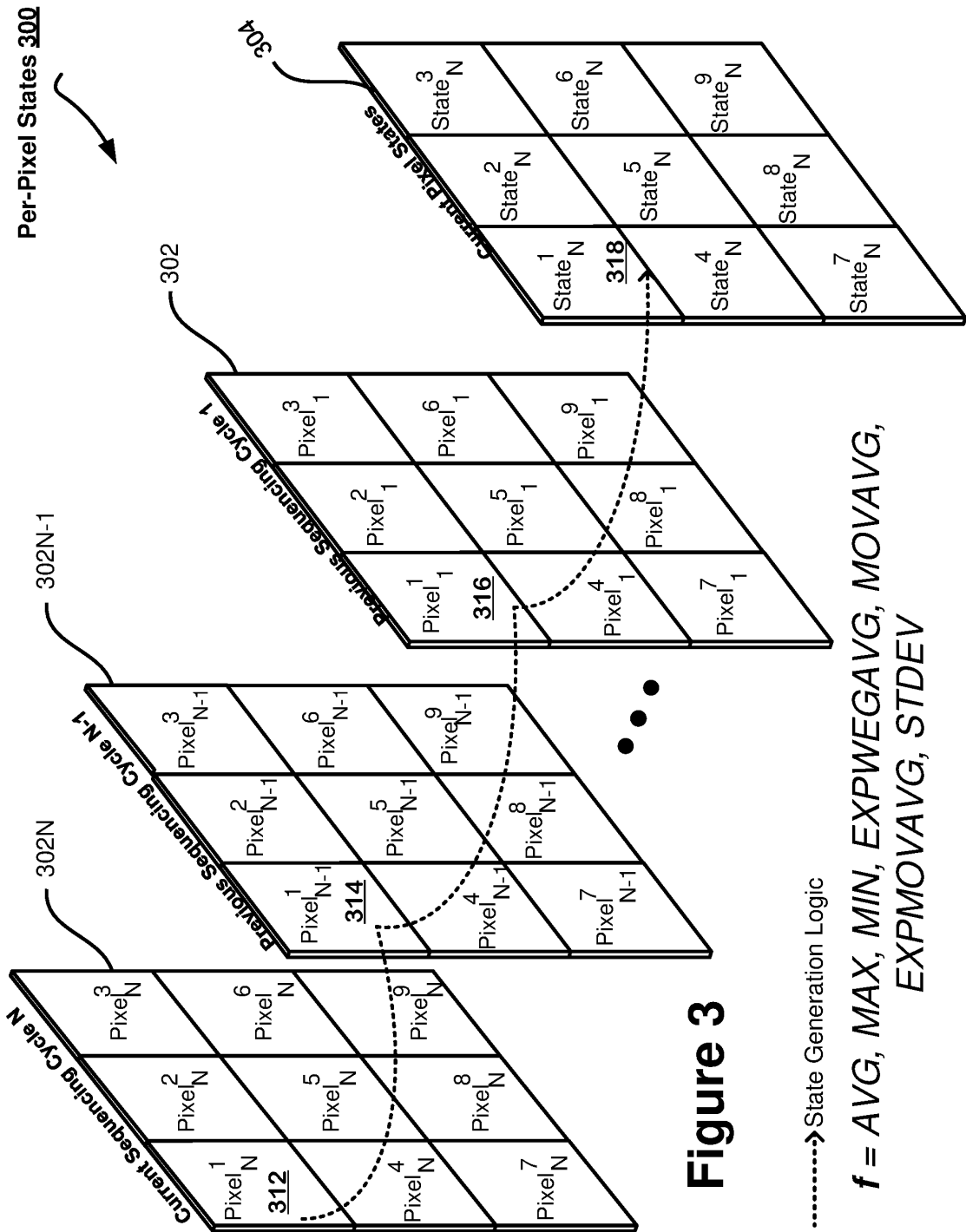


Figure 1

**Figure 2**



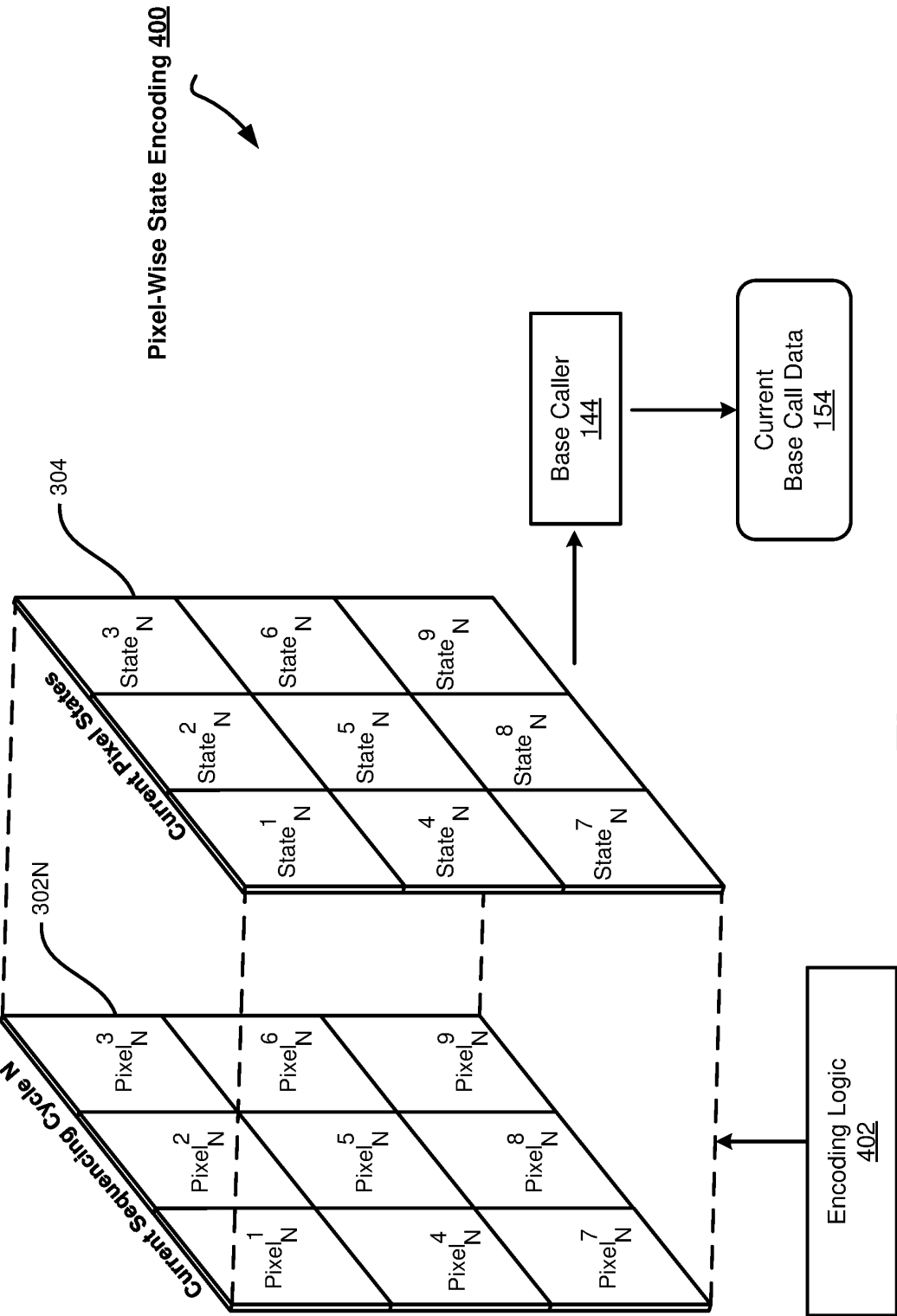
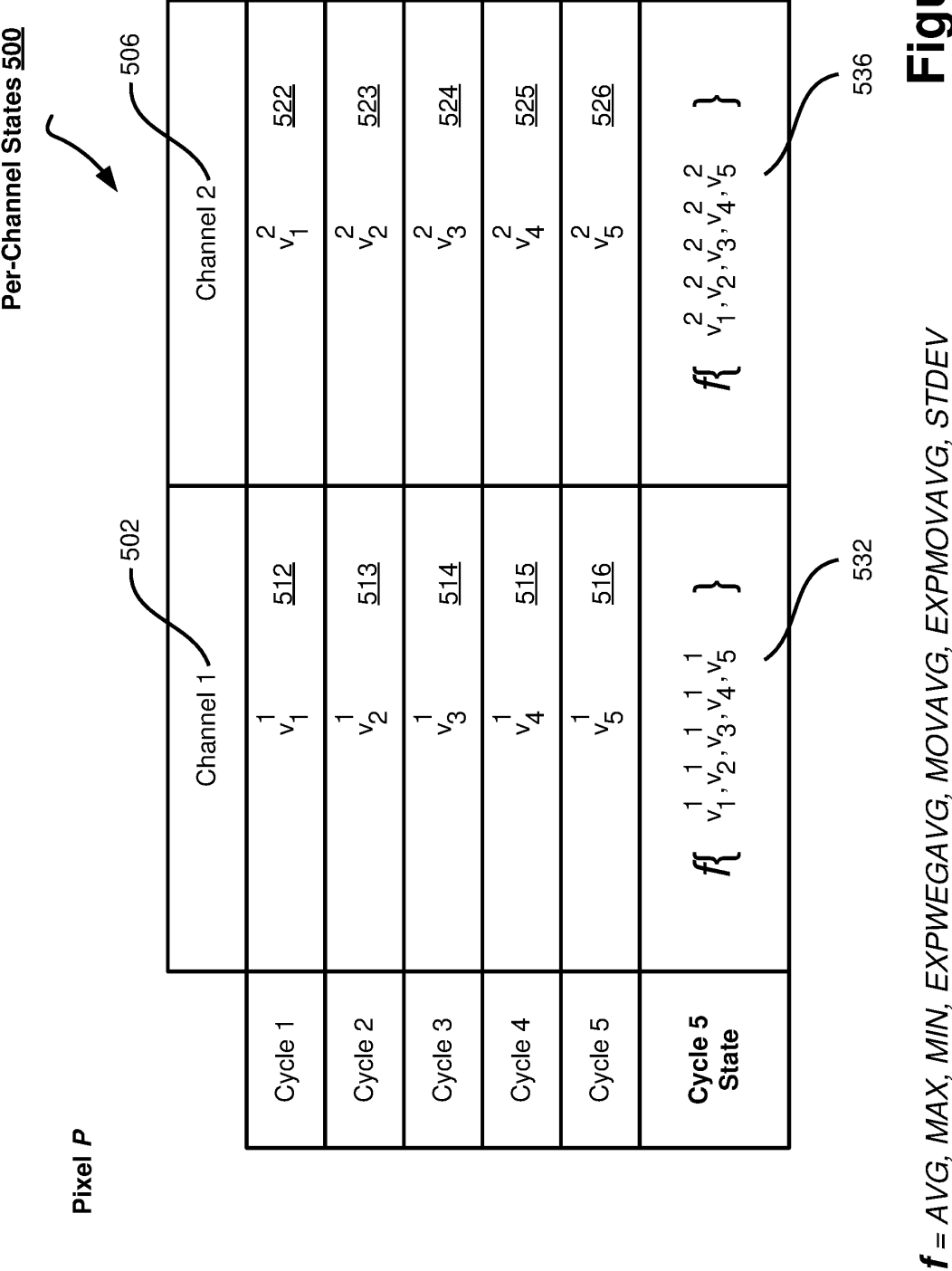


Figure 4



Per-Channel MIN States 600

Current Sequencing Cycle N

Pixels <u>601</u>	Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Channel 1 MIN State Values <u>604</u>	Channel 2 MIN State Values <u>605</u>
(1, 1)	x_N^1	y_N^1	$\text{MIN} \{x_N^1 \dots x_1^1\}$	$\text{MIN} \{y_N^1 \dots y_1^1\}$
(1, 2)	x_N^2	y_N^2	$\text{MIN} \{x_N^2 \dots x_1^2\}$	$\text{MIN} \{y_N^2 \dots y_1^2\}$
(1, 3)	x_N^3	y_N^3	$\text{MIN} \{x_N^3 \dots x_1^3\}$	$\text{MIN} \{y_N^3 \dots y_1^3\}$
(1, 4)	x_N^4	y_N^4	$\text{MIN} \{x_N^4 \dots x_1^4\}$	$\text{MIN} \{y_N^4 \dots y_1^4\}$
(1, 5)	x_N^5	y_N^5	$\text{MIN} \{x_N^5 \dots x_1^5\}$	$\text{MIN} \{y_N^5 \dots y_1^5\}$
...	...	...	...	...
(i, j)	x_N^k	y_N^k	$\text{MIN} \{x_N^k \dots x_1^k\}$	$\text{MIN} \{y_N^k \dots y_1^k\}$

Figure 6

Current Sequencing Cycle N			Pan-Channel MIN States 700	
Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Pan-Channel AVG MIN State Values 708	
(1, 1)	$\begin{smallmatrix} 1 \\ x \end{smallmatrix} N$	$\begin{smallmatrix} 1 \\ y \end{smallmatrix} N$	Pixel-Wise Averages of Columns 604 and 605 in Figure 6	
(1, 2)	$\begin{smallmatrix} 2 \\ x \end{smallmatrix} N$	$\begin{smallmatrix} 2 \\ y \end{smallmatrix} N$		
(1, 3)	$\begin{smallmatrix} 3 \\ x \end{smallmatrix} N$	$\begin{smallmatrix} 3 \\ y \end{smallmatrix} N$		
(1, 4)	$\begin{smallmatrix} 4 \\ x \end{smallmatrix} N$	$\begin{smallmatrix} 4 \\ y \end{smallmatrix} N$		
(1, 5)	$\begin{smallmatrix} 5 \\ x \end{smallmatrix} N$	$\begin{smallmatrix} 5 \\ y \end{smallmatrix} N$		
...	...	...	...	...
(i, j)	$\begin{smallmatrix} k \\ x \end{smallmatrix} N$	$\begin{smallmatrix} k \\ y \end{smallmatrix} N$		

Figure 7

Current Sequencing Cycle N			Per-Channel MAX States 800		
Pixels <u>601</u>	Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Channel 1 MAX State Values <u>804</u>	Channel 2 MAX State Values <u>805</u>	
(1, 1)	x_N^1	y_N^1	$\text{MAX}\{x_N^1 \dots x_N^1\}$	$\text{MAX}\{y_N^1 \dots y_N^1\}$	
(1, 2)	x_N^2	y_N^2	$\text{MAX}\{x_N^2 \dots x_N^2\}$	$\text{MAX}\{y_N^2 \dots y_N^2\}$	
(1, 3)	x_N^3	y_N^3	$\text{MAX}\{x_N^3 \dots x_N^3\}$	$\text{MAX}\{y_N^3 \dots y_N^3\}$	
(1, 4)	x_N^4	y_N^4	$\text{MAX}\{x_N^4 \dots x_N^4\}$	$\text{MAX}\{y_N^4 \dots y_N^4\}$	
(1, 5)	x_N^5	y_N^5	$\text{MAX}\{x_N^5 \dots x_N^5\}$	$\text{MAX}\{y_N^5 \dots y_N^5\}$	
...	...	...	...	...	
(i, j)	x_N^k	y_N^k	$\text{MAX}\{x_N^k \dots x_N^k\}$	$\text{MAX}\{y_N^k \dots y_N^k\}$	

Figure 8

Current Sequencing Cycle N			Pan-Channel AVG MAX States <u>900</u>	
Pixels <u>601</u>	Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Pan-Channel AVG MAX State Values <u>908</u>	
(1, 1)	$\begin{matrix} 1 \\ x \\ N \end{matrix}$	$\begin{matrix} 1 \\ y \\ N \end{matrix}$		
(1, 2)	$\begin{matrix} 2 \\ x \\ N \end{matrix}$	$\begin{matrix} 2 \\ y \\ N \end{matrix}$		
(1, 3)	$\begin{matrix} 3 \\ x \\ N \end{matrix}$	$\begin{matrix} 3 \\ y \\ N \end{matrix}$	Pixel-Wise Averages of Columns <u>804</u> and <u>805</u> in Figure 8	
(1, 4)	$\begin{matrix} 4 \\ x \\ N \end{matrix}$	$\begin{matrix} 4 \\ y \\ N \end{matrix}$		
(1, 5)	$\begin{matrix} 5 \\ x \\ N \end{matrix}$	$\begin{matrix} 5 \\ y \\ N \end{matrix}$		
...	...	...	...	...
(i, j)	$\begin{matrix} k \\ x \\ N \end{matrix}$	$\begin{matrix} k \\ y \\ N \end{matrix}$		

Figure 9

Current Sequencing Cycle N

Per-Channel AVG States 1000

Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Channel 1 AVG State Values 1004	Channel 2 AVG State Values 1005
(1, 1)	x_N^1	y_N^1	$AVG\{x_N^1 \dots x_1^1\}$	$AVG\{y_N^1 \dots y_1^1\}$
(1, 2)	x_N^2	y_N^2	$AVG\{x_N^2 \dots x_1^2\}$	$AVG\{y_N^2 \dots y_1^2\}$
(1, 3)	x_N^3	y_N^3	$AVG\{x_N^3 \dots x_1^3\}$	$AVG\{y_N^3 \dots y_1^3\}$
(1, 4)	x_N^4	y_N^4	$AVG\{x_N^4 \dots x_1^4\}$	$AVG\{y_N^4 \dots y_1^4\}$
(1, 5)	x_N^5	y_N^5	$AVG\{x_N^5 \dots x_1^5\}$	$AVG\{y_N^5 \dots y_1^5\}$
...	...	...	...	...
(i, j)	x_N^k	y_N^k	$AVG\{x_N^k \dots x_1^k\}$	$AVG\{y_N^k \dots y_1^k\}$

Figure 10

Pan-Channel AVG AVG States 1100

Current Sequencing Cycle N

Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Pan-Channel AVG AVG State Values 1108
(1, 1)	1 x N	1 y N	
(1, 2)	2 x N	2 y N	
(1, 3)	3 x N	3 y N	
(1, 4)	4 x N	4 y N	Pixel-Wise Averages of Columns 1004 and 1005 in Figure 10
(1, 5)	5 x N	5 y N	
...	...	...	...
(i, j)	k x N	k y N	

Figure 11

Current Sequencing Cycle N				Per-Channel MIN MAX States 1200			
Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Channel 1 MIN State Values 604	Channel 2 MIN State Values 605	Channel 1 MAX State Values 804	Channel 2 MAX State Values 805	
(1, 1)	x_N^1	y_N^1					
(1, 2)	x_N^2	y_N^2					
(1, 3)	x_N^3	y_N^3	600 (Figure 6)	800 (Figure 8)			
(1, 4)	x_N^4	y_N^4					
(1, 5)	x_N^5	y_N^5					
...	...	...					
(i, j)	x_N^k	y_N^k					

Figure 12

Current Sequencing Cycle N						Per-Channel MIN AVG States <u>1300</u>			
Pixels <u>601</u>	Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Channel 1 MIN State Values <u>604</u>	Channel 2 MIN State Values <u>605</u>	Channel 1 AVG State Values <u>1004</u>	Channel 2 AVG State Values <u>1005</u>			
(1, 1)	x_N^1	y_N^1							
(1, 2)	x_N^2	y_N^2							
(1, 3)	x_N^3	y_N^3	<u>600</u> Figure 6		<u>1000</u> Figure 10				
(1, 4)	x_N^4	y_N^4							
(1, 5)	x_N^5	y_N^5							
...	...	...							
(i, j)	x_N^k	y_N^k							

Figure 13

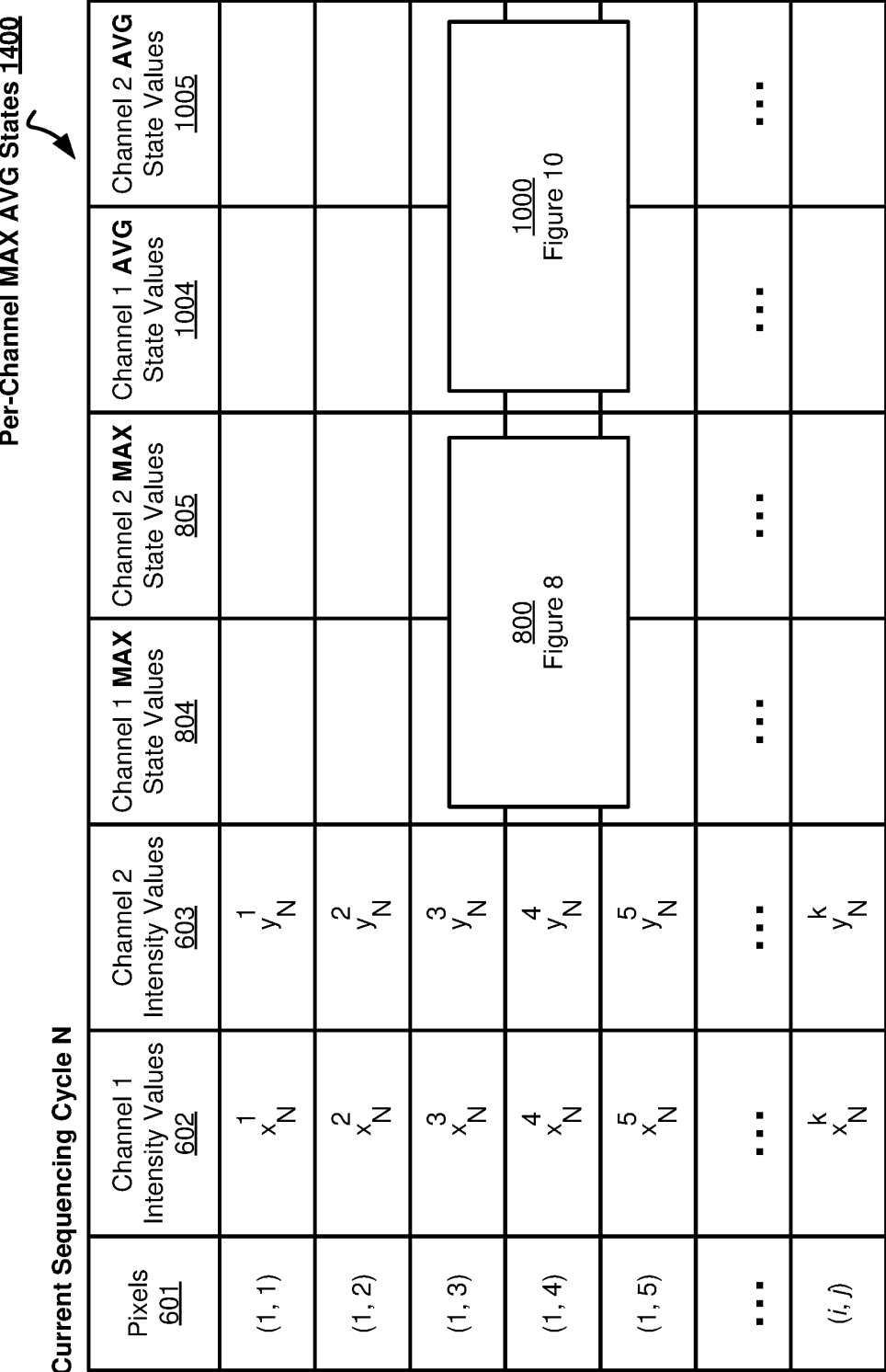
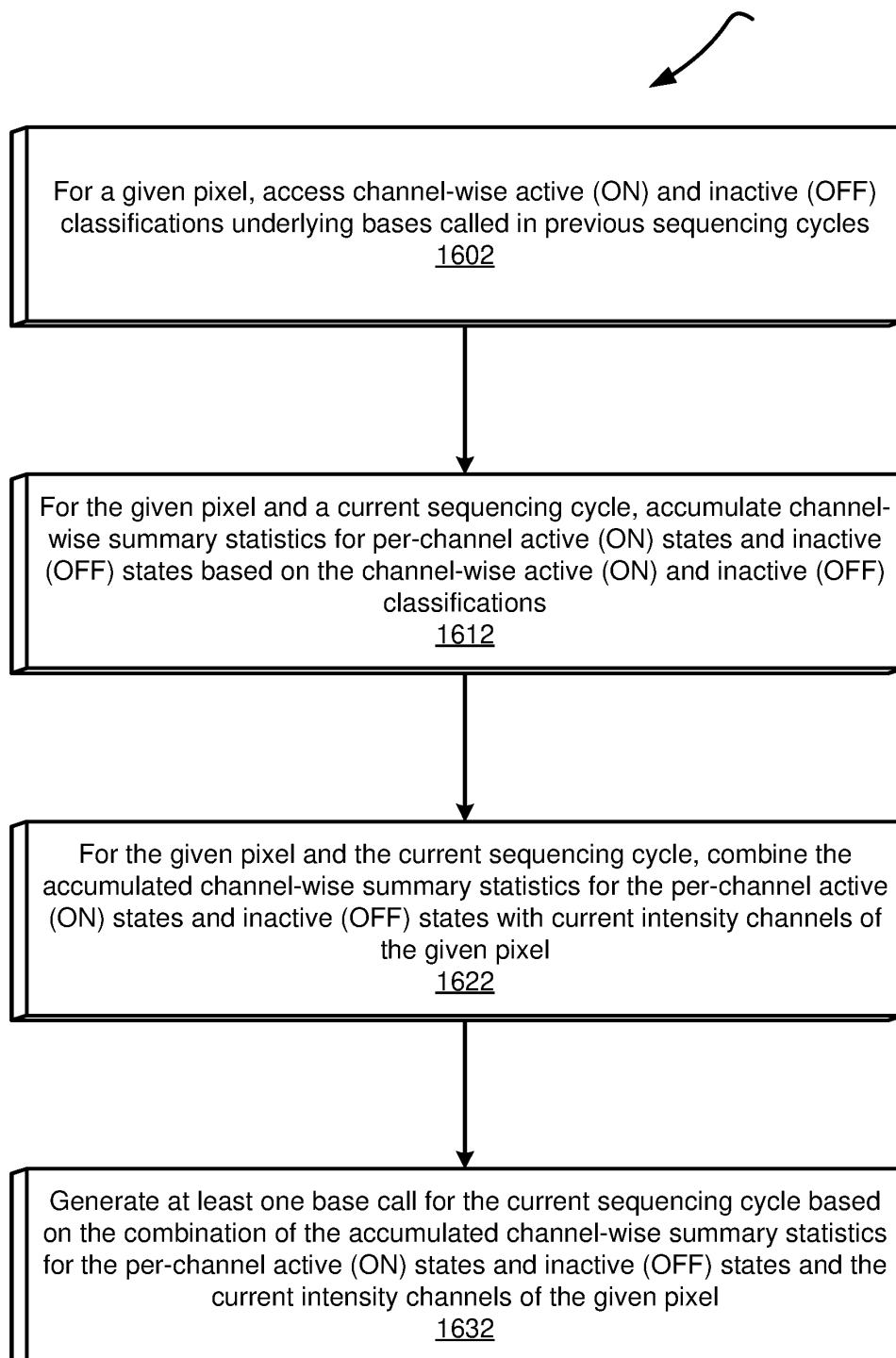


Figure 14

Current Sequencing Cycle N

Pixels <u>601</u>	Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Channel 1 MIN State Values <u>604</u>	Channel 2 MIN State Values <u>605</u>	Channel 1 MAX State Values <u>804</u>	Channel 2 MAX State Values <u>805</u>	Channel 1 AVG State Values <u>1004</u>	Channel 2 AVG State Values <u>1005</u>
(1, 1)	x_N^1	y_N^1						
(1, 2)	x_N^2	y_N^2						
(1, 3)	x_N^3	y_N^3						
(1, 4)	x_N^4	y_N^4						
(1, 5)	x_N^5	y_N^5						
...	...	...	...	...	...	...	...	...
(i, j)	x_N^k	y_N^k						

Figure 15

Base Call-Directed State Generation 1600**Figure 16**

Base Call-Directed ON and OFF State Generation 1700

Pixel <i>P</i>		Channel 1	Channel 2
Cycle 1	Base Call G	OFF x_1^P	OFF y_1^P
Cycle 2	Base Call C	OFF x_2^P	ON y_2^P
Cycle 3	Base Call T	ON x_3^P	ON y_3^P
Cycle 4	Base Call A	ON x_4^P	OFF y_4^P
Cycle 5	Base Call C	OFF x_5^P	ON y_5^P
Cycle 6	Base Call G	OFF x_6^P	OFF y_6^P
Cycle 7	Base Call T	ON x_7^P	ON y_7^P
Cycle 8	Base Call A	ON x_8^P	OFF y_8^P
Cycle 9	Base Call C	OFF x_9^P	ON y_9^P
Cycle 10	Base Call T	ON x_{10}^P	ON y_{10}^P

Figure 17A

Per-Channel State Calculation for Cycle 11		$f = \text{AVG, MAX, MIN, EXPWEGAVG, MOVAVG, EXPMOVAVG, STDEV}$
Channel 1 INACTIVE (OFF) State	1702	$f\{x_1^P, x_2^P, x_5^P, x_6^P, x_9^P\}$
Channel 1 ACTIVE (ON) State	1712	$f\{x_3^P, x_4^P, x_7^P, x_8^P, x_{10}^P\}$
Channel 2 INACTIVE (OFF) State	1722	$f\{y_1^P, y_4^P, y_6^P, y_8^P\}$
Channel 2 ACTIVE (ON) State	1732	$f\{y_2^P, y_3^P, y_5^P, y_7^P, y_9^P, y_{10}^P\}$

Figure 17B

Cycle 11		Channel 1	Channel 2	1702	1712	1722	1732
		x_{11}^P	y_{11}^P				

Figure 17C

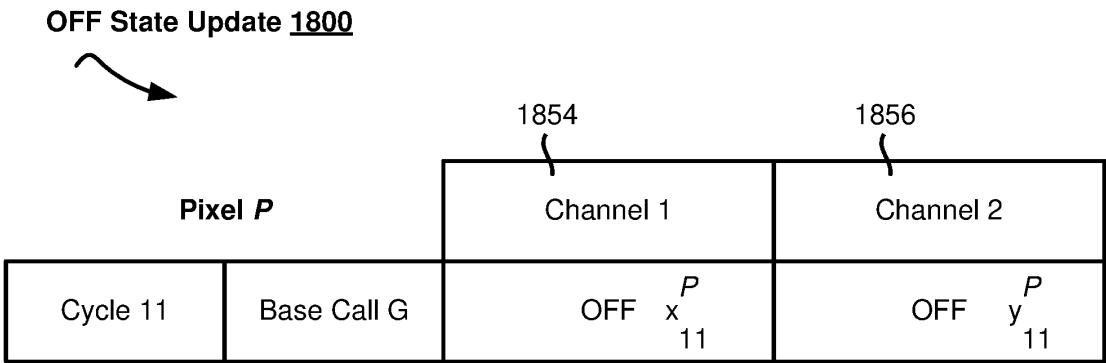


Figure 18A

Per-Channel State Calculation for Cycle 12		$f = \text{AVG, MAX, MIN, EXPWEGAVG, MOVAVG, EXPMOVAVG, STDEV}$
Channel 1 INACTIVE (OFF) State	1802	$f\{ \underline{1702}, x_{11}^P \}$
Channel 1 ACTIVE (ON) State	1812	<u>1712</u> (no change)
Channel 2 INACTIVE (OFF) State	1822	$f\{ \underline{1722}, y_{11}^P \}$
Channel 2 ACTIVE (ON) State	1832	<u>1732</u> (no change)

Figure 18B

Cycle 12	Channel 1	Channel 2	<u>1802</u>	<u>1812</u>	<u>1822</u>	<u>1832</u>
	x_{12}^P	y_{12}^P				

Figure 18C

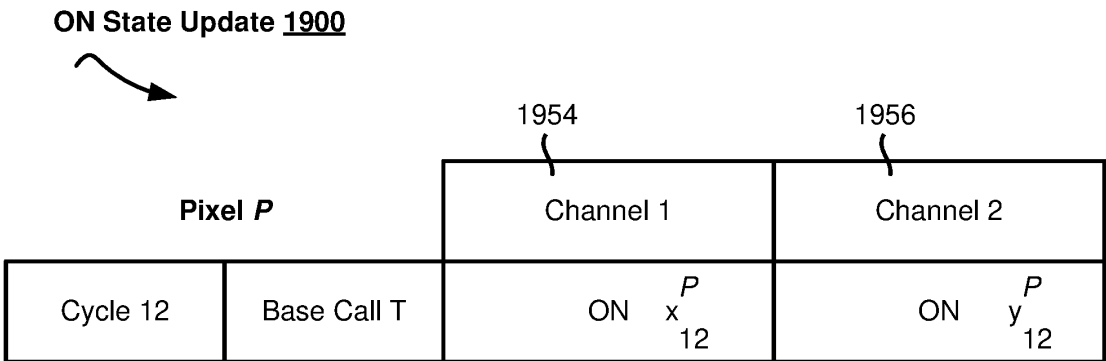


Figure 19A

Per-Channel State Calculation for Cycle 13			$f = \text{AVG, MAX, MIN, EXPWEGAVG, MOVAVG, EXPMOVAVG, STDEV}$
Channel 1 INACTIVE (OFF) State	1902	<u>1802</u> (no change)	
Channel 1 ACTIVE (ON) State	1912	$f\{ \text{1812}, x_{12}^P \}$	
Channel 2 INACTIVE (OFF) State	1922	<u>1822</u> (no change)	
Channel 2 ACTIVE (ON) State	1932	$f\{ \text{1832}, y_{12}^P \}$	

Figure 19B

Cycle 13	1964 Channel 1	1966 Channel 2	<u>1902</u>	<u>1913</u>	<u>1922</u>	<u>1932</u>
	x_{13}^P	y_{13}^P				

Figure 19C

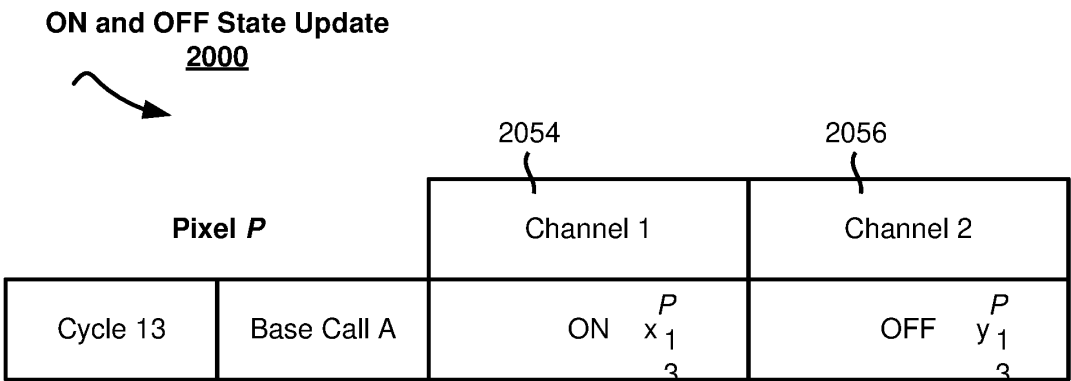


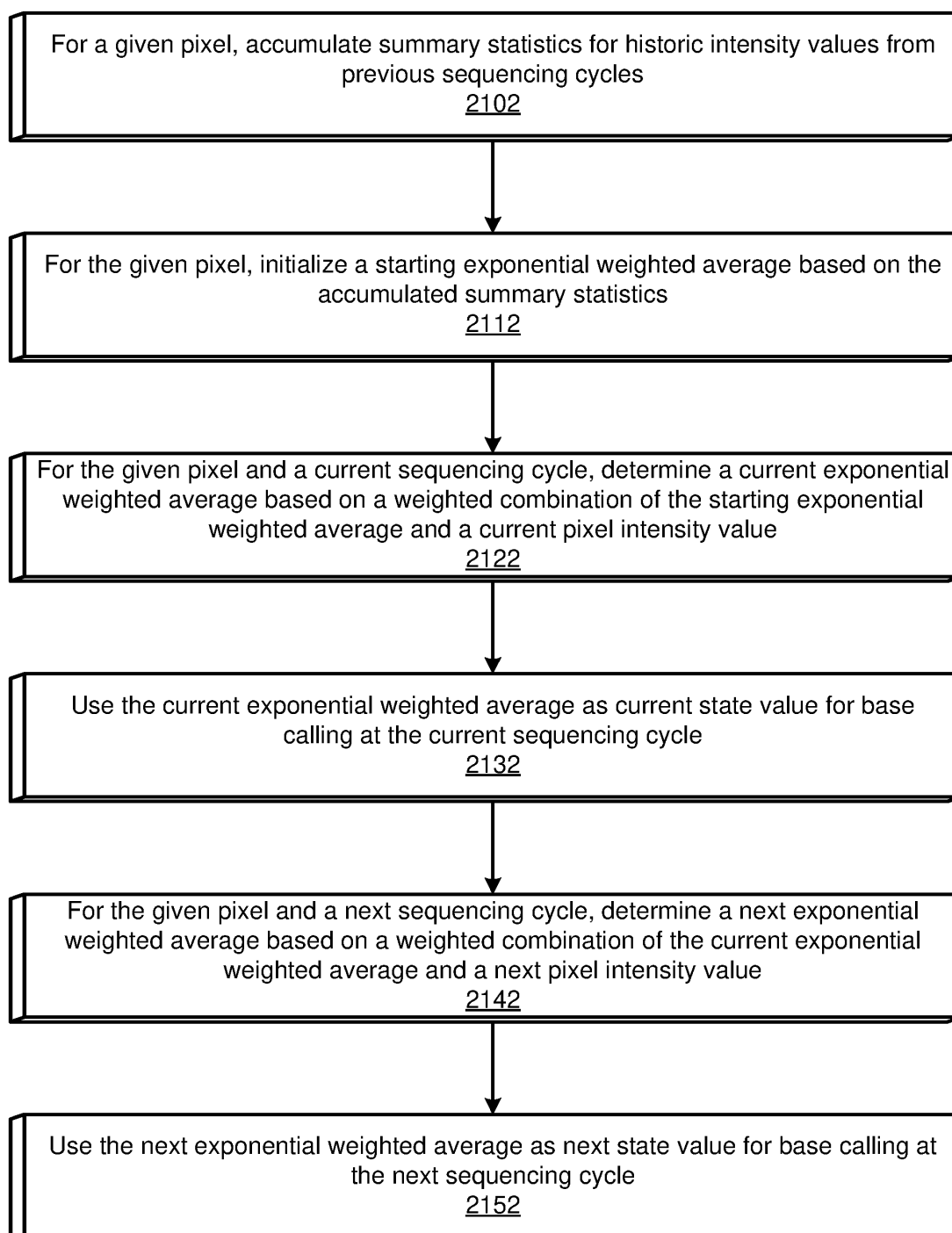
Figure 20A

$f = \text{AVG, MAX, MIN, EXPWEGAVG, MOVAVG, EXPMOVAVG, STDEV}$		
Per-Channel State Calculation for Cycle 14		
Channel 1 INACTIVE (OFF) State	2002	<u>1902</u> (no change)
Channel 1 ACTIVE (ON) State	2012	$f\{ \underline{1912}, x_{13}^P \}$
Channel 2 INACTIVE (OFF) State	2022	$f\{ \underline{1922}, y_{13}^P \}$
Channel 2 ACTIVE (ON) State	2032	<u>1932</u> (no change)

Figure 20B

Cycle 14	Channel 1	Channel 2	<u>2002</u>	<u>2014</u>	<u>2022</u>	<u>2032</u>
	x_{14}^P	y_{14}^P				

Figure 20C

Exponential Weighted Averaging 2100**Figure 21**

Per-Channel Exponential Weighted Averaging 2200

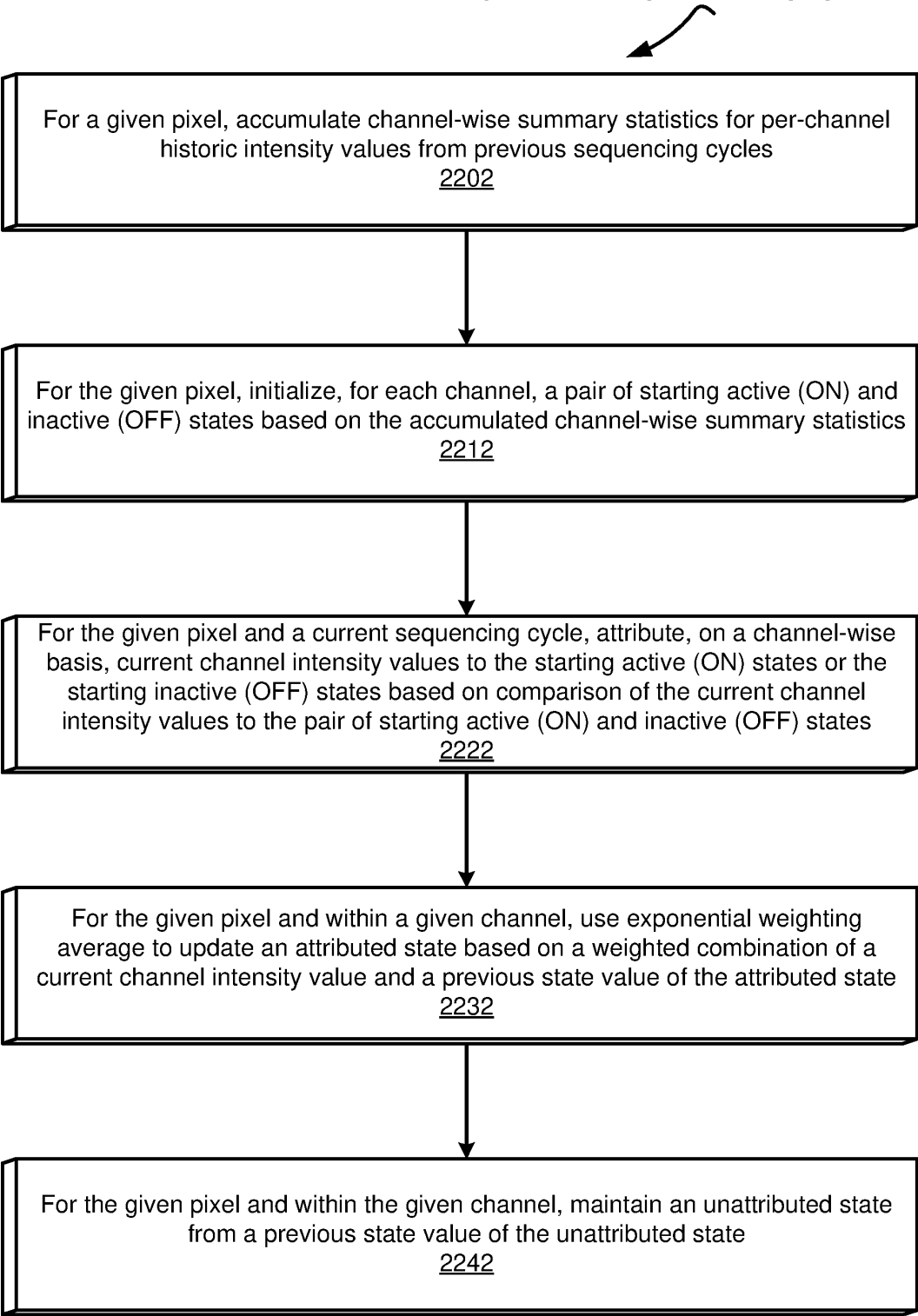
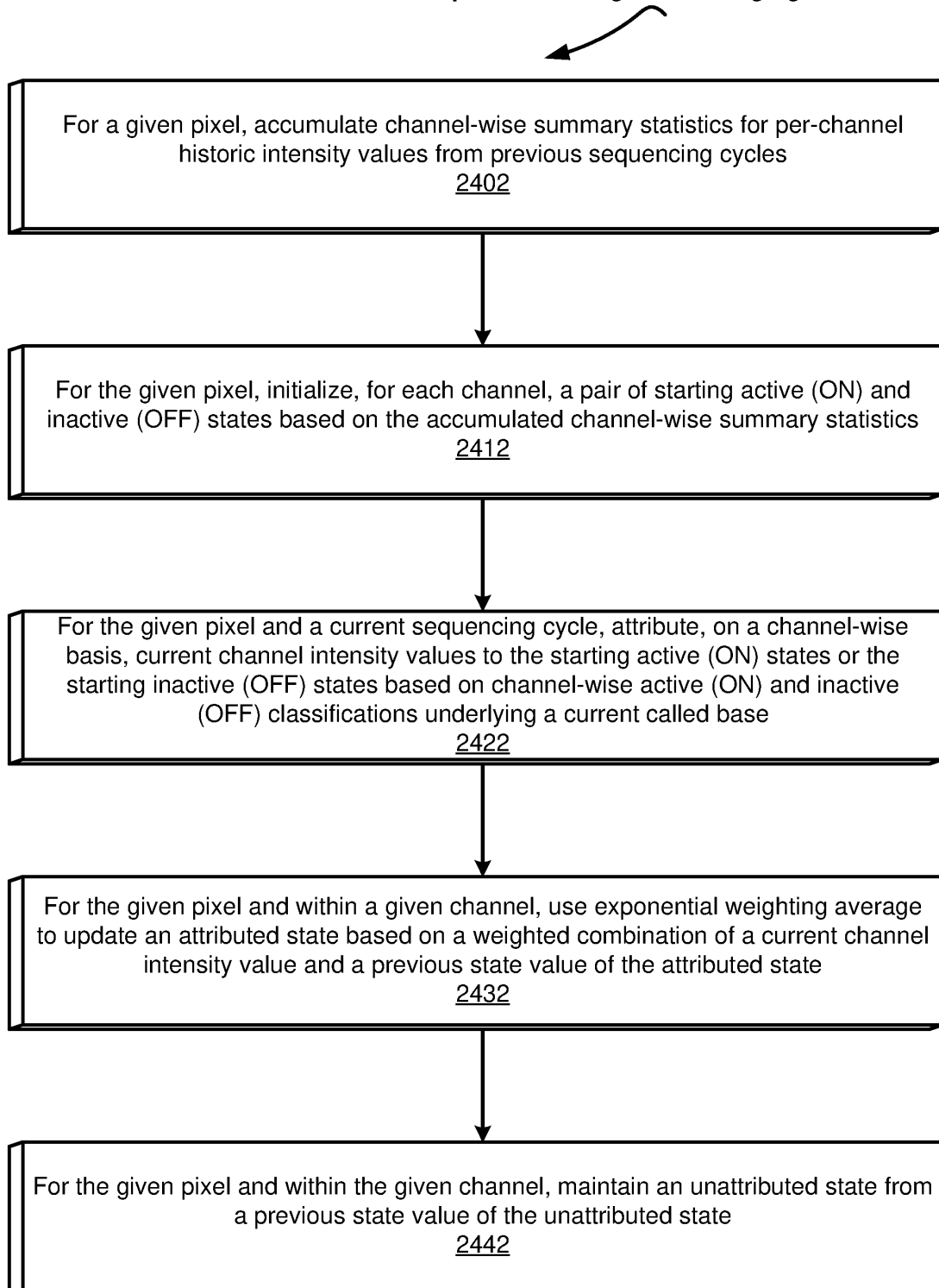


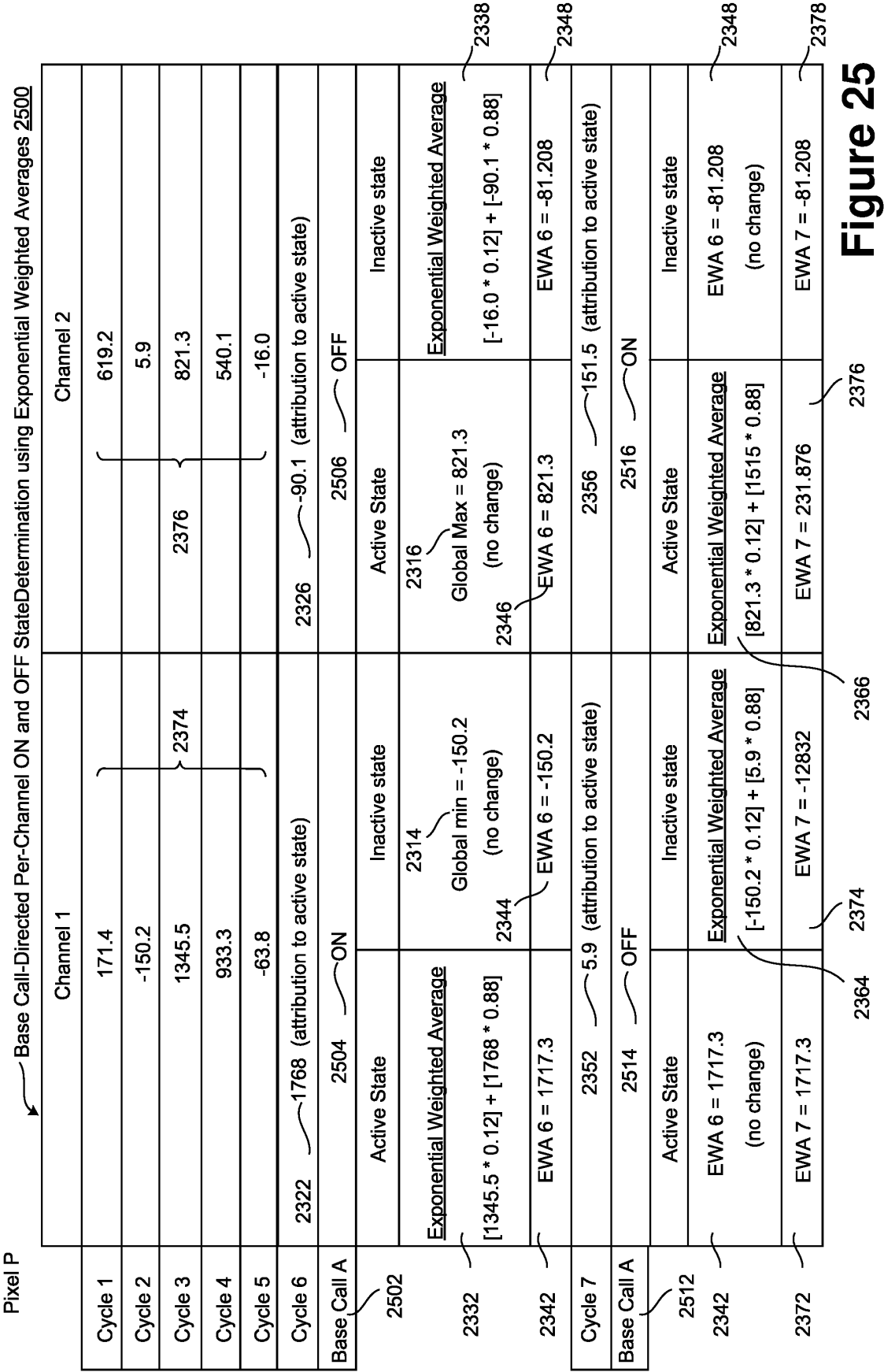
Figure 22

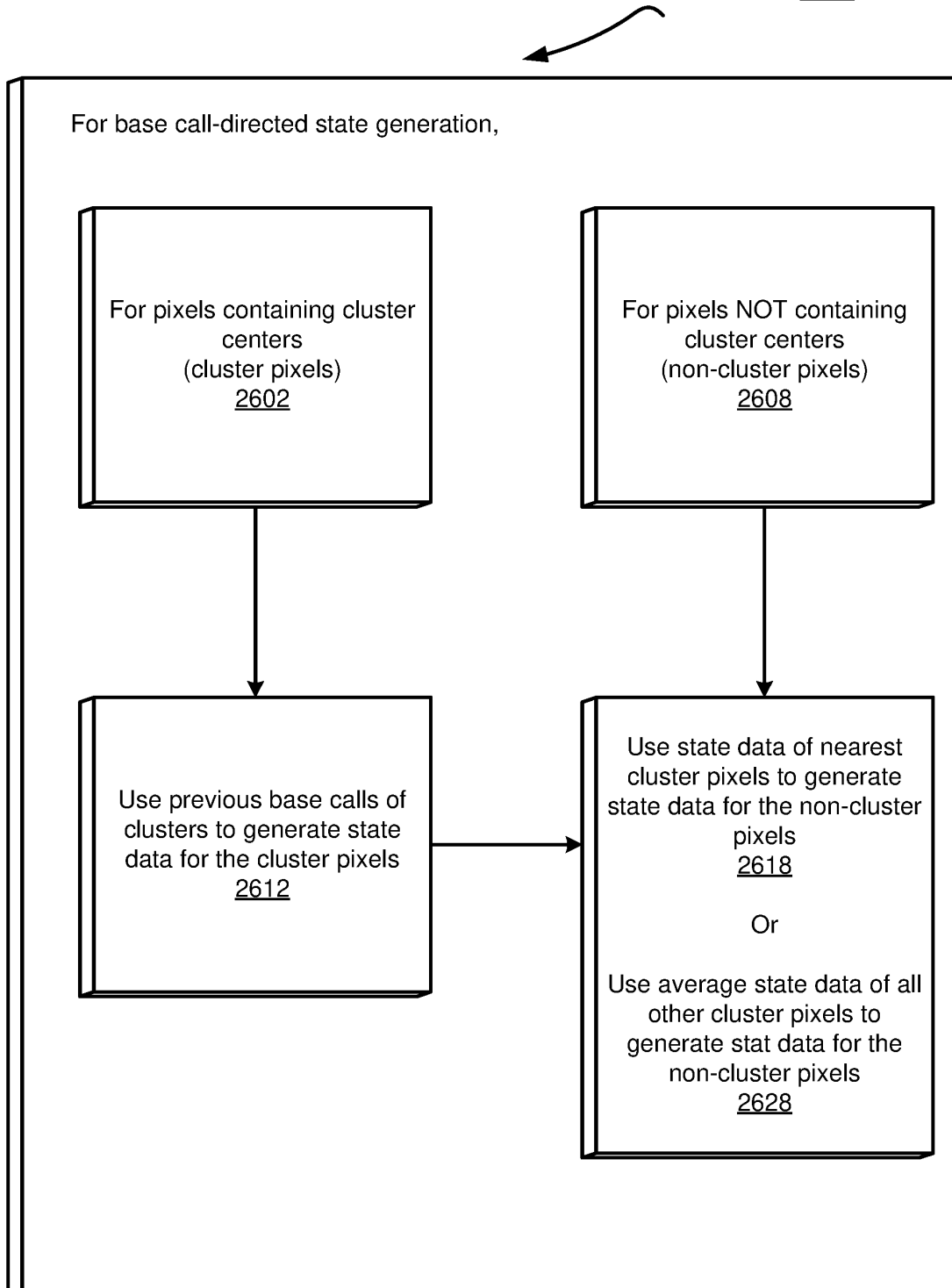
Pixel P Per-Channel ON and OFF State Determination using GlobalMAX and MIN and Exponential Weighted Averages 2300

	Channel 1		Channel 2	
Cycle 1	171.4		619.2	
Cycle 2	-150.2		5.9	
Cycle 3	1345.5	2374	2376	821.3
Cycle 4	933.3			540.1
Cycle 5	-63.8	2314	2316	-16.0
	Global Max = 1345.5		Global Min = -150.2	
Cycle 6	2322 (attribution to active state)		2326 (attribution to active state)	
	Active State	Inactive state	Active State	Inactive state
	Exponential Weighted Average	2314	2316	Exponential Weighted Average
2332	$[1345.5 * 0.12] + [1768 * 0.88]$	Global min = -150.2 (no change)	Global Max = 821.3 (no change)	$[-16.0 * 0.12] + [-90.1 * 0.88]$
2342	EWA 6 = 1717.3	EWA 6 = -150.2	EWA 6 = 821.3	EWA 6 = -81.208
Cycle 7	2352 (attribution to active state)	2356 (attribution to active state)	2356 (attribution to active state)	2348
	Active State	Inactive state	Active State	Inactive state
2342	EWA 6 = 1717.3 (no change)	Exponential Weighted Average $[-150.2 * 0.12] + [5.9 * 0.88]$	Exponential Weighted Average $[821.3 * 0.12] + [1515 * 0.88]$	EWA 6 = -81.208 (no change)
2372	EWA 7 = 1717.3	EWA 7 = -12832	EWA 7 = 231.876	EWA 7 = -81.208
	2364 2374 2366 2376			2378

Figure 23

Base Call-Directed Per-Channel Exponential Weighted Averaging 2400**Figure 24**



Base Call-Directed State Generation for Non-Cluster Pixels 2600**Figure 26**

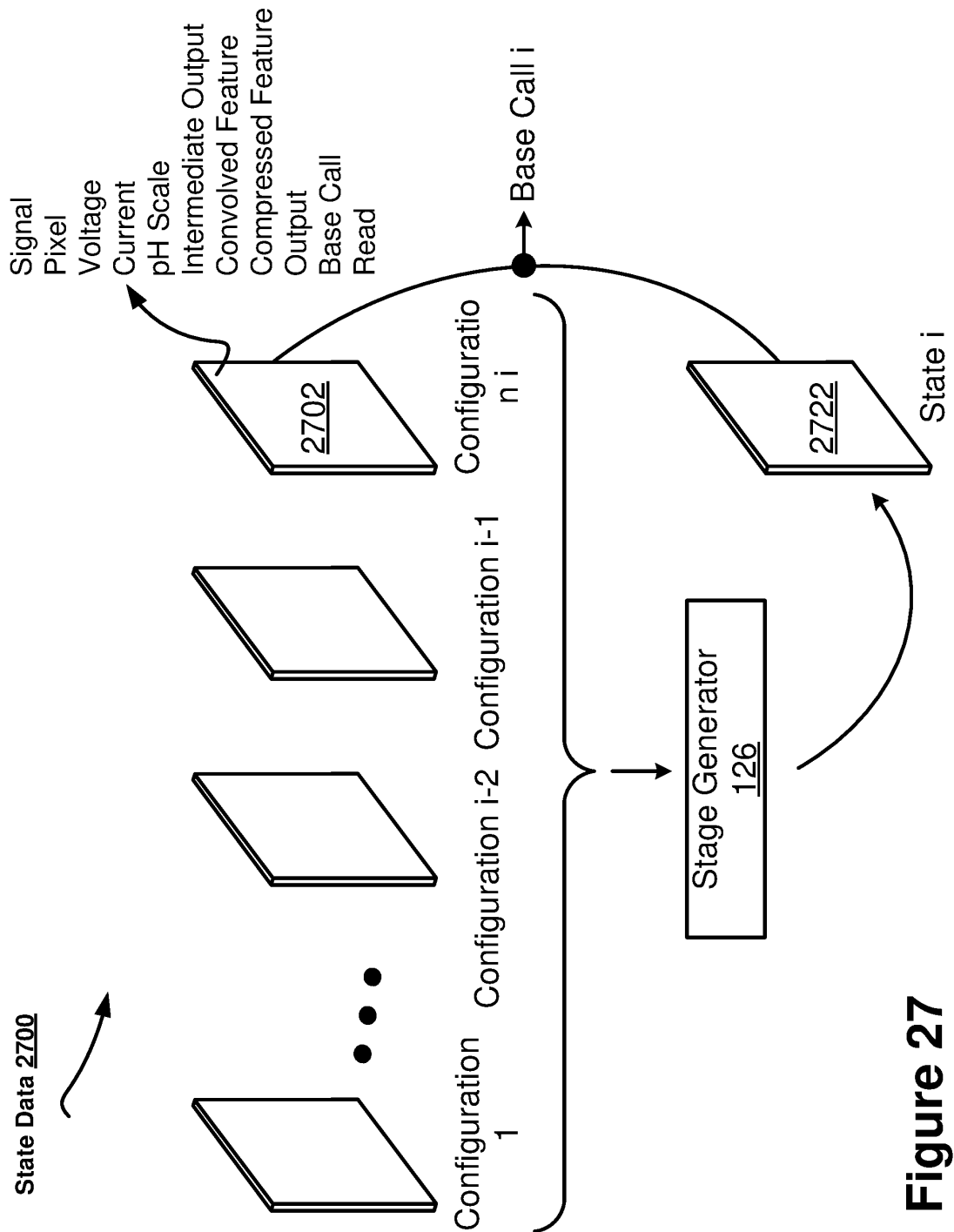


Figure 27

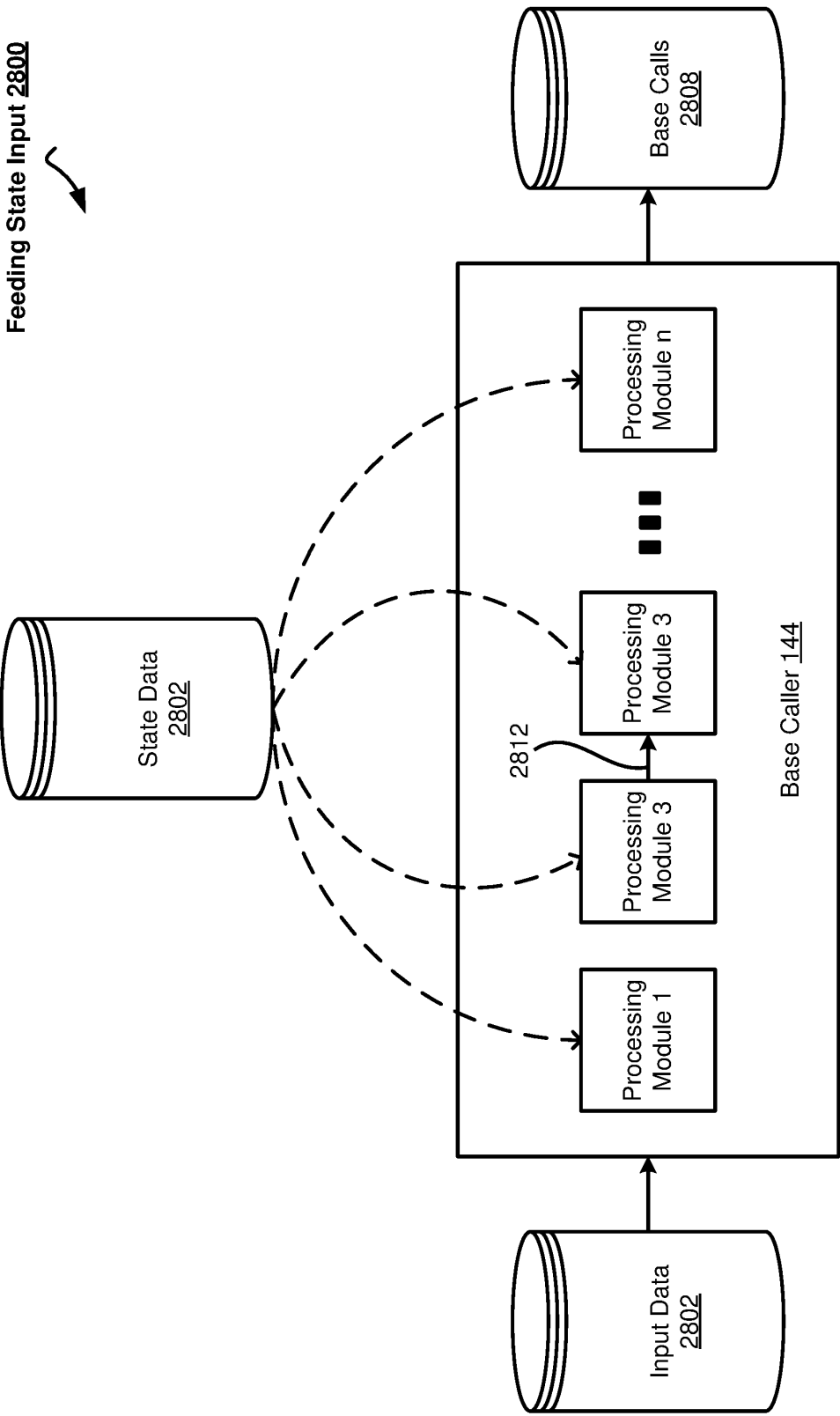


Figure 28

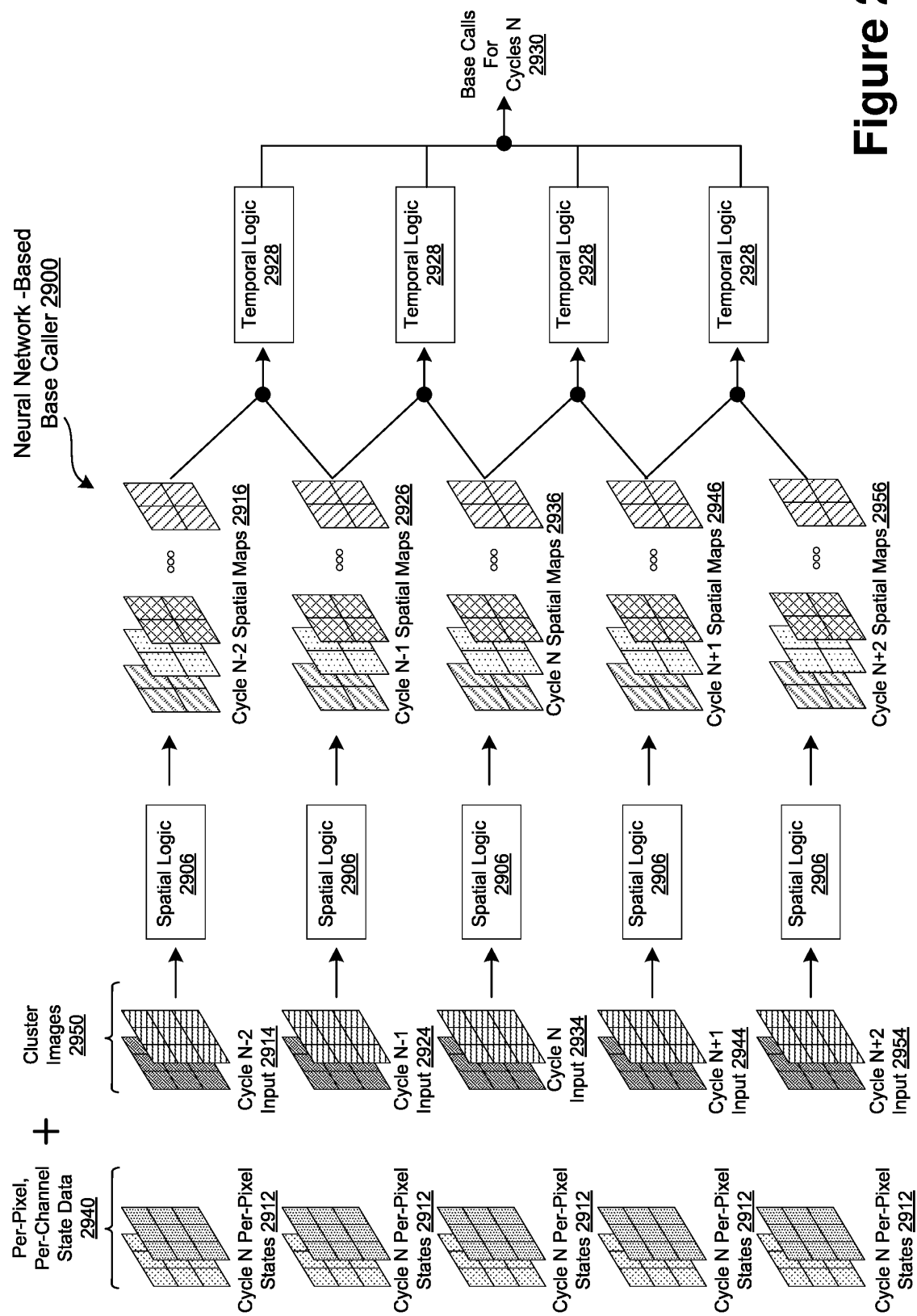


Figure 29

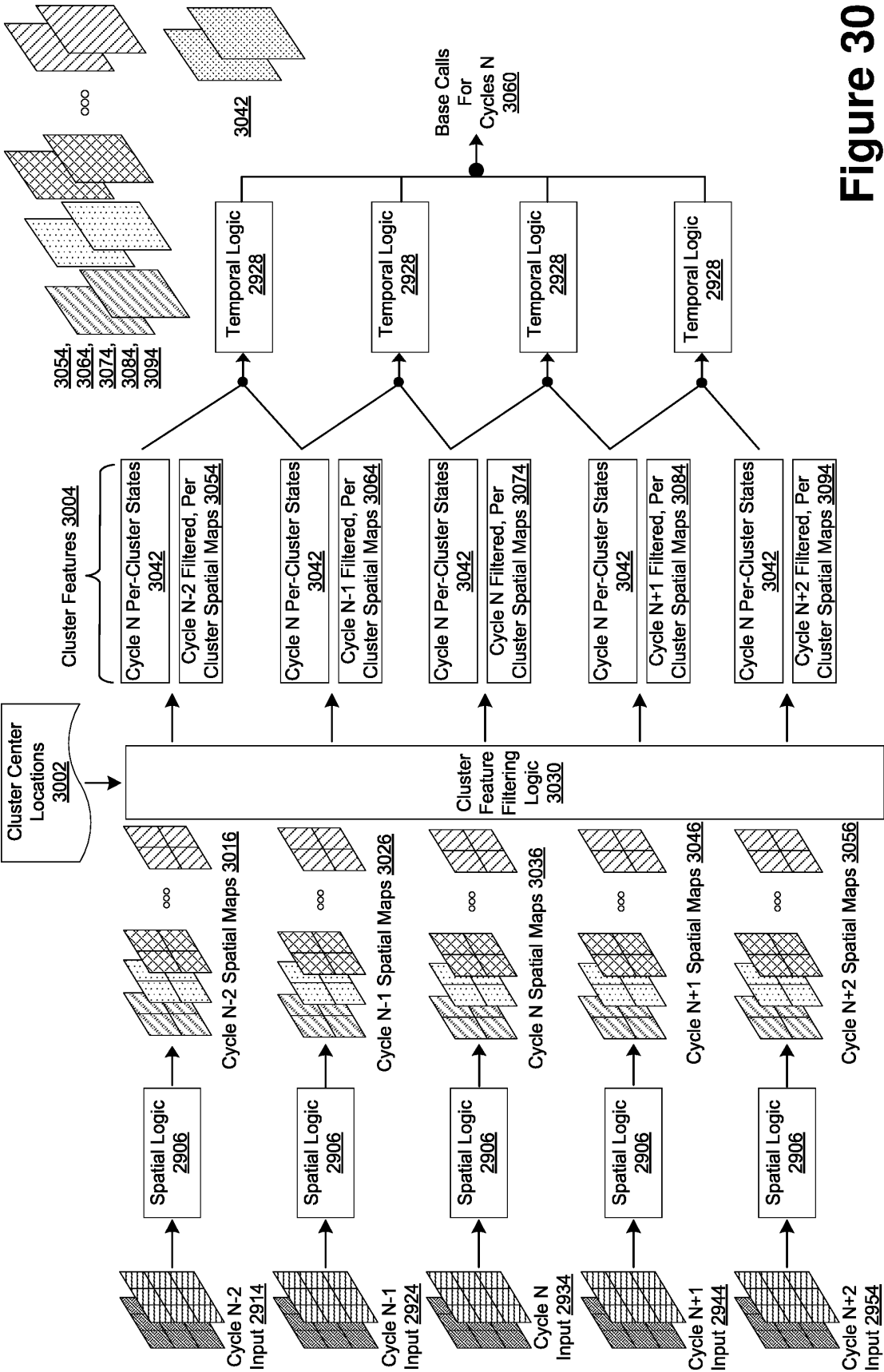
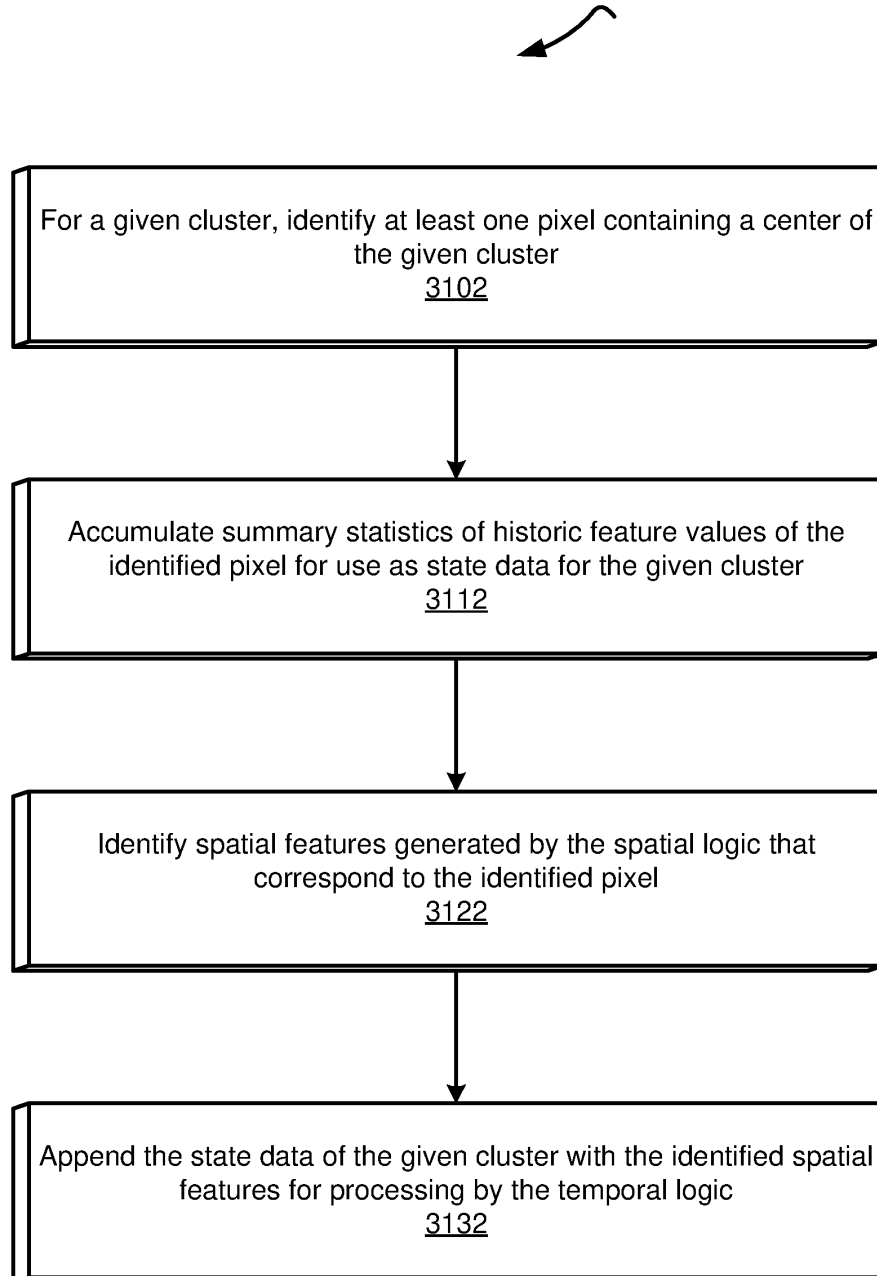
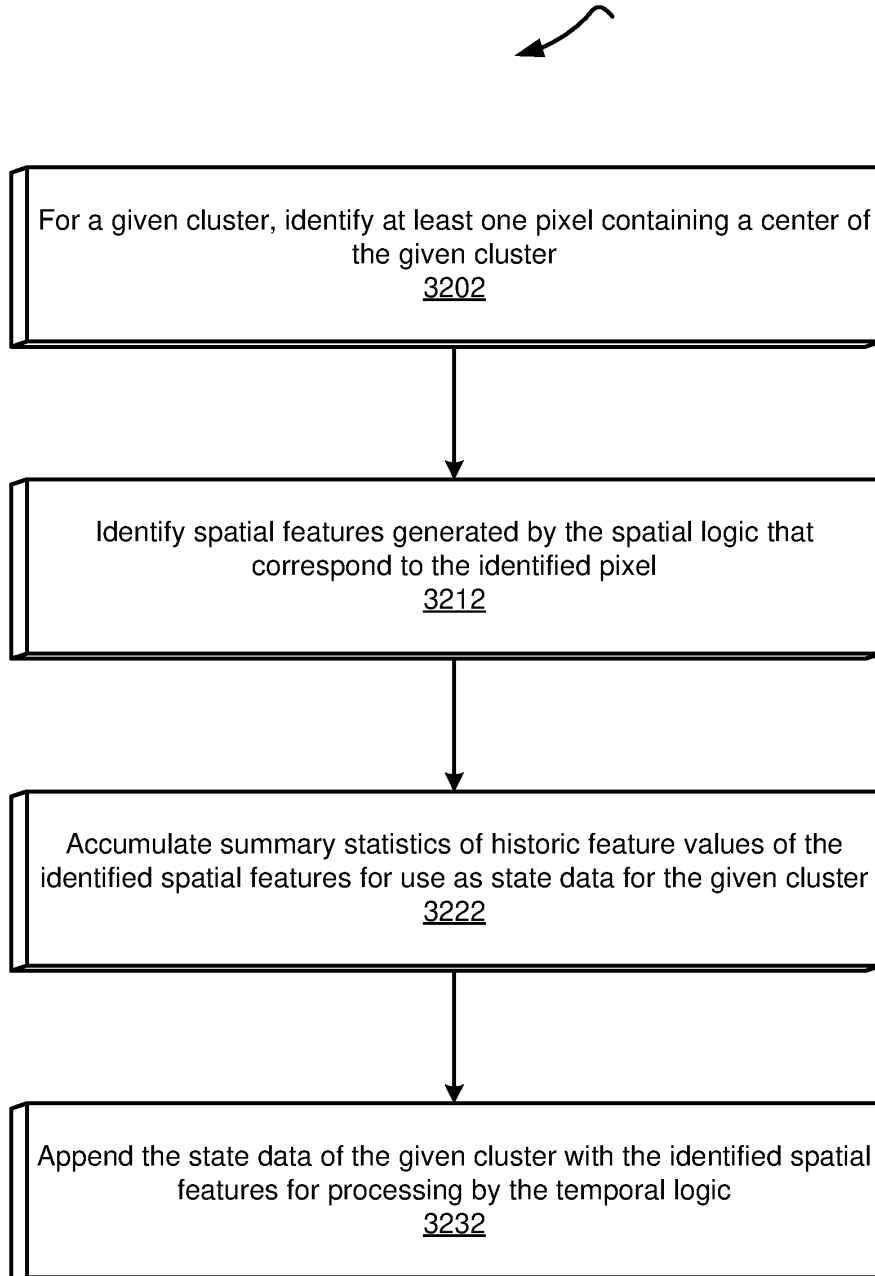
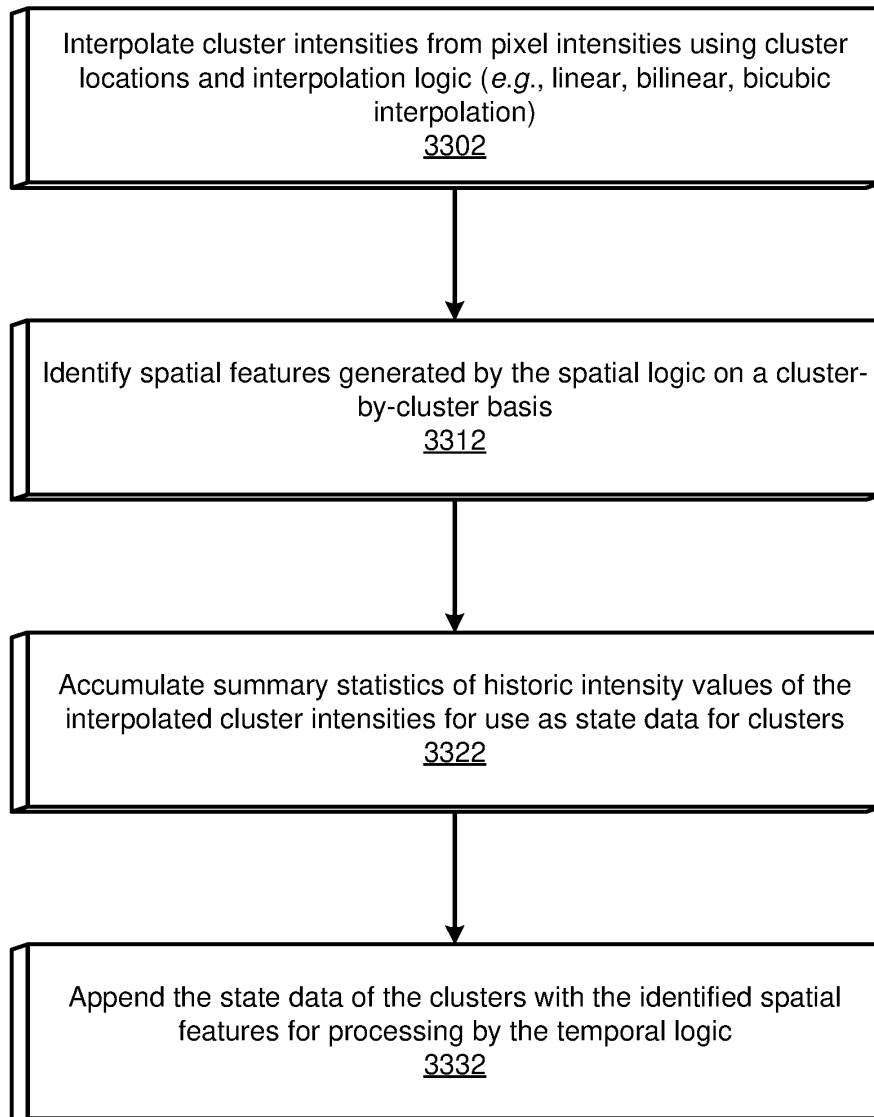
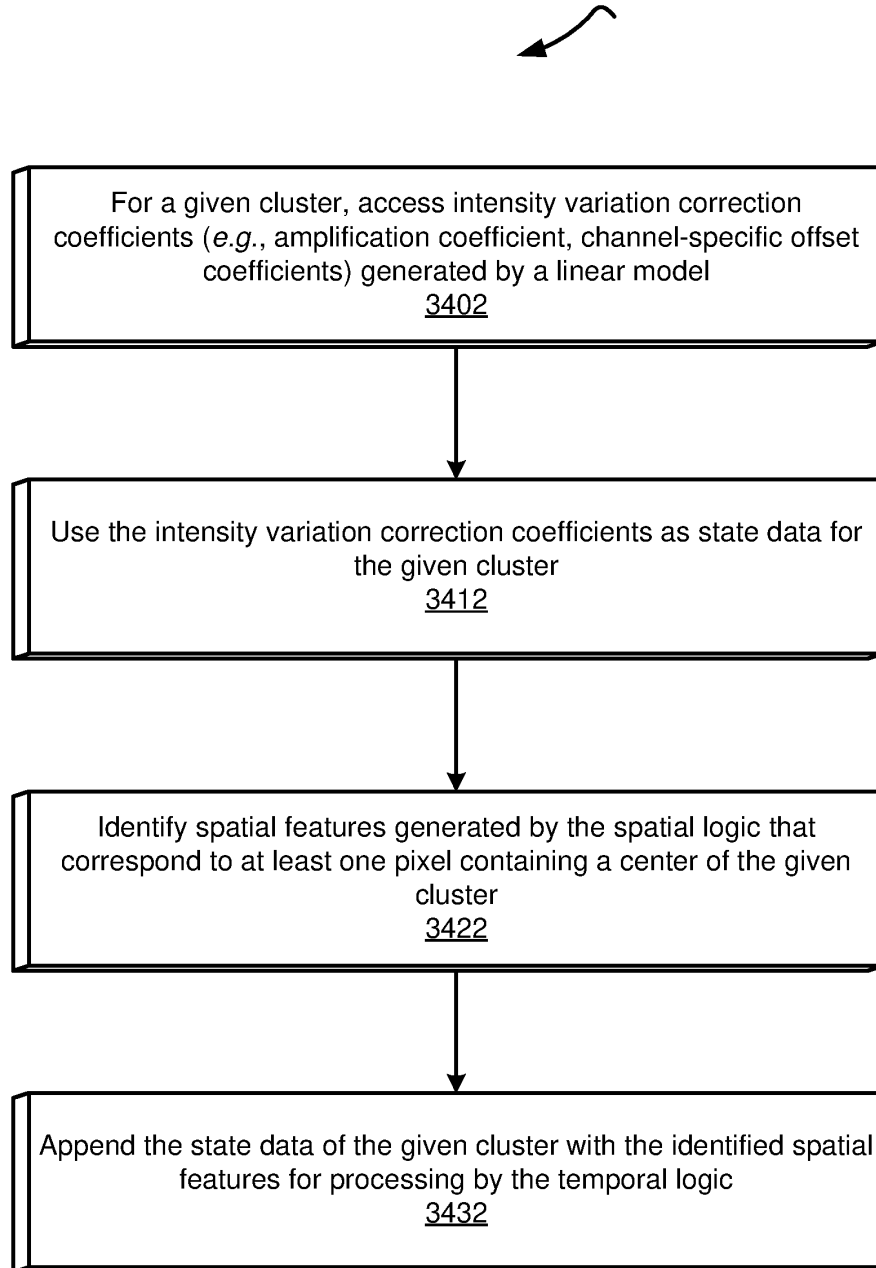


Figure 30

Per-Cluster Pixel-Based State Generation 3100**Figure 31**

Per-Cluster Spatial Features-Based State Generation 3200**Figure 32**

Per-Cluster Interpolated Features-Based State Generation 3300**Figure 33**

Per-Cluster RTA Coefficients-Based State Generation 3400**Figure 34**

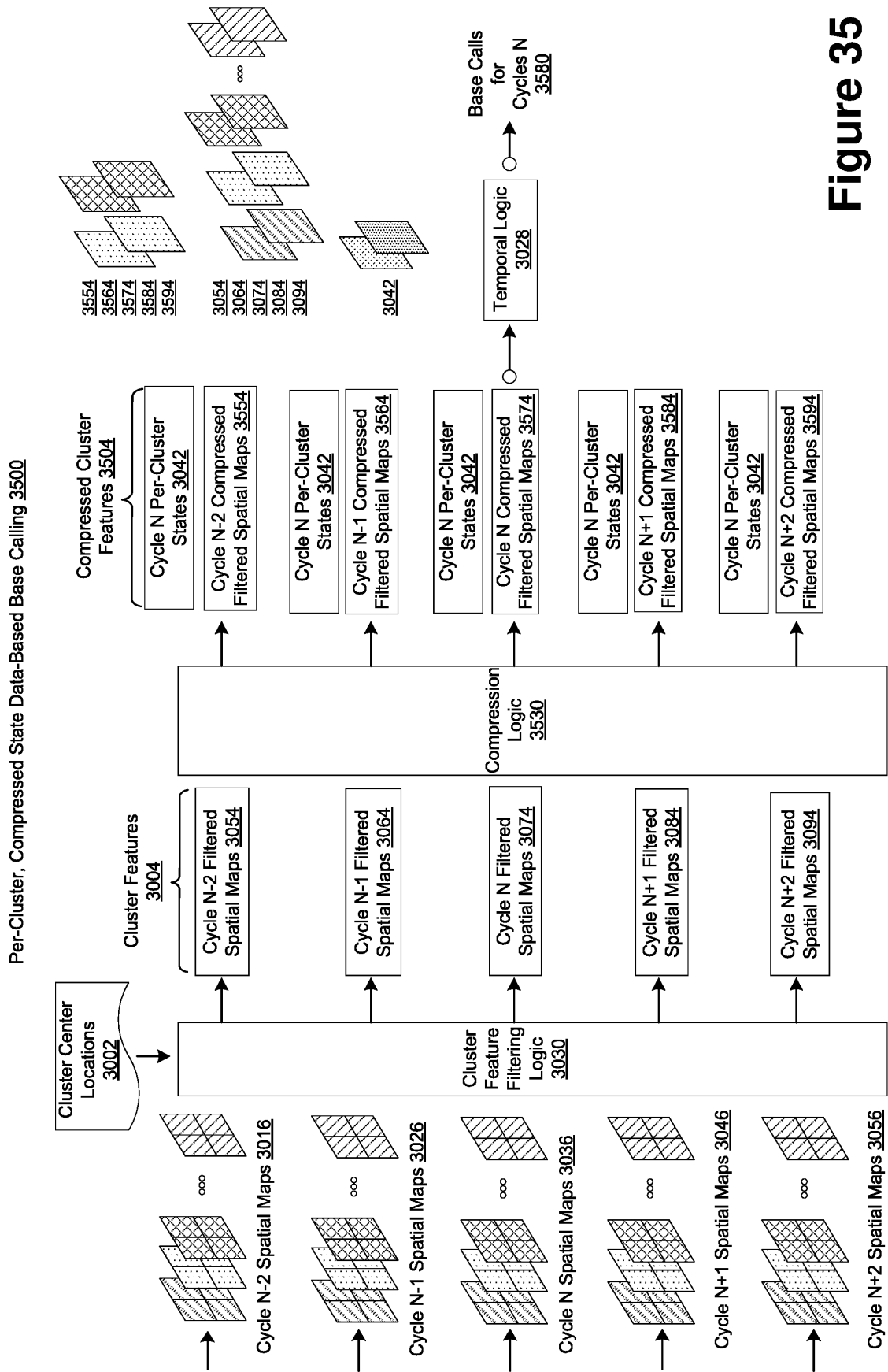
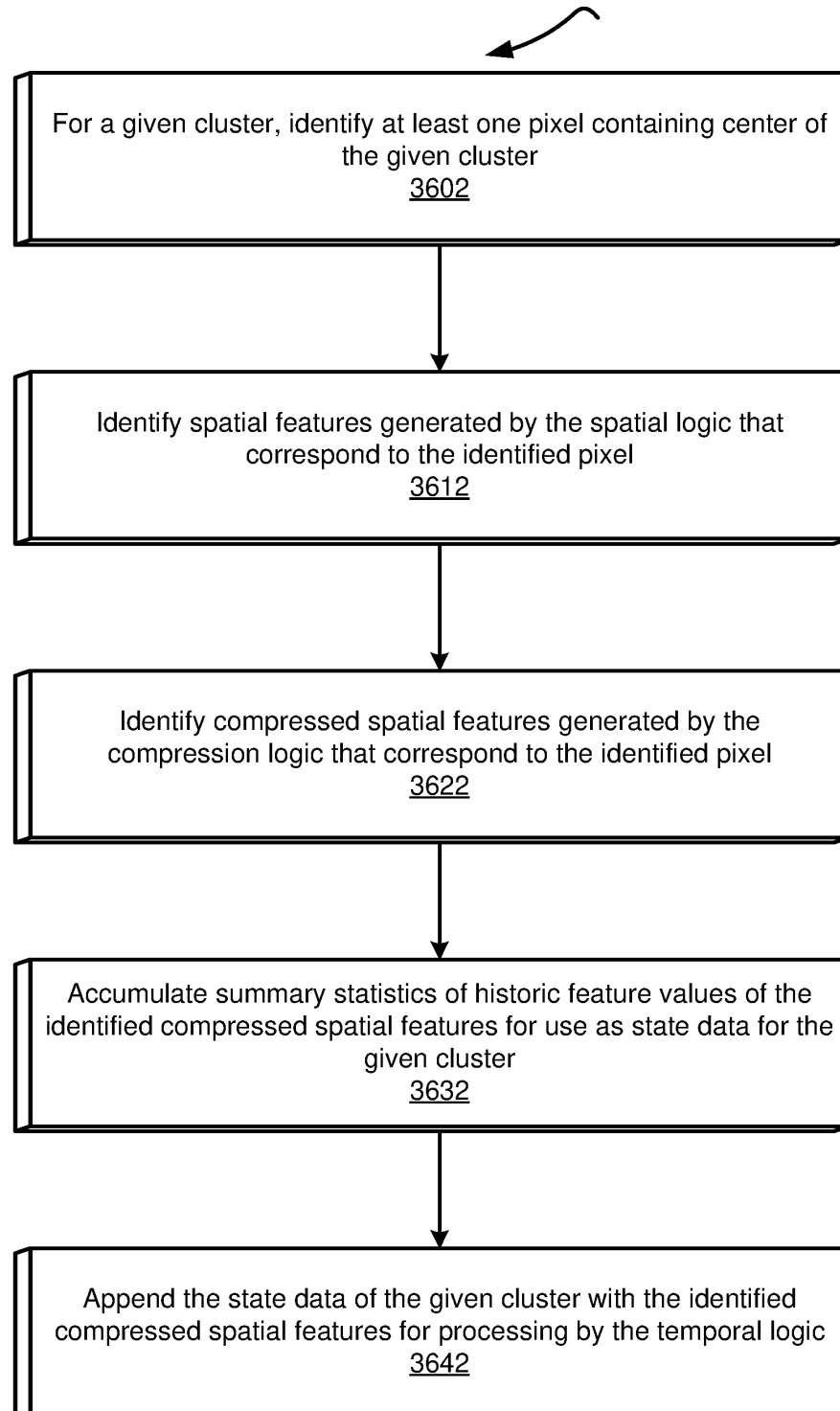
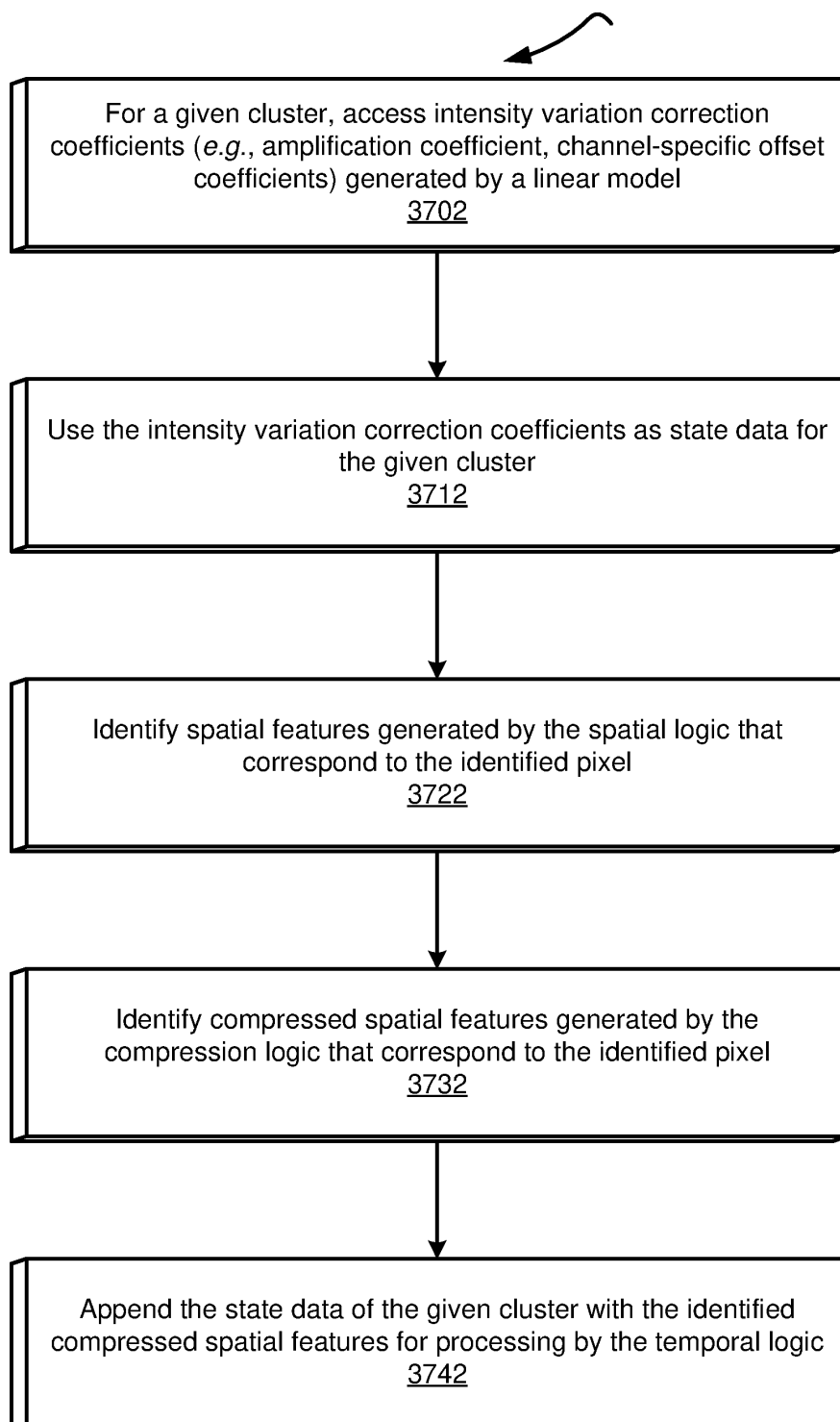
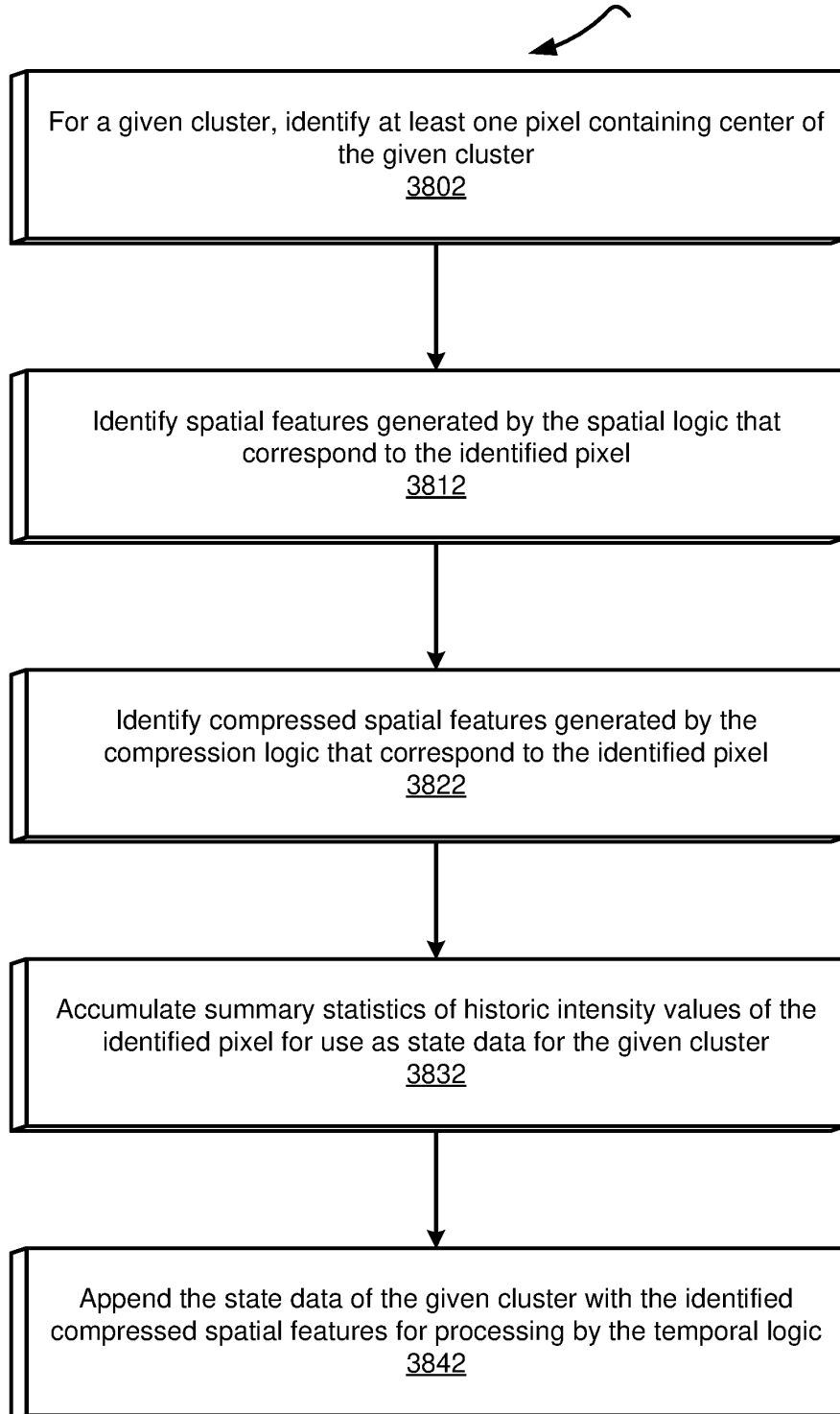


Figure 35

Per-Cluster Compressed Spatial Features-Based State Generation 3600**Figure 36**

Per-Cluster RTA Compressed Features-Based State Generation 3700**Figure 37**

Per-Cluster Compressed Pixel-Based State Generation 3800**Figure 38**

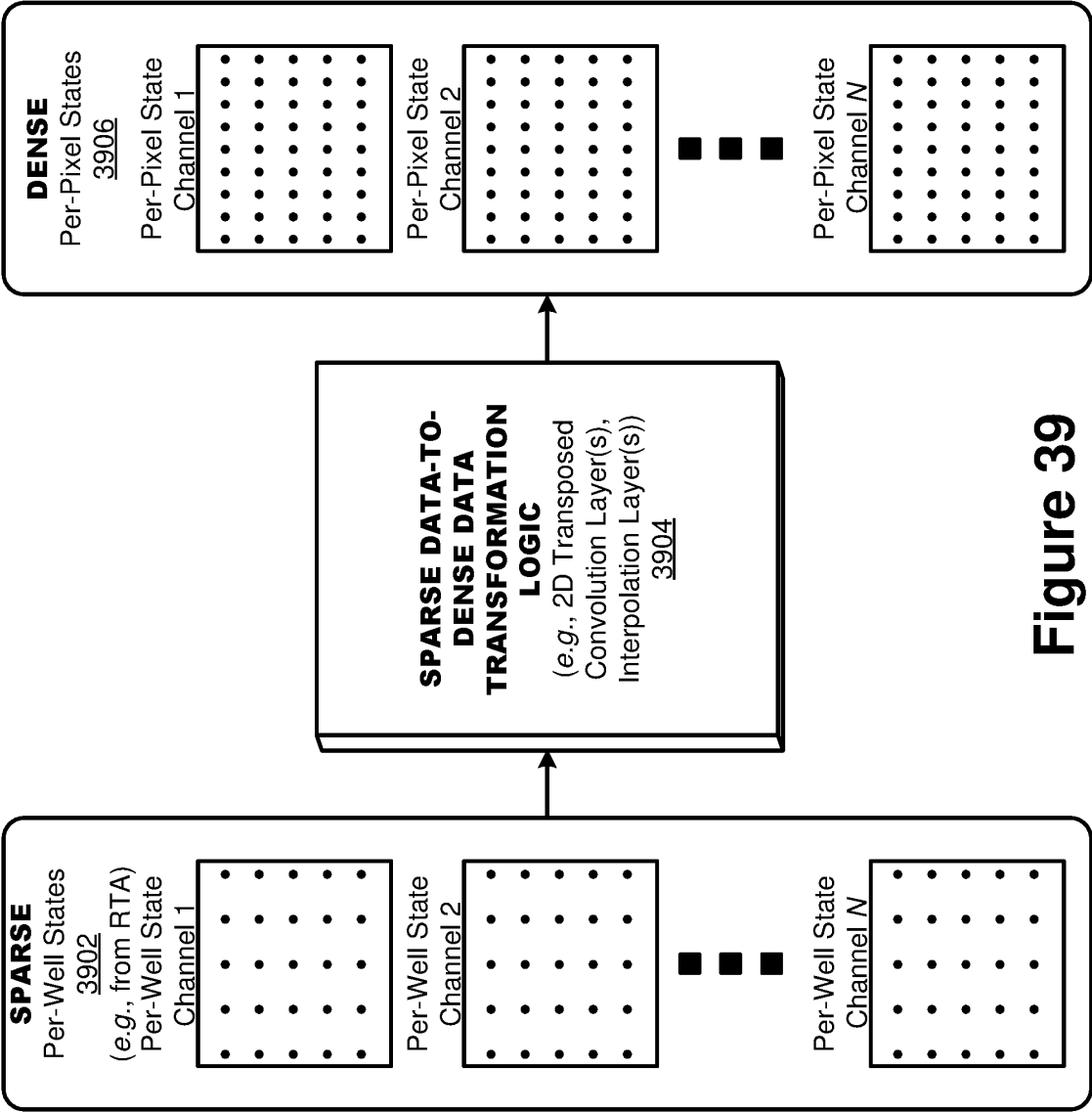


Figure 39

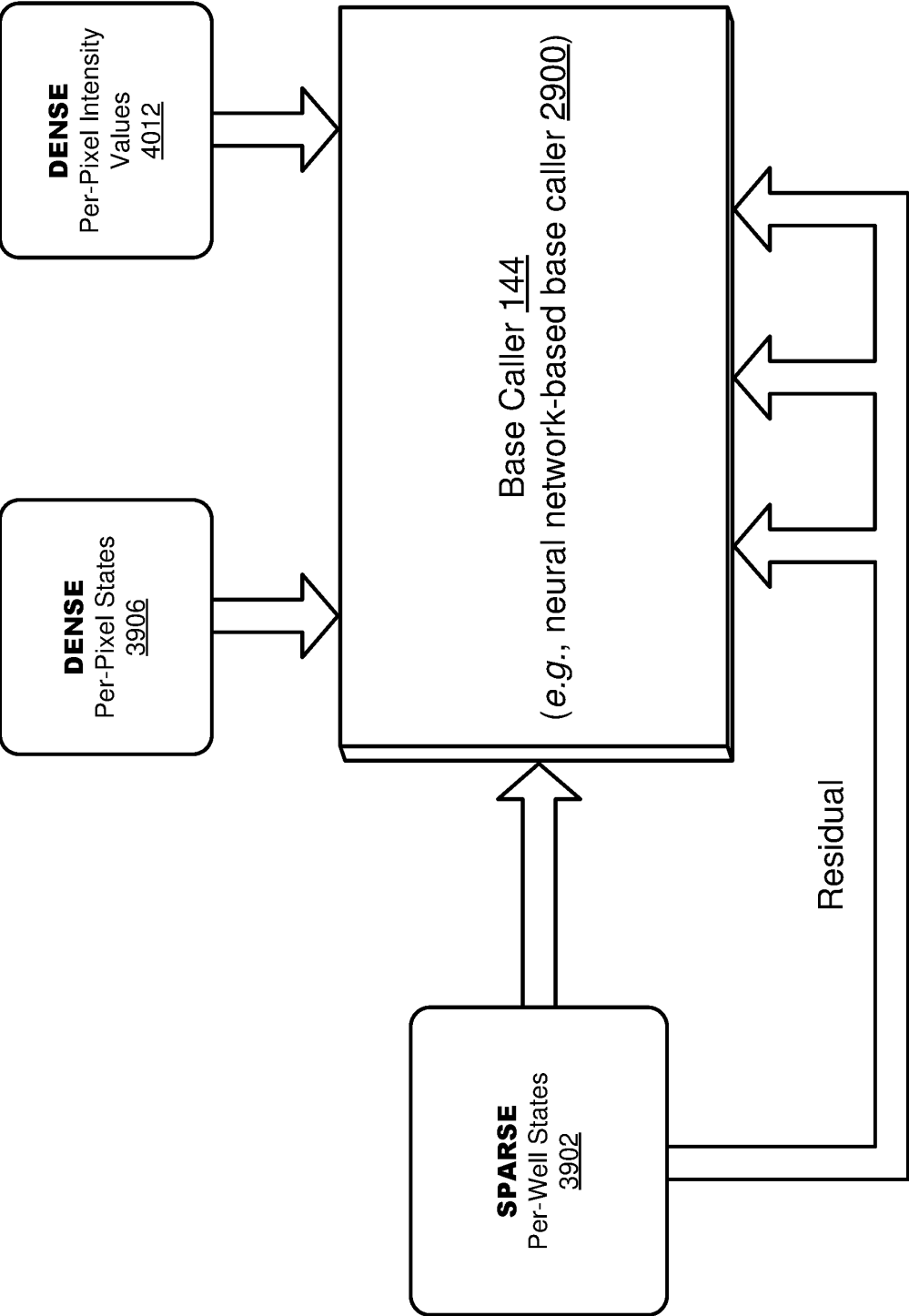


Figure 40

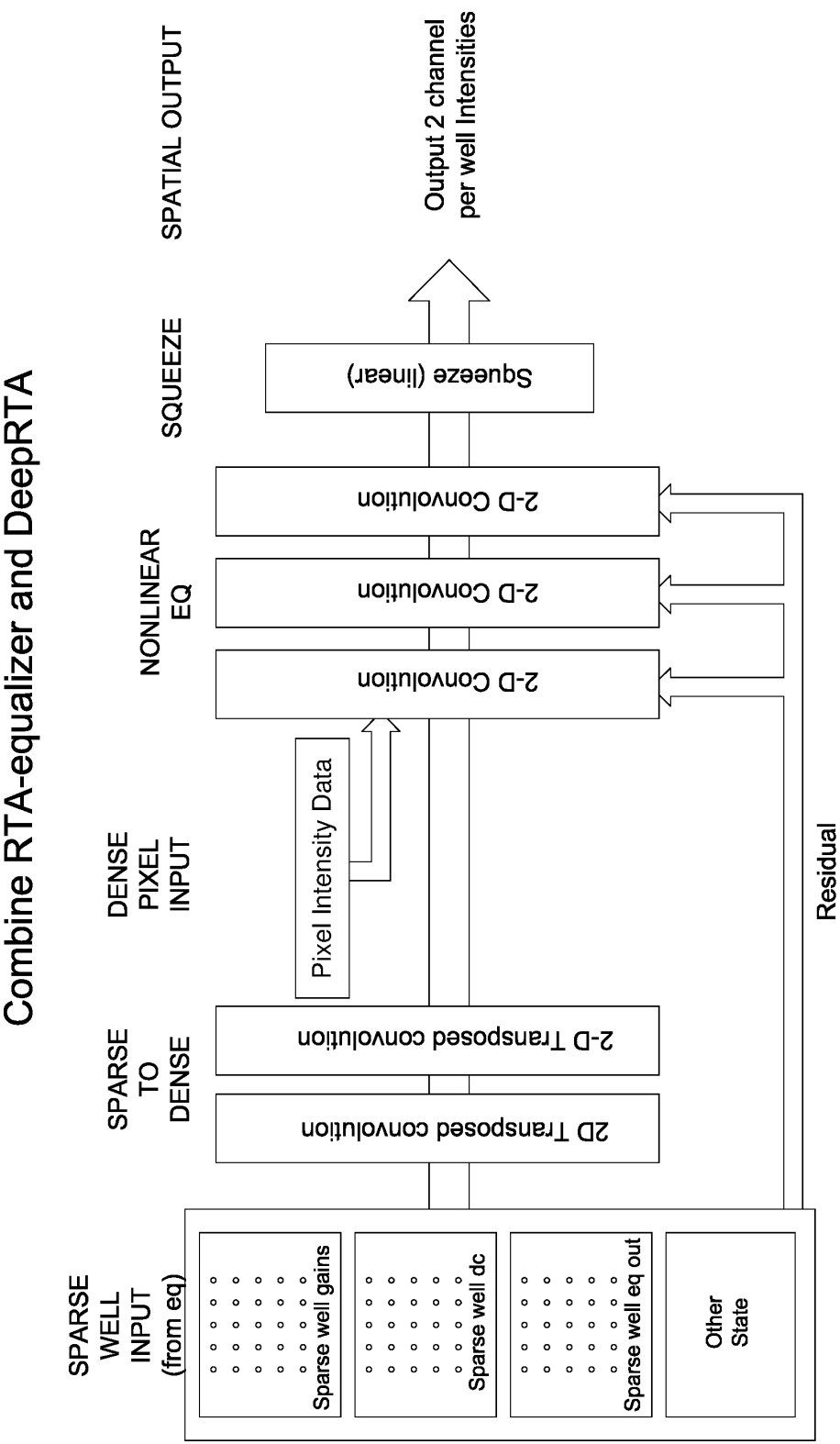


Figure 41

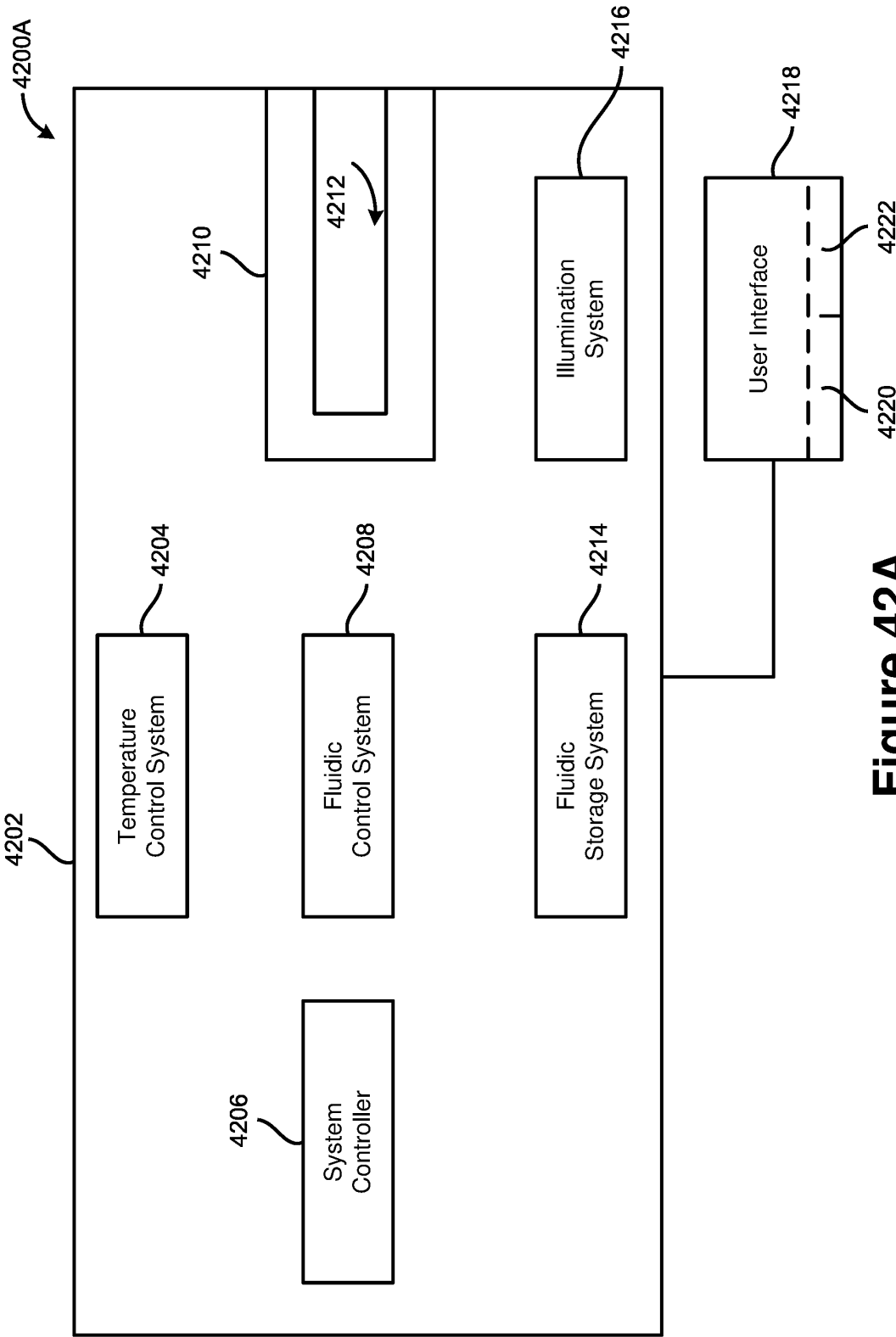


Figure 42A

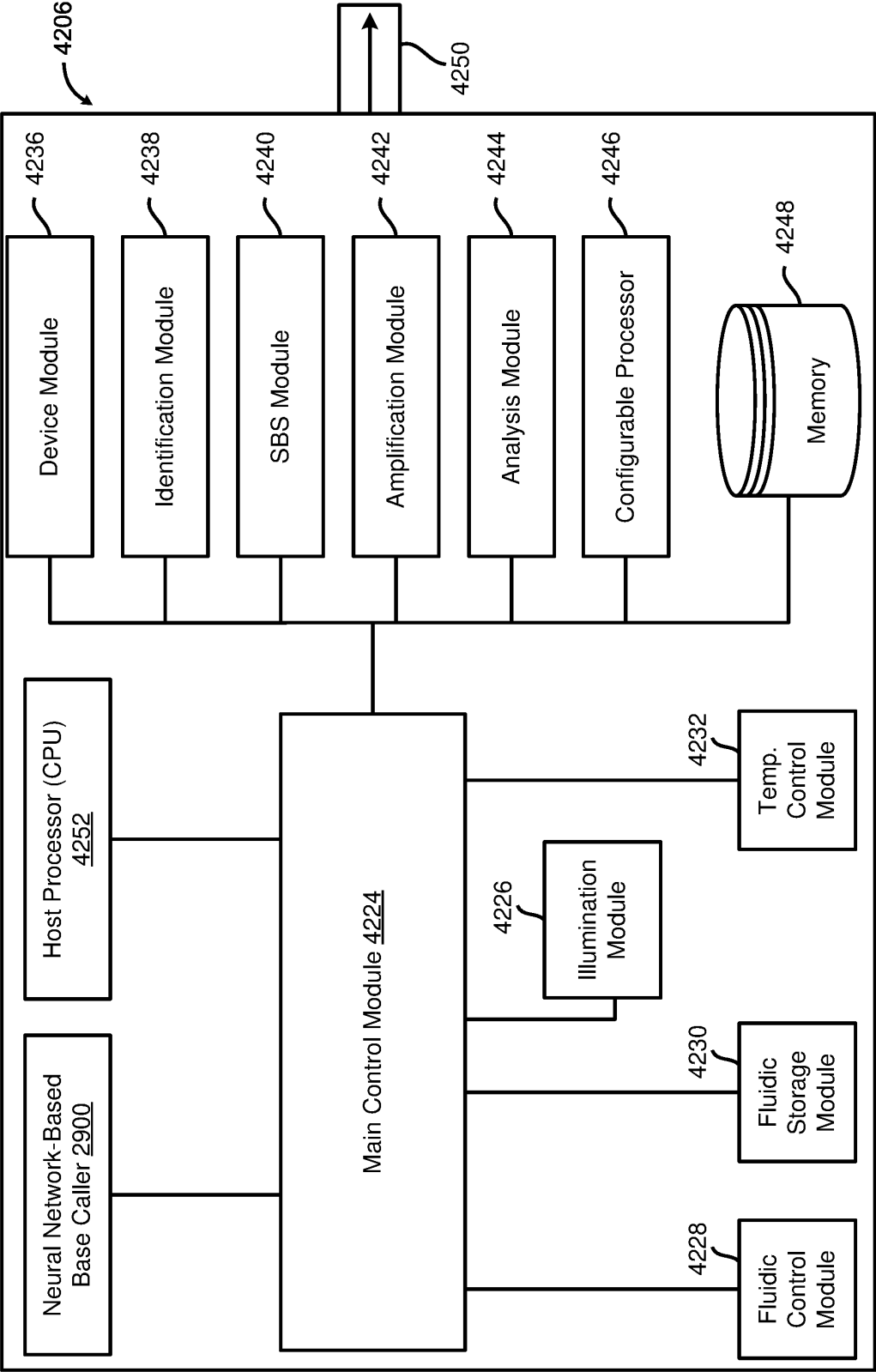


Figure 42B

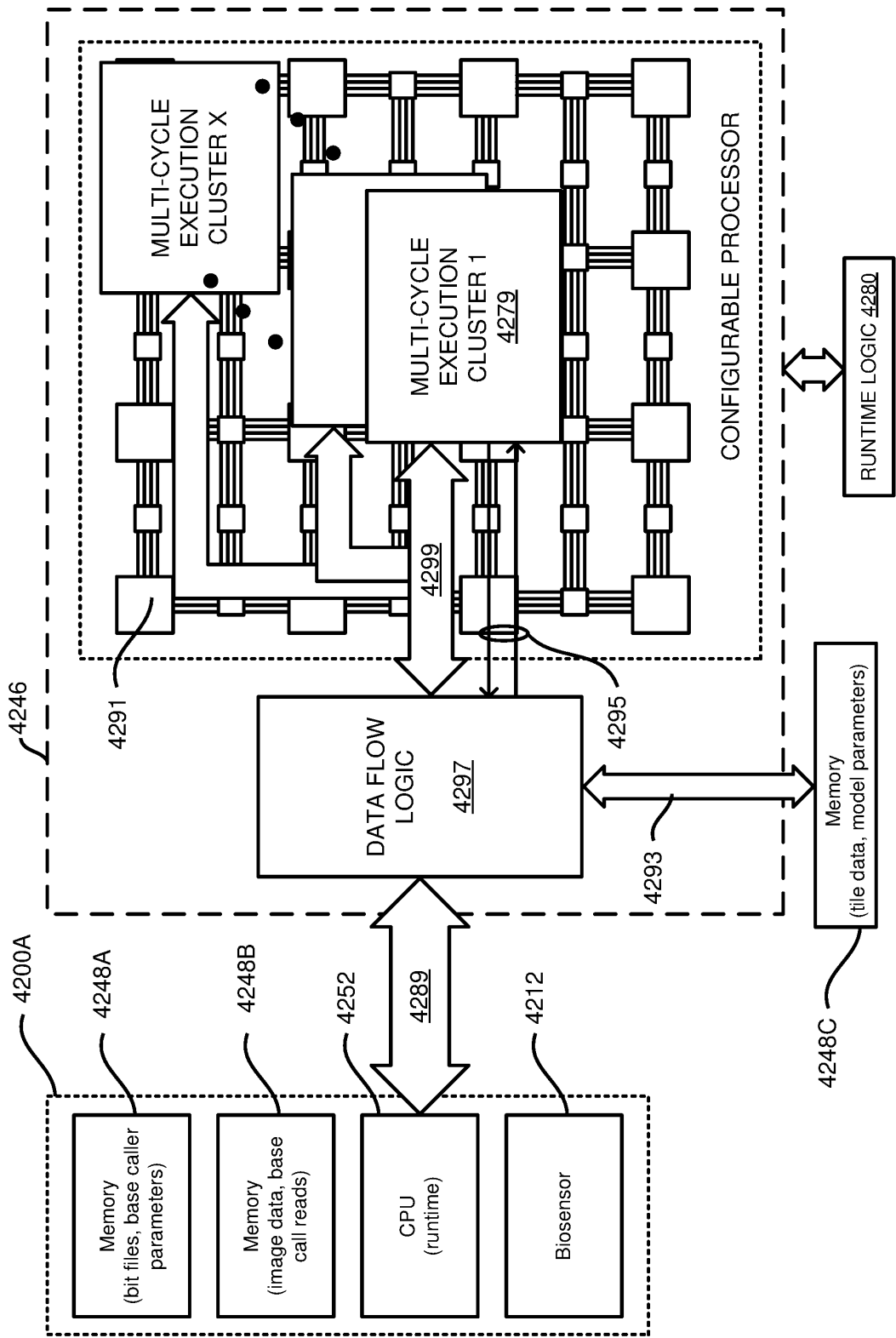


Figure 42C

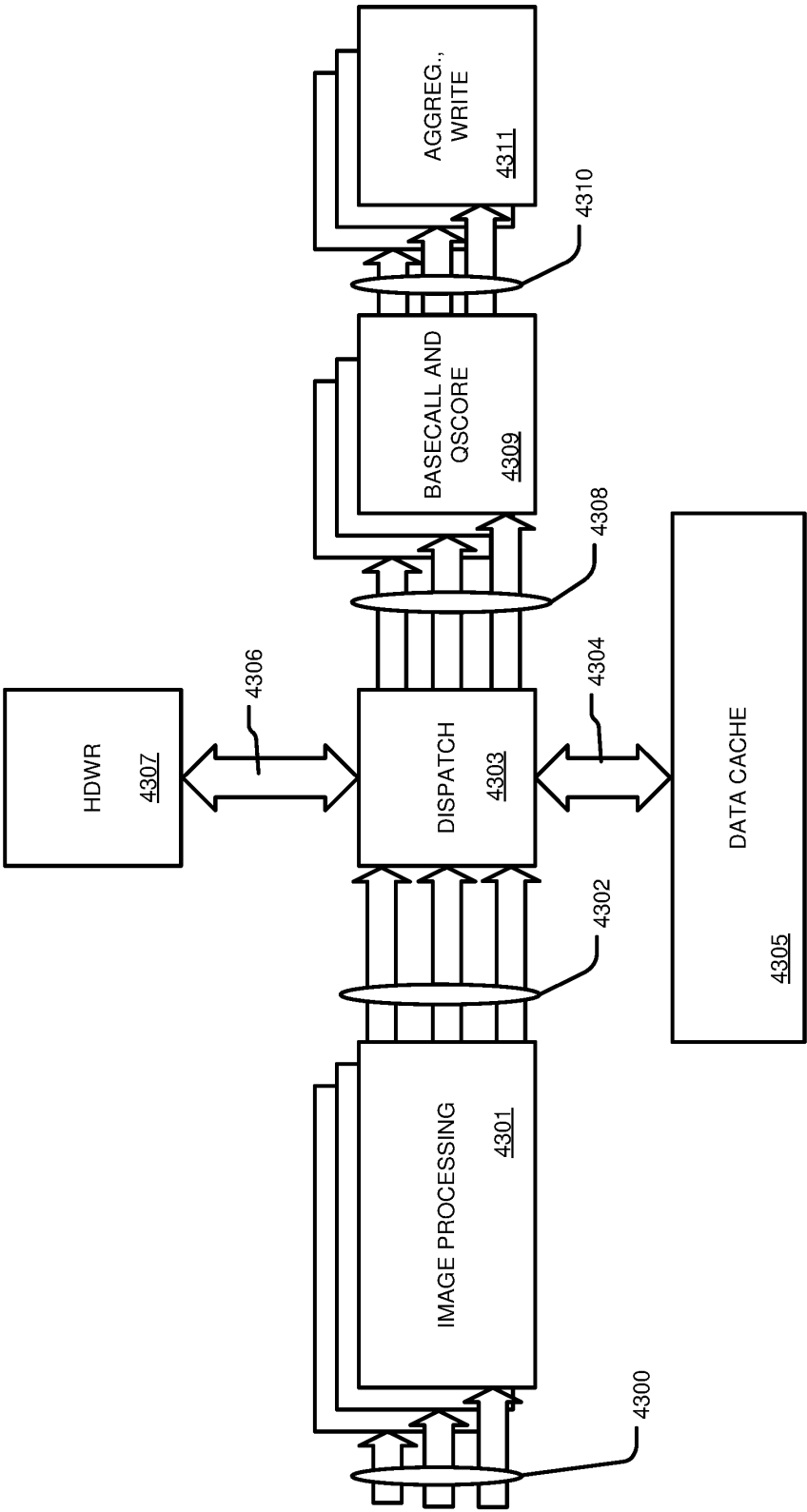


Figure 43A

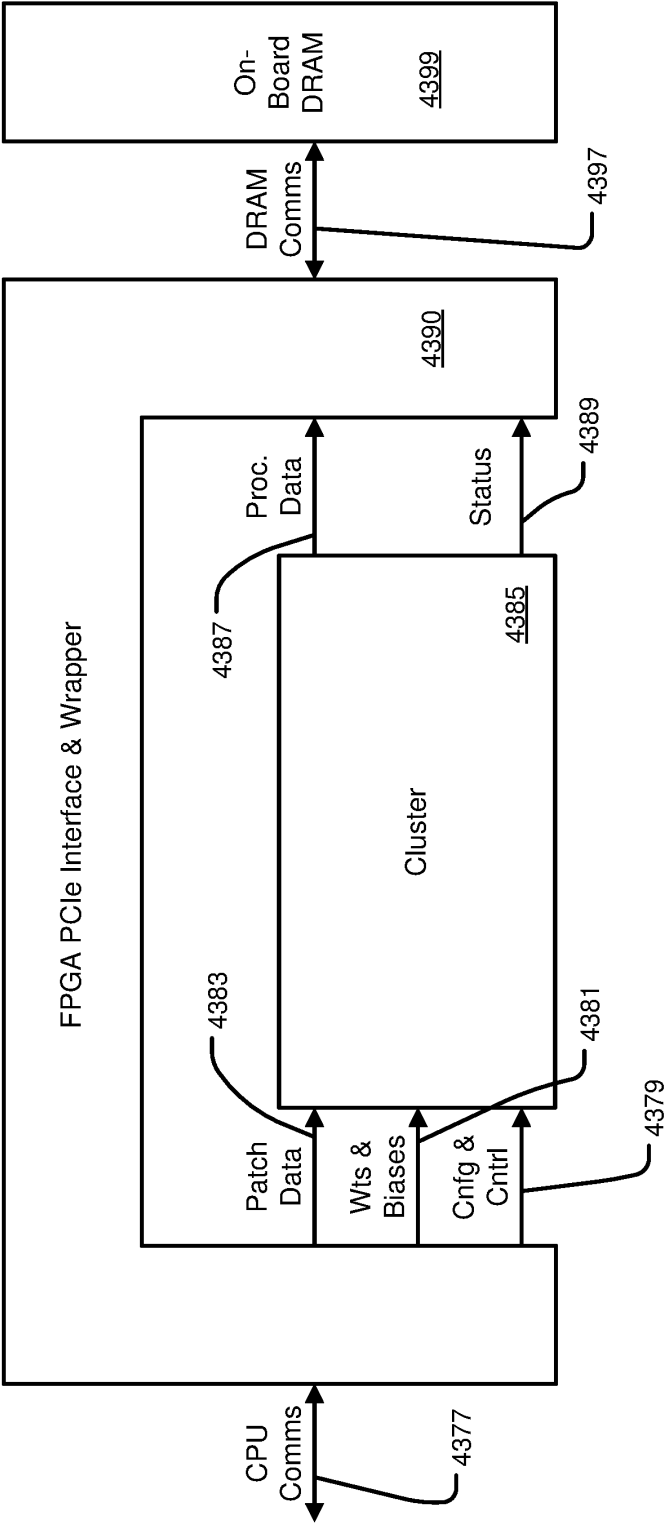


Figure 43B

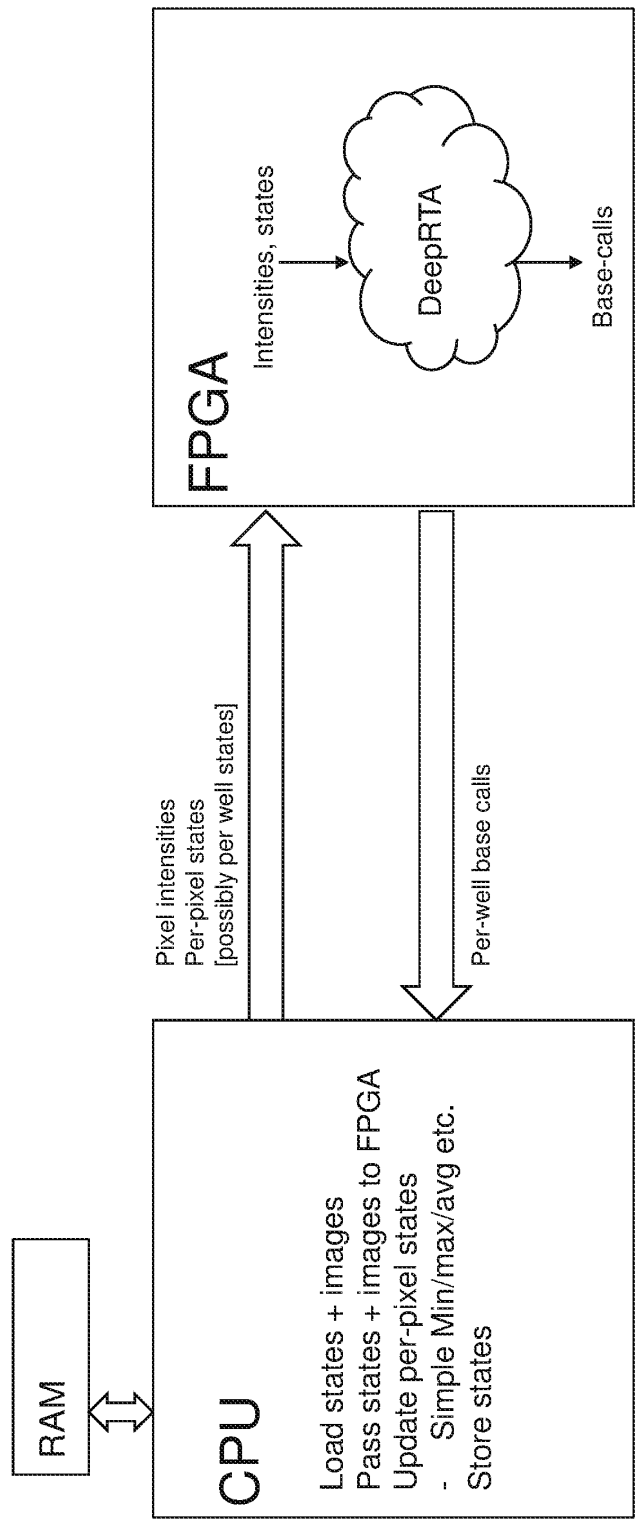


Figure 44

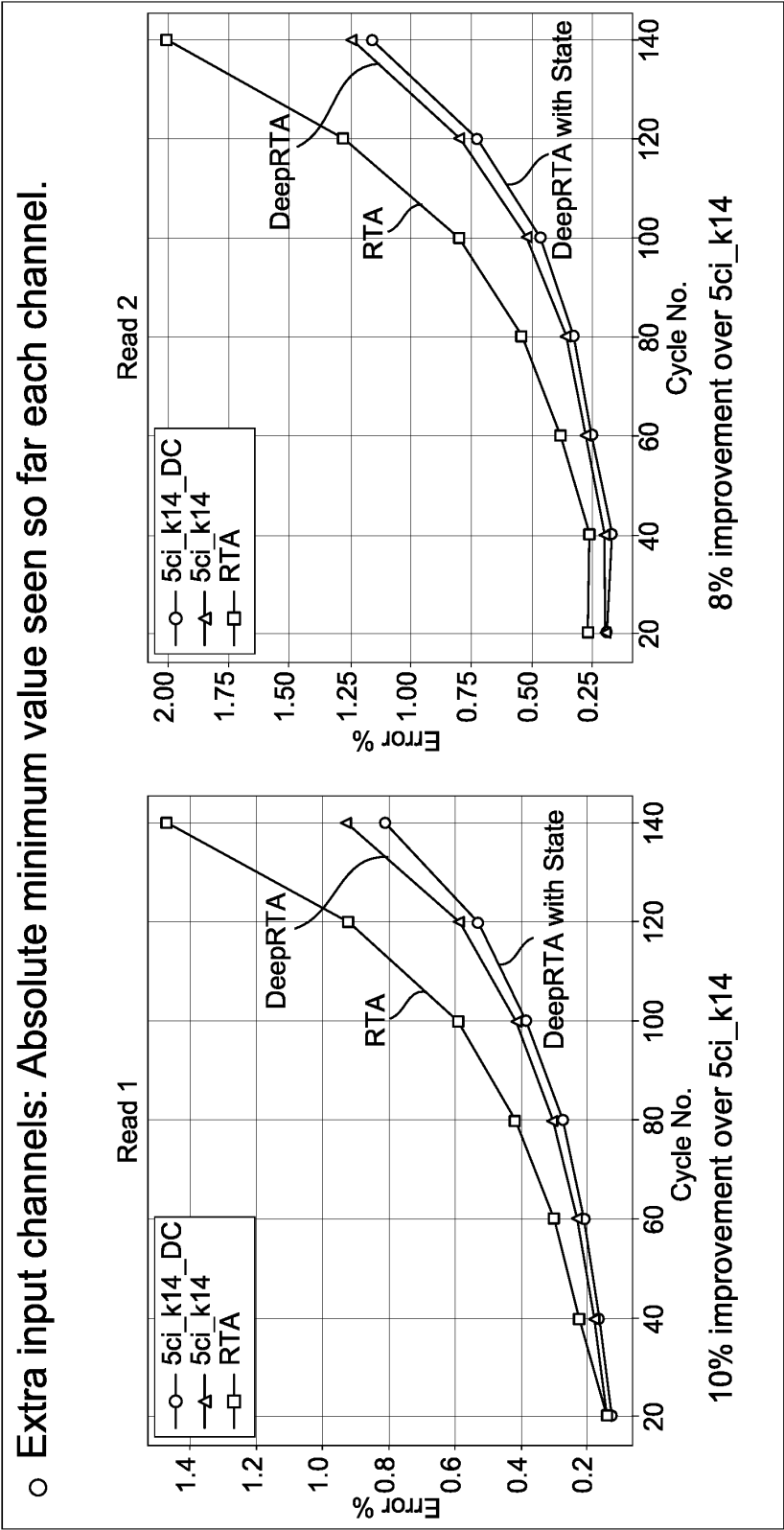


Figure 45

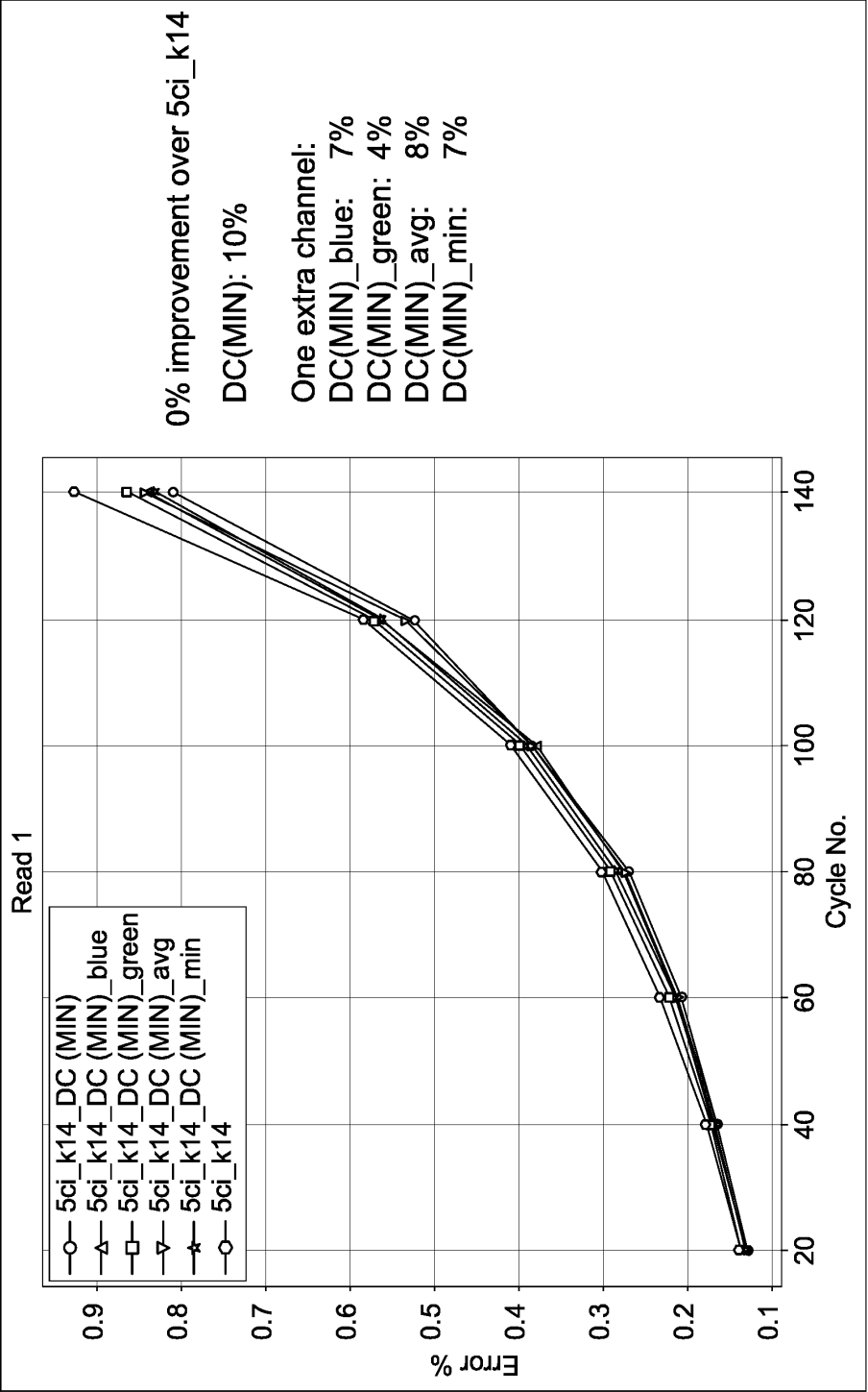


Figure 46

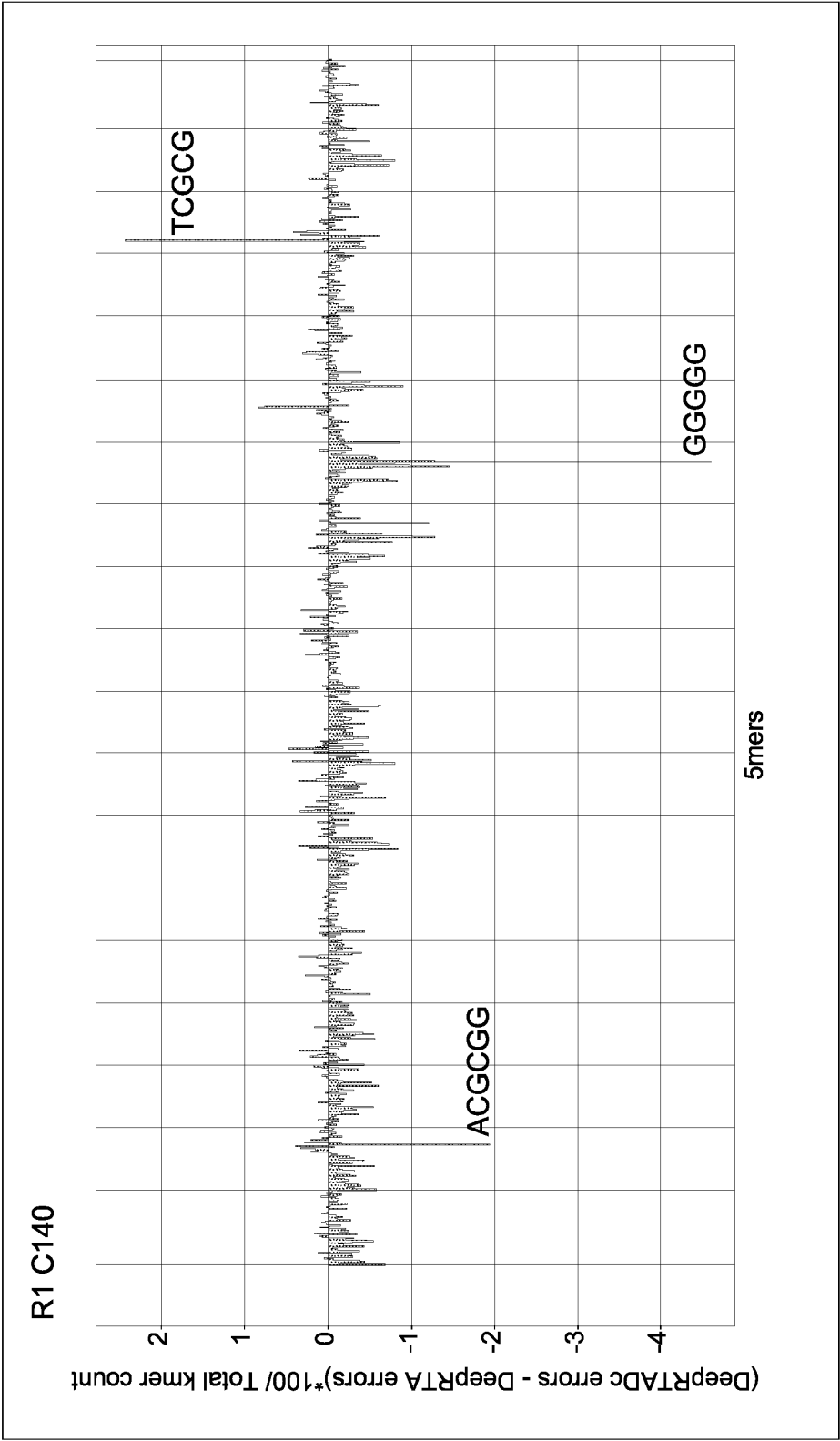
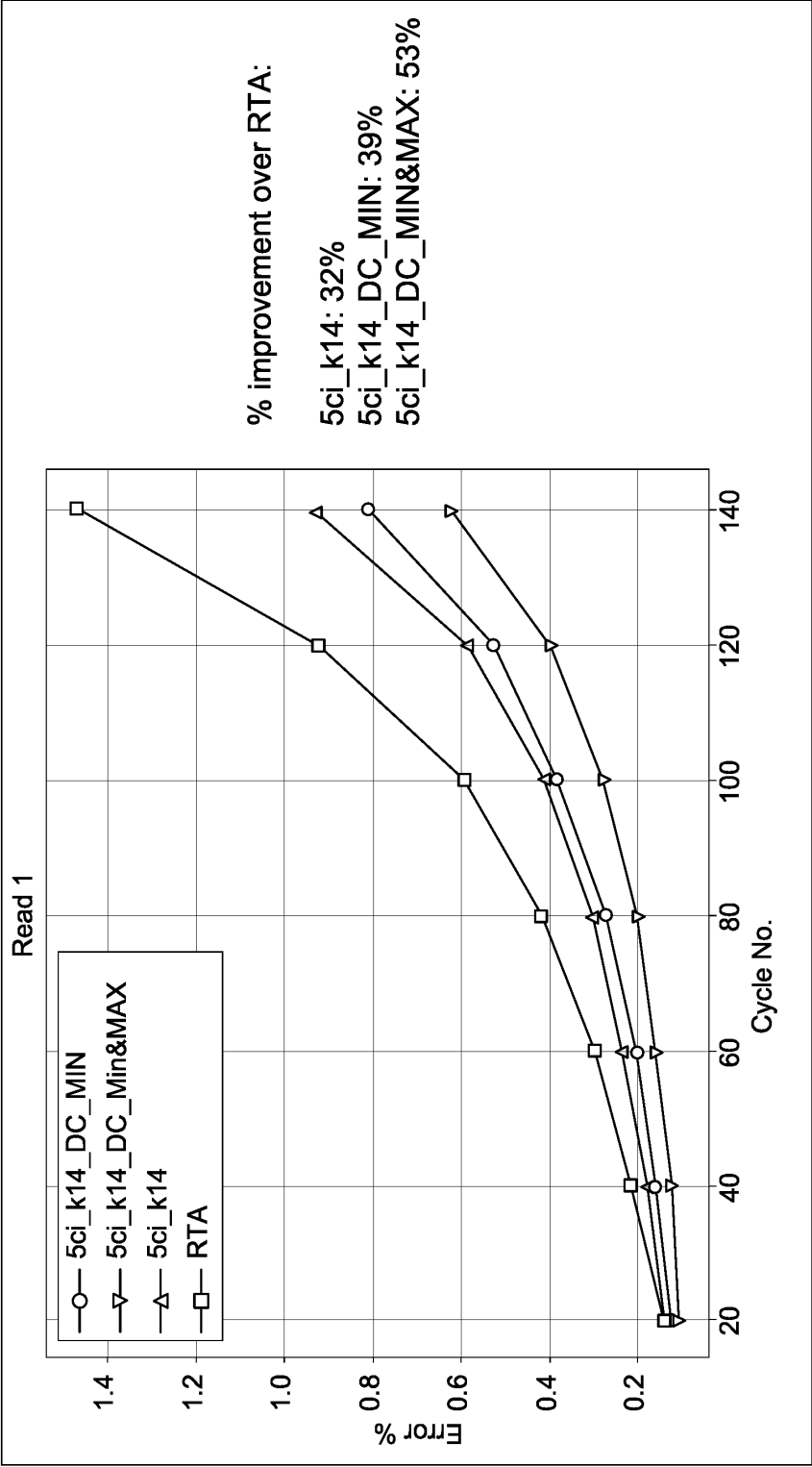


Figure 47



Reduction in error rates of 30% have been demonstrate, compared to DeepRTA system without state

- 'compute' cost is negligible
- Hardware compatible

Figure 48

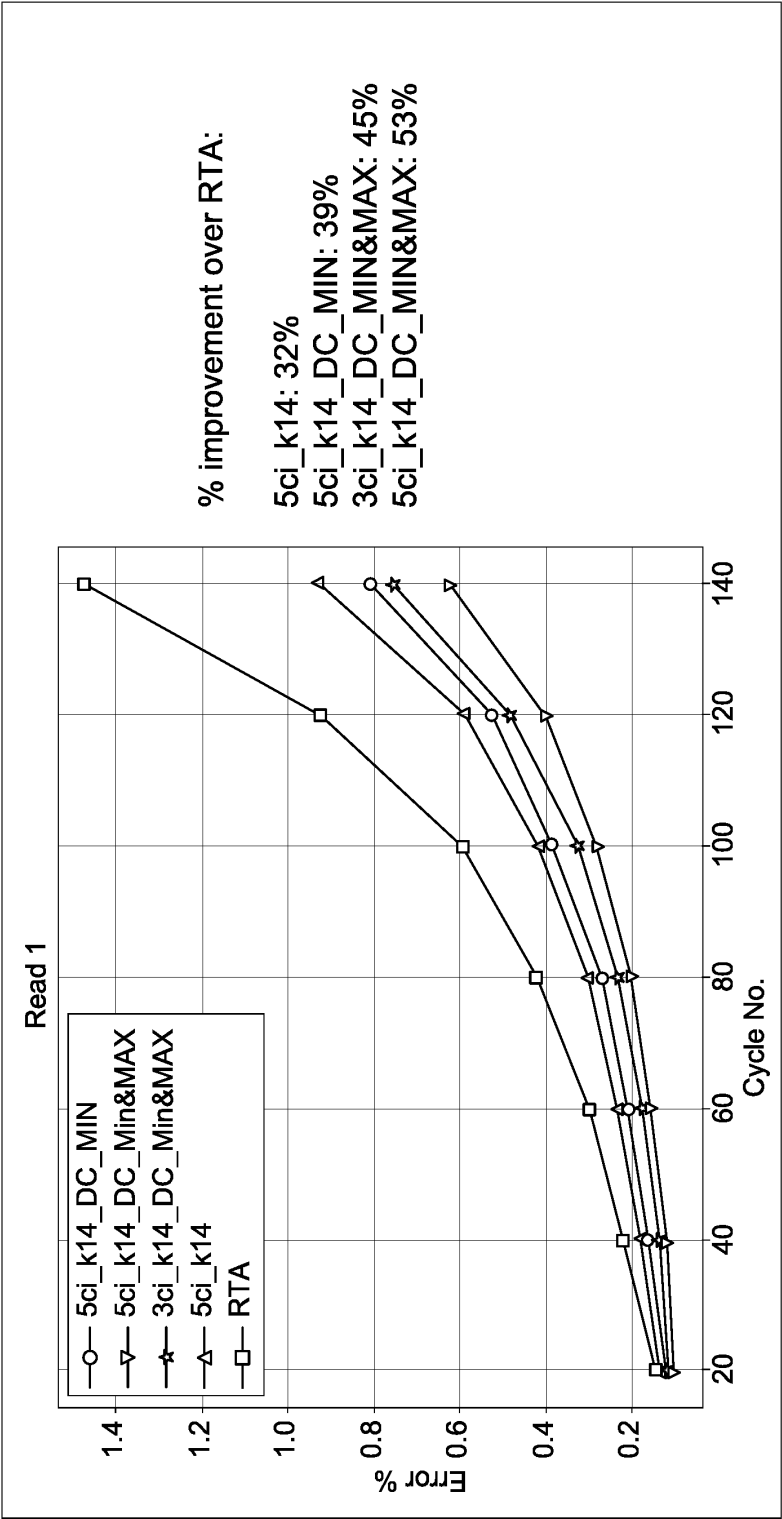


Figure 49

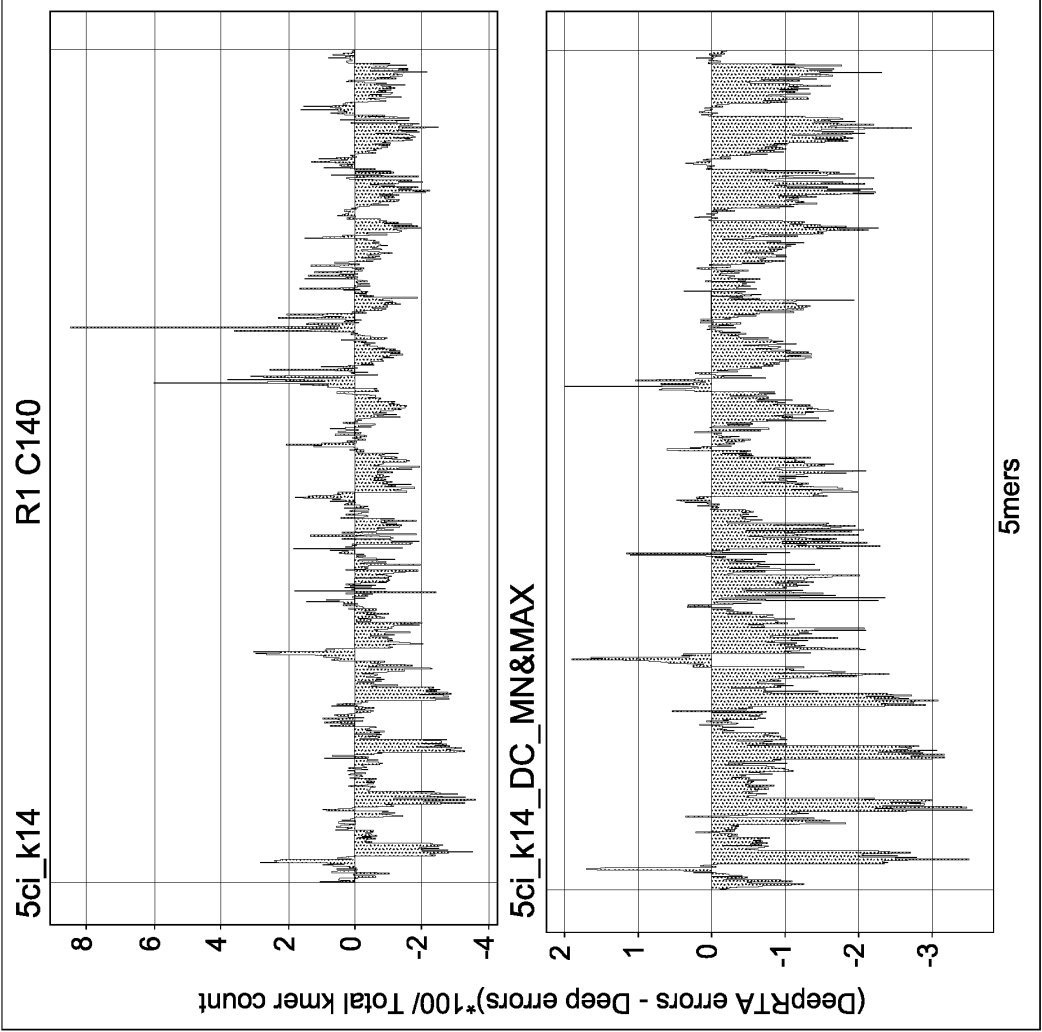


Figure 50

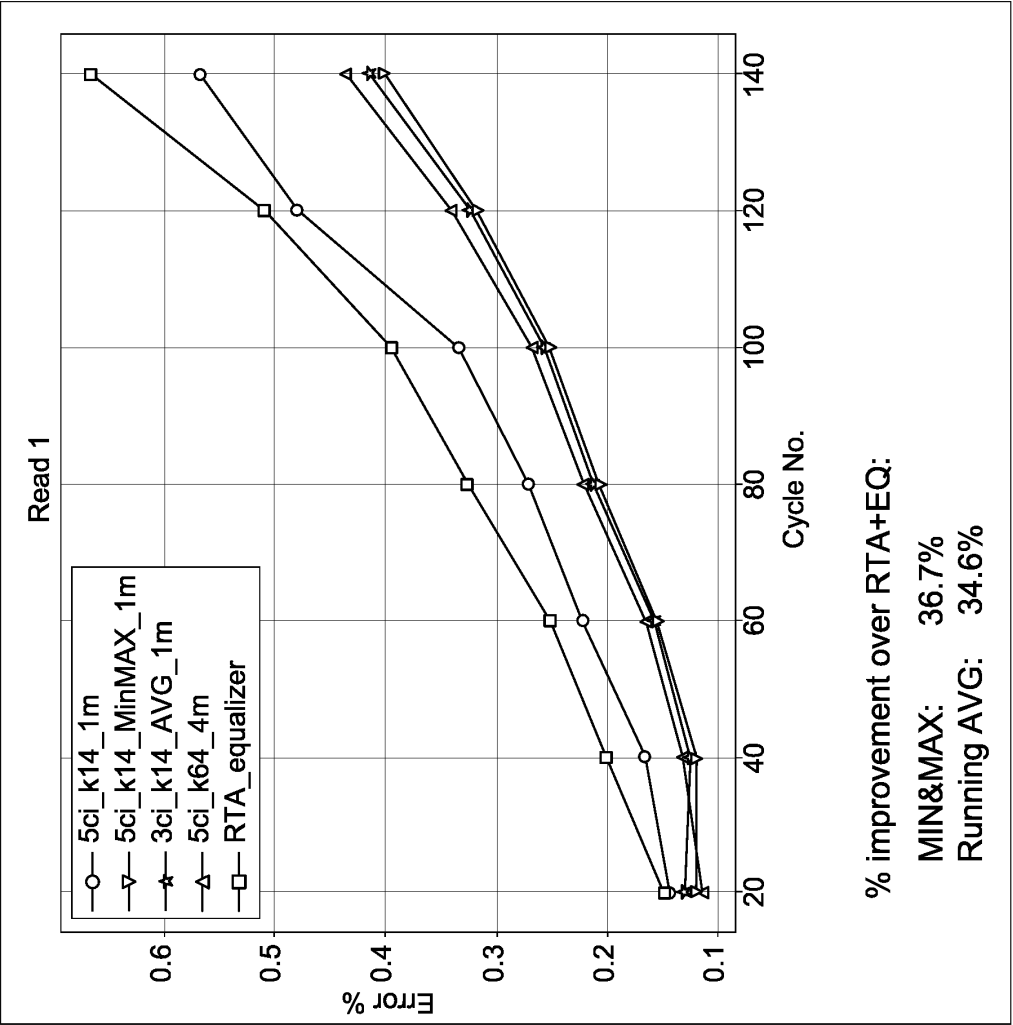


Figure 51

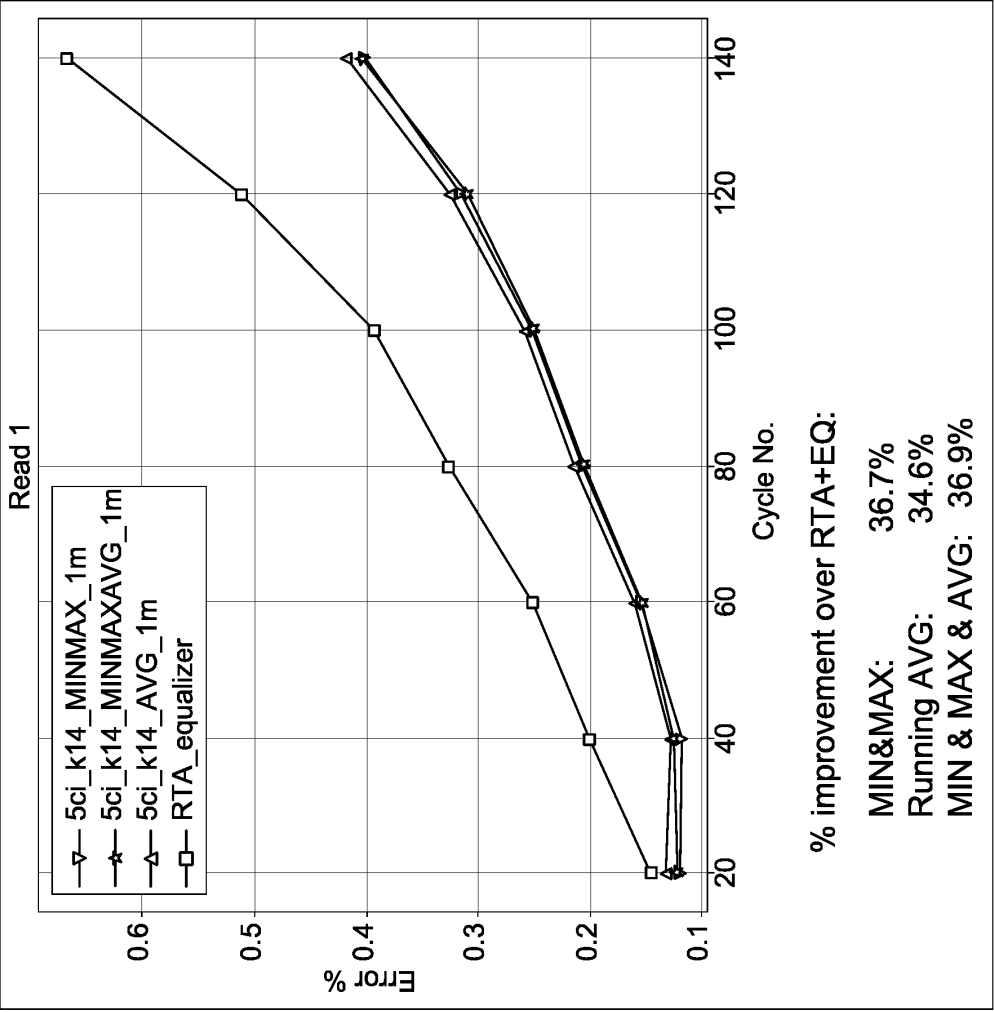


Figure 52

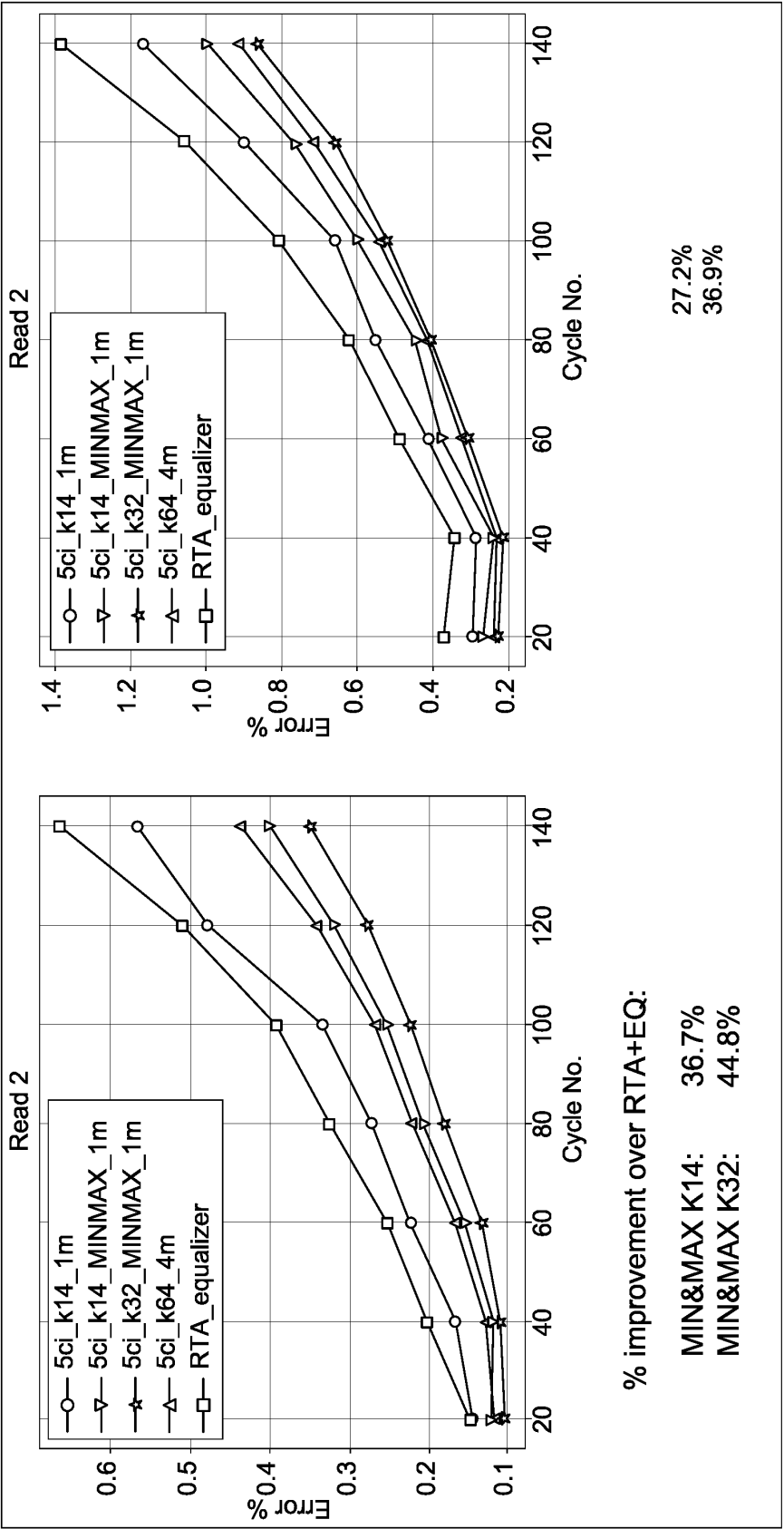


Figure 53

Using Per-Cluster Information

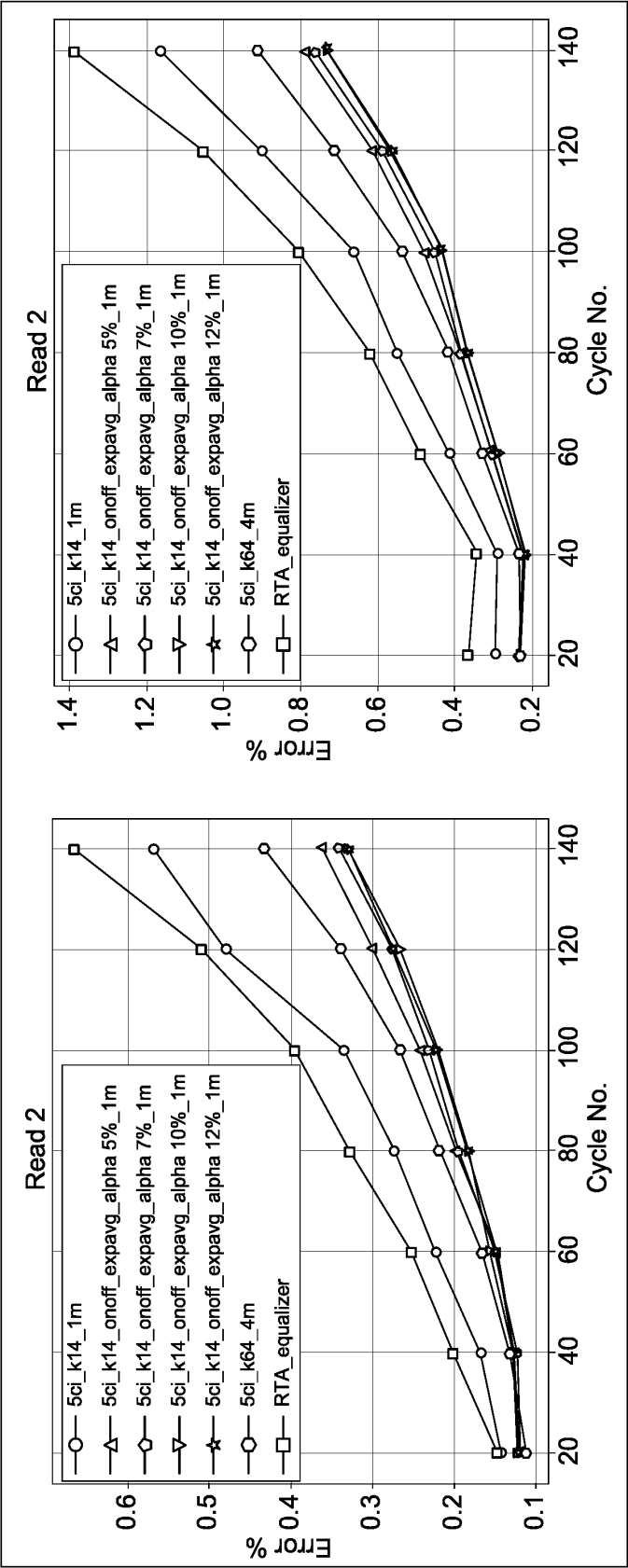


Figure 54

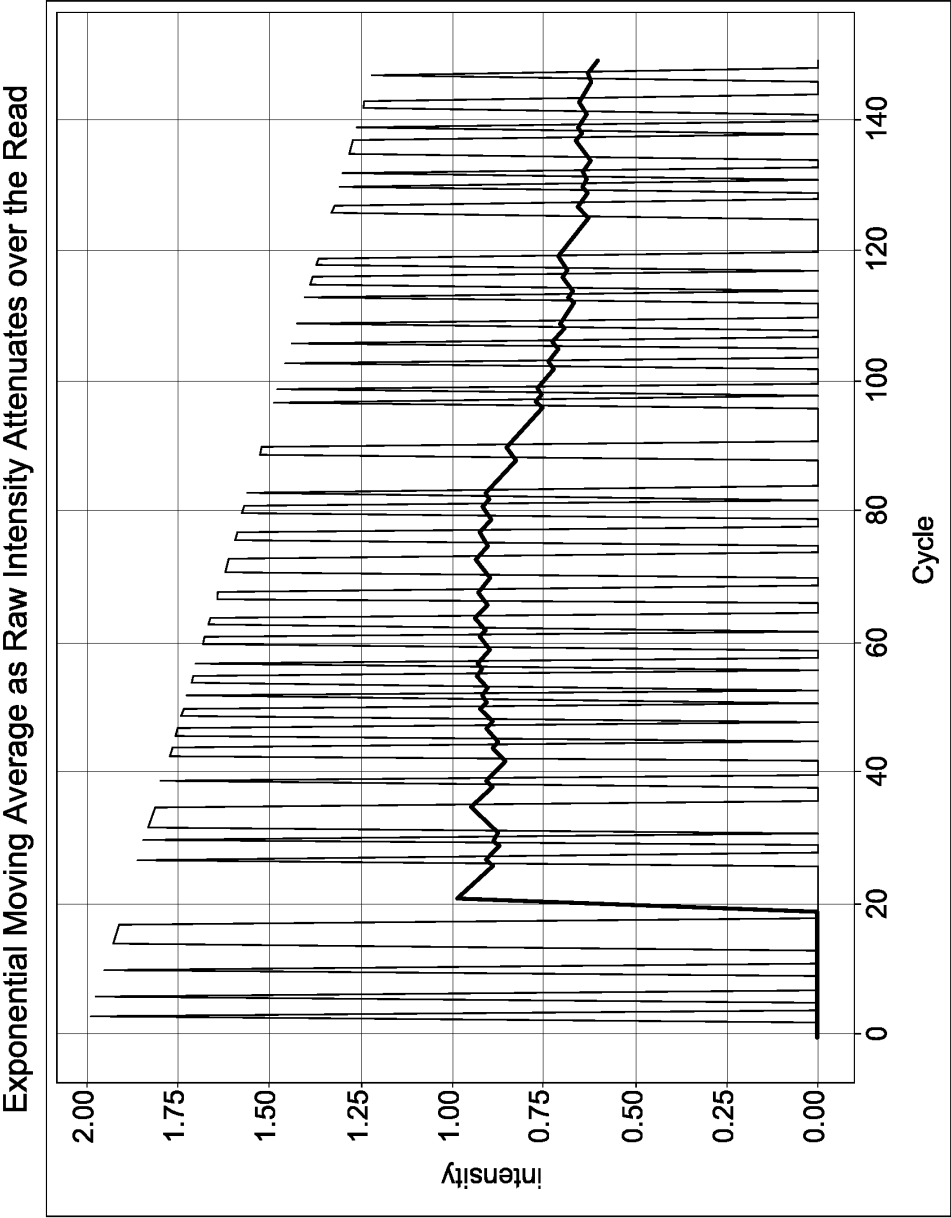


Figure 55

Exponential Moving Average with Step Change

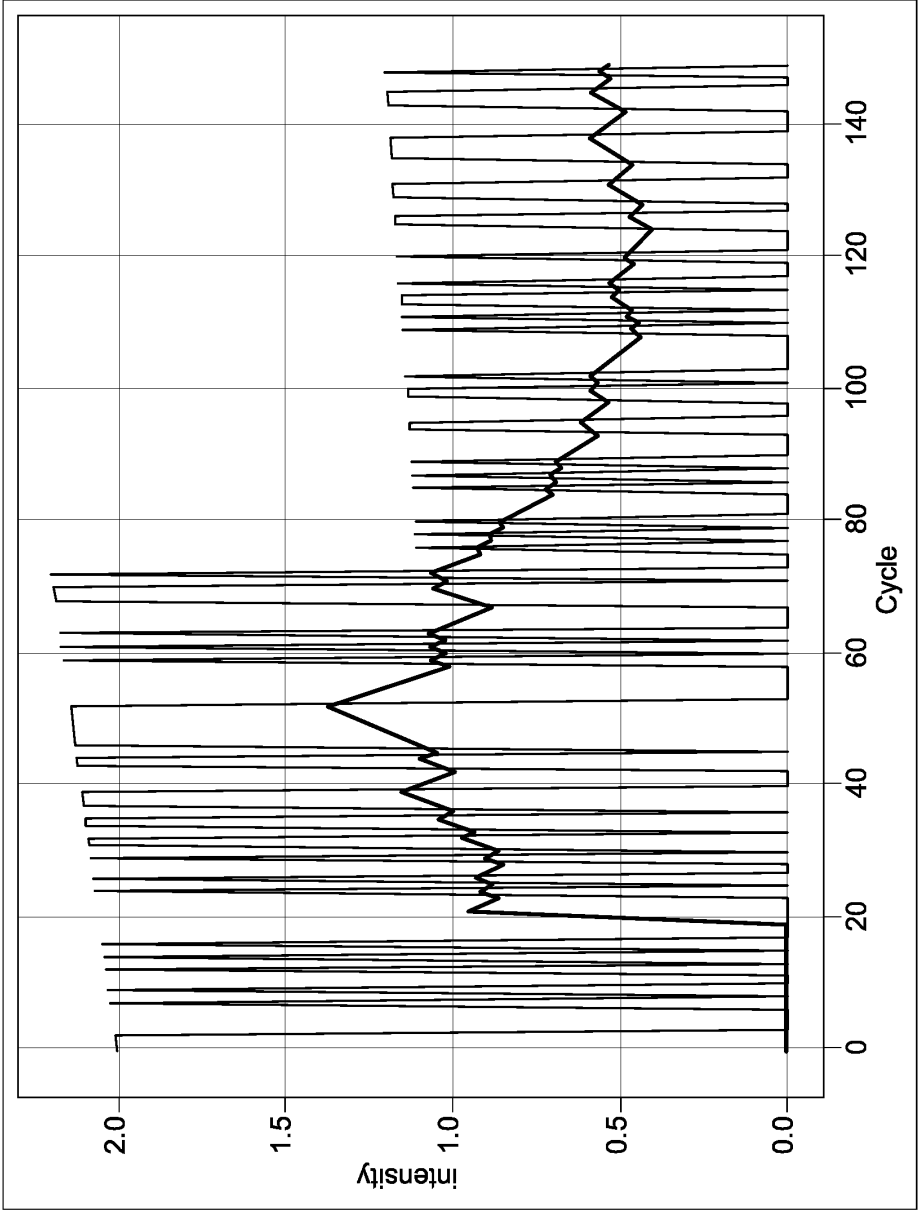


Figure 56

Inference Results on 25X Human Build

	Number of reads	Error rate (R1, R2, avg)	SNP Recall	SNP Precision	SNP F1	Indel Recall	Indel Precision	Indel F1
RTA + Eq	605,717,554	0.41,0.72,0.56	0.990142	0.998558	0.994332	0.971573	0.978162	0.974856
DeepRTA (k14_1m	602,022,776	0.36,0.63,0.50	0.990882	0.998508	0.994680	0.976982	0.977608	0.977295
DeepRTA_extrachannels (k14_1m_onoff_expavg	609,209,246	0.31,0.54,0.42	0.990985	0.99849	0.994724	0.977727	0.977748	0.977737

Figure 57