

1/60

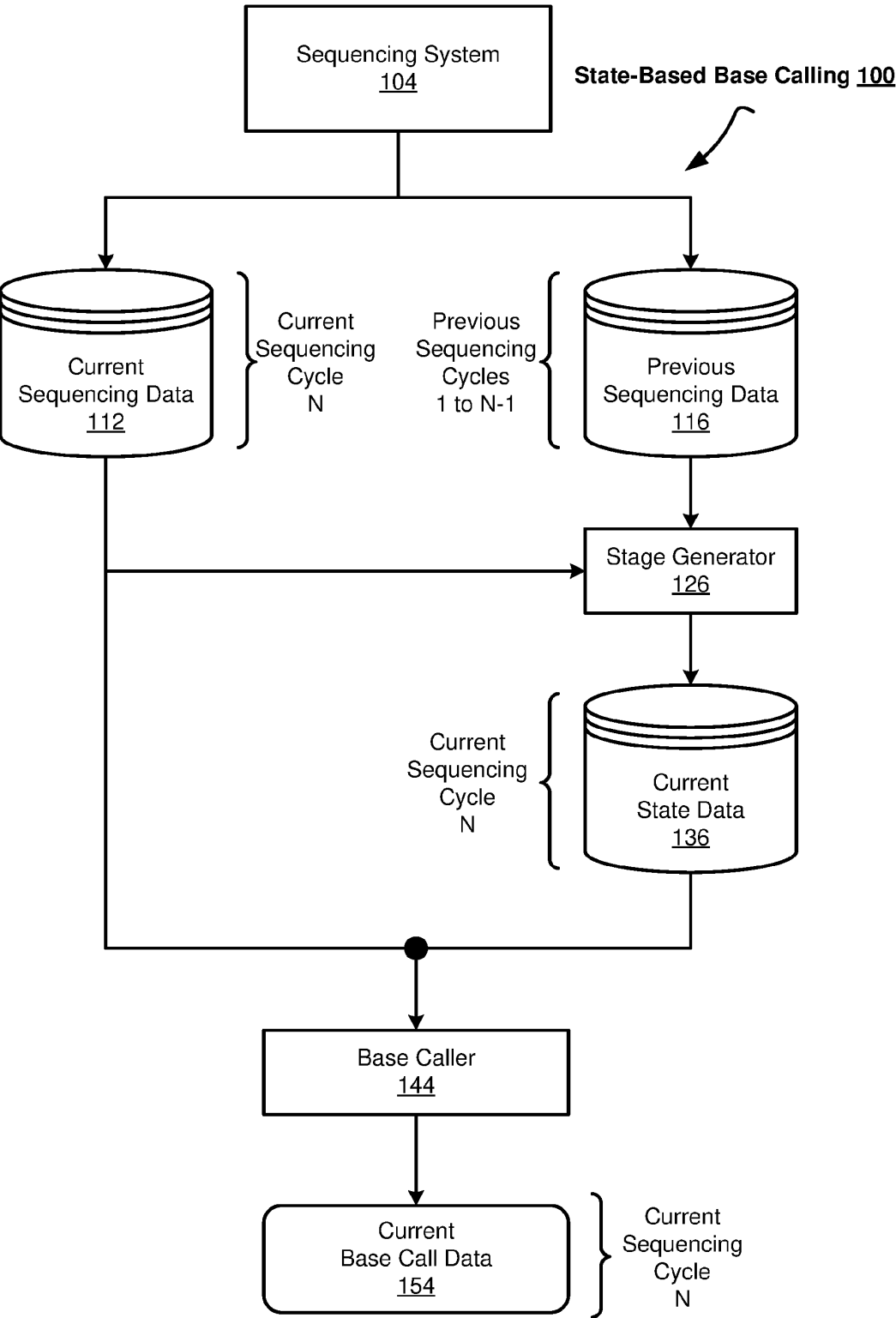
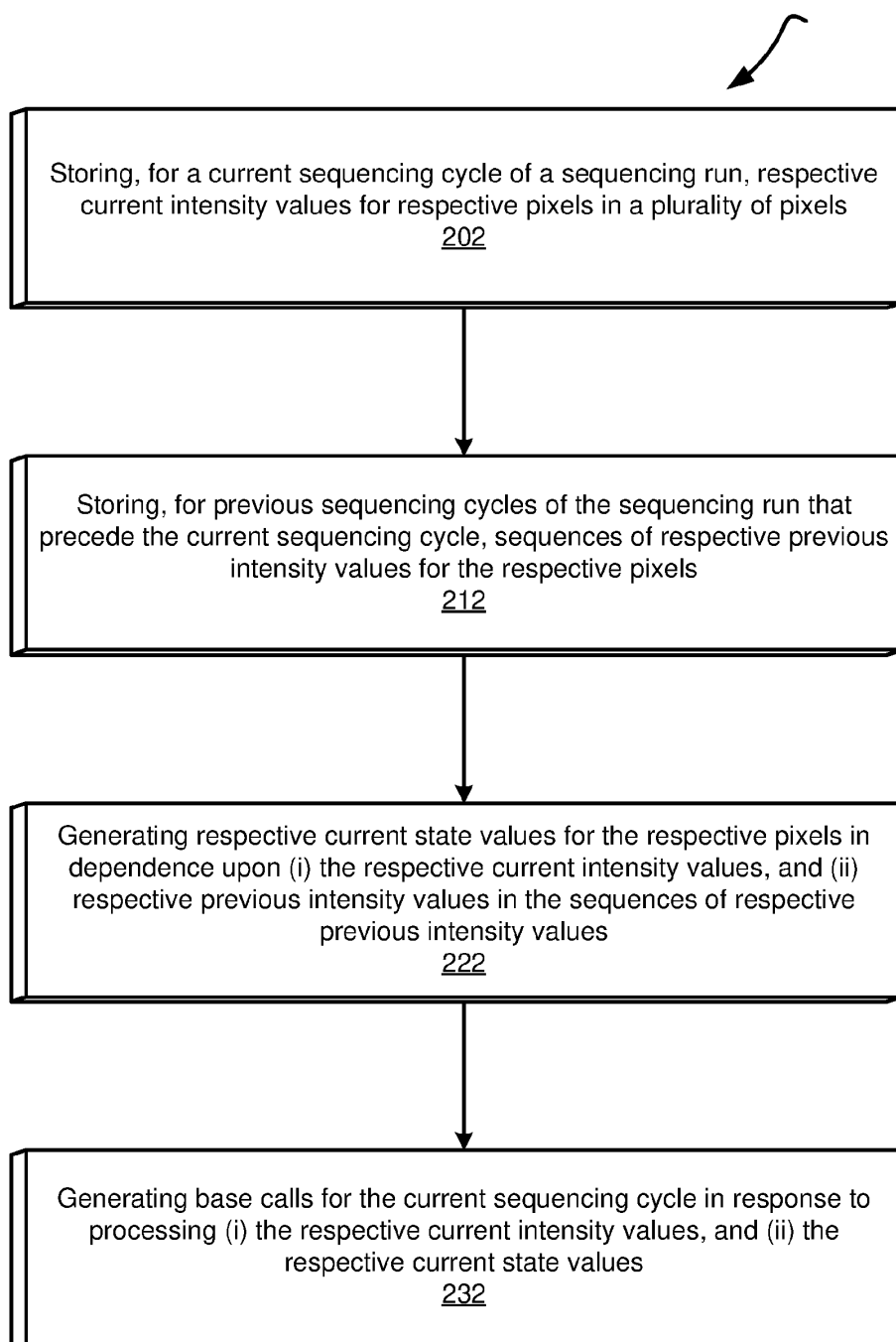
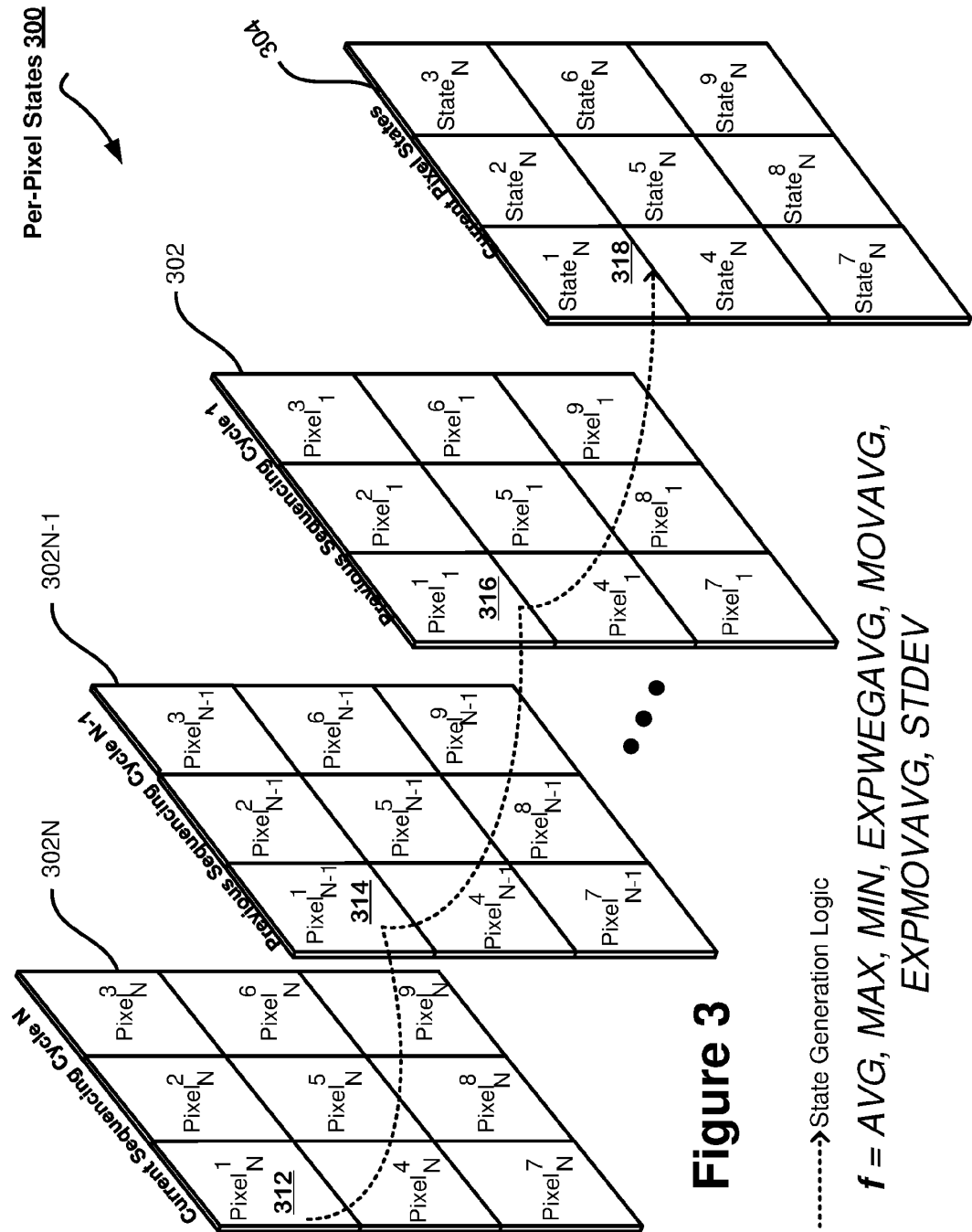


Figure 1

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Pixelated State Data 200**Figure 2**



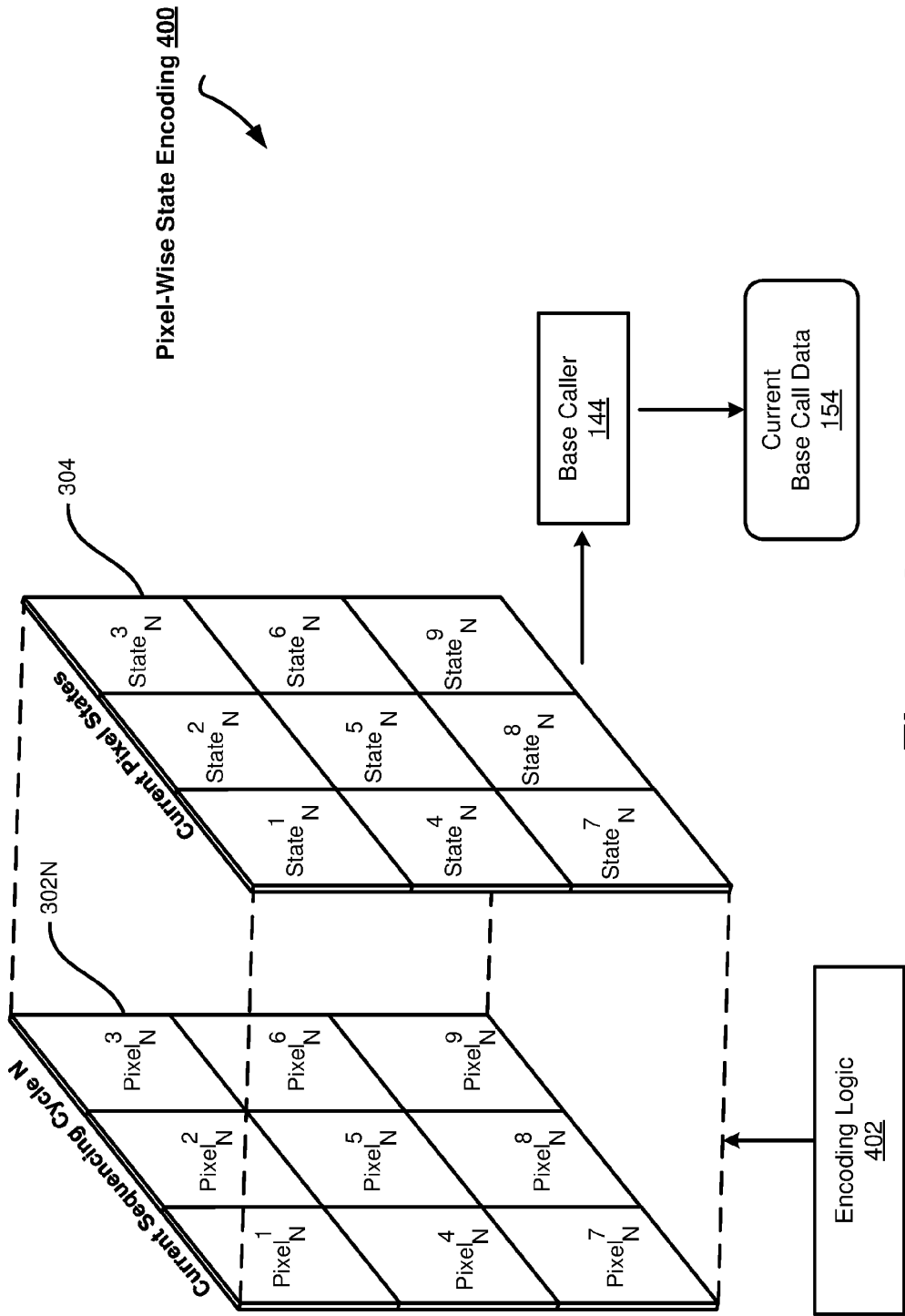


Figure 4

Pixel *P*

Per-Channel States 500

Cycle 1 Cycle 2 Cycle 3 Cycle 4 Cycle 5 Cycle 5 State	Channel 1 Channel 2	
	v_1^1	v_1^2
	v_2^1	v_2^2
	v_3^1	v_3^2
	v_4^1	v_4^2
	v_5^1	v_5^2
	$f\{v_1^1, v_2^1, v_3^1, v_4^1, v_5^1\}$	$f\{v_1^2, v_2^2, v_3^2, v_4^2, v_5^2\}$

f = AVG, MAX, MIN, EXPWEGAVG, MOVAVG, EXPMOVAVG, STDEV

Figure 5

Current Sequencing Cycle N			Per-Channel MIN States 600		
Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Channel 1 MIN State Values 604	Channel 2 MIN State Values 605	
(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)	$\begin{matrix} 1 \\ x \\ N \end{matrix}$	$\begin{matrix} 1 \\ y \\ N \end{matrix}$	Pixel-Wise Averages of Columns 604 and 605 in Figure 6	
(1, 2)	$\begin{matrix} 2 \\ x \\ N \end{matrix}$	$\begin{matrix} 2 \\ y \\ N \end{matrix}$		
(1, 3)	$\begin{matrix} 3 \\ x \\ N \end{matrix}$	$\begin{matrix} 3 \\ y \\ N \end{matrix}$		
(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 7

Current Sequencing Cycle N			Per-Channel MAX States 800	
Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Channel 1 MAX State Values 804	Channel 2 MAX State Values 805
(1, 1)	x_N^1	y_N^1	$\text{MAX}\{x_N^1 \dots x_1^1\}$	$\text{MAX}\{y_N^1 \dots y_1^1\}$
(1, 2)	x_N^2	y_N^2	$\text{MAX}\{x_N^2 \dots x_1^2\}$	$\text{MAX}\{y_N^2 \dots y_1^2\}$
(1, 3)	x_N^3	y_N^3	$\text{MAX}\{x_N^3 \dots x_1^3\}$	$\text{MAX}\{y_N^3 \dots y_1^3\}$
(1, 4)	x_N^4	y_N^4	$\text{MAX}\{x_N^4 \dots x_1^4\}$	$\text{MAX}\{y_N^4 \dots y_1^4\}$
(1, 5)	x_N^5	y_N^5	$\text{MAX}\{x_N^5 \dots x_1^5\}$	$\text{MAX}\{y_N^5 \dots y_1^5\}$
...	...	...	...	...
(i, j)	x_N^k	y_N^k	$\text{MAX}\{x_N^k \dots x_1^k\}$	$\text{MAX}\{y_N^k \dots y_1^k\}$

Figure 8

Current Sequencing Cycle N			Pan-Channel AVG MAX States 900	
Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Pan-Channel AVG MAX State Values 908	
(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 804 and 805 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 <u>1000</u>		
Pixels <u>601</u>	Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Channel 1 AVG State Values <u>1004</u>	Channel 2 AVG State Values <u>1005</u>
(1, 1)	$\begin{matrix} 1 \\ x_N \end{matrix}$	$\begin{matrix} 1 \\ y_N \end{matrix}$	AVG $\{x_N^1 \dots x_1^1\}$	AVG $\{y_N^1 \dots y_1^1\}$
(1, 2)	$\begin{matrix} 2 \\ x_N \end{matrix}$	$\begin{matrix} 2 \\ y_N \end{matrix}$	AVG $\{x_N^2 \dots x_1^2\}$	AVG $\{y_N^2 \dots y_1^2\}$
(1, 3)	$\begin{matrix} 3 \\ x_N \end{matrix}$	$\begin{matrix} 3 \\ y_N \end{matrix}$	AVG $\{x_N^3 \dots x_1^3\}$	AVG $\{y_N^3 \dots y_1^3\}$
(1, 4)	$\begin{matrix} 4 \\ x_N \end{matrix}$	$\begin{matrix} 4 \\ y_N \end{matrix}$	AVG $\{x_N^4 \dots x_1^4\}$	AVG $\{y_N^4 \dots y_1^4\}$
(1, 5)	$\begin{matrix} 5 \\ x_N \end{matrix}$	$\begin{matrix} 5 \\ y_N \end{matrix}$	AVG $\{x_N^5 \dots x_1^5\}$	AVG $\{y_N^5 \dots y_1^5\}$
...	...	...	...	...
(i, j)	$\begin{matrix} k \\ x_N \end{matrix}$	$\begin{matrix} k \\ y_N \end{matrix}$	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		Channel 1 Intensity Values <u>602</u>	Channel 2 Intensity Values <u>603</u>	Pan-Channel AVG AVG State Values <u>1108</u>
Pixels <u>601</u>				
(1, 1)		$\begin{smallmatrix} 1 \\ x \\ N \end{smallmatrix}$	$\begin{smallmatrix} 1 \\ y \\ N \end{smallmatrix}$	
(1, 2)		$\begin{smallmatrix} 2 \\ x \\ N \end{smallmatrix}$	$\begin{smallmatrix} 2 \\ y \\ N \end{smallmatrix}$	
(1, 3)		$\begin{smallmatrix} 3 \\ x \\ N \end{smallmatrix}$	$\begin{smallmatrix} 3 \\ y \\ N \end{smallmatrix}$	
(1, 4)		$\begin{smallmatrix} 4 \\ x \\ N \end{smallmatrix}$	$\begin{smallmatrix} 4 \\ y \\ N \end{smallmatrix}$	Pixel-Wise Averages of Columns <u>1004</u> and <u>1005</u> in Figure 10
(1, 5)		$\begin{smallmatrix} 5 \\ x \\ N \end{smallmatrix}$	$\begin{smallmatrix} 5 \\ y \\ N \end{smallmatrix}$	
...		...	...	
(i, j)		$\begin{smallmatrix} k \\ x \\ N \end{smallmatrix}$	$\begin{smallmatrix} k \\ y \\ N \end{smallmatrix}$	...

Figure 11

Current Sequencing Cycle N					Per-Channel MIN MAX States 1200		
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>	
(1, 1)	^1x_N	^1y_N					
(1, 2)	^2x_N	^2y_N					
(1, 3)	^3x_N	^3y_N	<u>600</u> (Figure 6)	<u>600</u> (Figure 6)	<u>800</u> (Figure 8)	<u>800</u> (Figure 8)	
(1, 4)	^4x_N	^4y_N					
(1, 5)	^5x_N	^5y_N					
...	...	...					
(i, j)	^kx_N	^ky_N					

Figure 12

Current Sequencing Cycle N				Per-Channel MIN AVG States 1300			
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 AVG State Values 1004	Channel 2 AVG State Values 1005	
(1, 1)	1 x_N	1 y_N					
(1, 2)	2 x_N	2 y_N					
(1, 3)	3 x_N	3 y_N	600 Figure 6				1000 Figure 10
(1, 4)	4 x_N	4 y_N					
(1, 5)	5 x_N	5 y_N					
...	...	...	...	...	...	...	...
(i, j)	k x_N	k y_N					

Figure 13

Per-Channel MAX AVG States 1400

Current Sequencing Cycle N

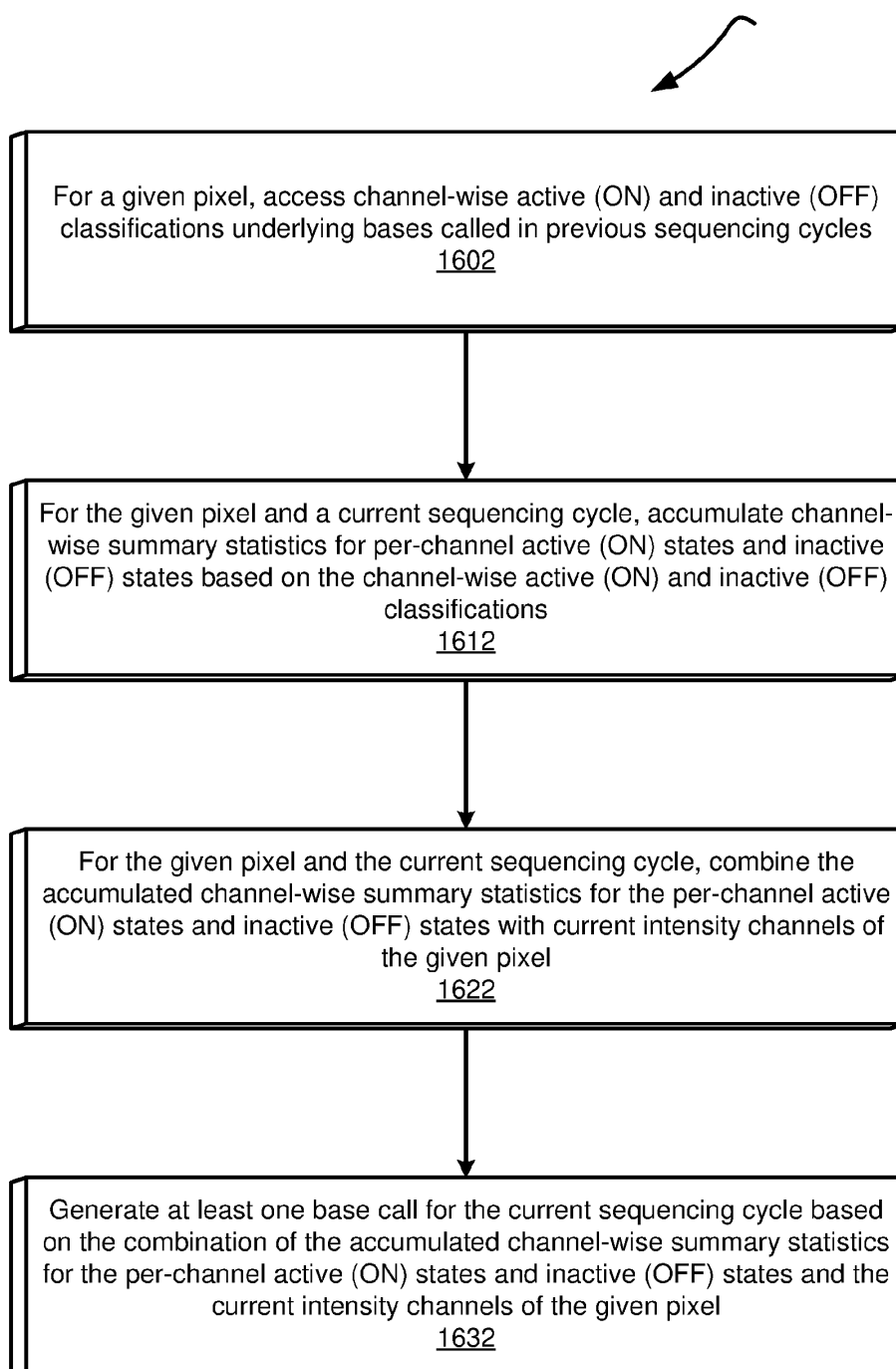
Pixels 601	Channel 1 Intensity Values 602	Channel 2 Intensity Values 603	Channel 1 MAX State Values 804	Channel 2 MAX State Values 805	Channel 1 AVG State Values 1004	Channel 2 AVG State Values 1005
(1, 1)	1 x_N^1	1 y_N^1				
(1, 2)	2 x_N^2	2 y_N^2				
(1, 3)	3 x_N^3	3 y_N^3				
(1, 4)	4 x_N^4	4 y_N^4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

Figure 14

Current Sequencing Cycle N						Per-Channel MIN MAX AVG States 1500			
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	Channel 1 AVG State Values 1004	Channel 2 AVG State Values 1005	
(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							
(1, 5)	5 x_N	5 y_N							
...	...	...	...	...	...	...	...	...	...
(i, j)	k x_N	k y_N							

Figure 15

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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

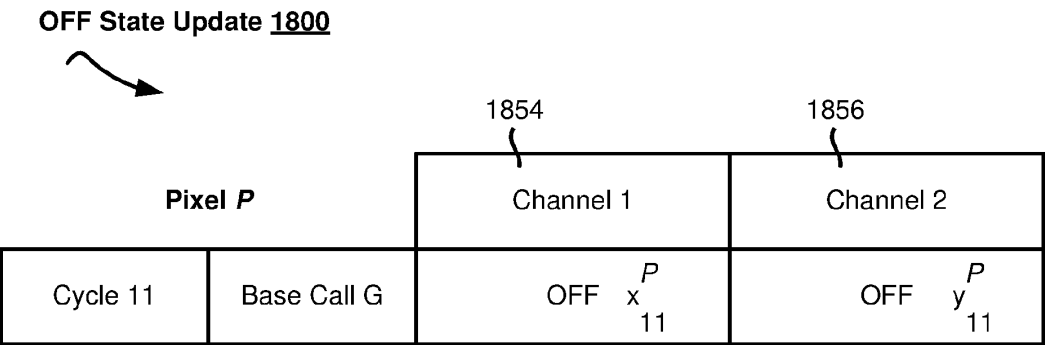


Figure 18A

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	1864 Channel 1	1866 Channel 2				
	x_{12}^P	y_{12}^P	<u>1802</u>	<u>1812</u>	<u>1822</u>	<u>1832</u>

Figure 18C

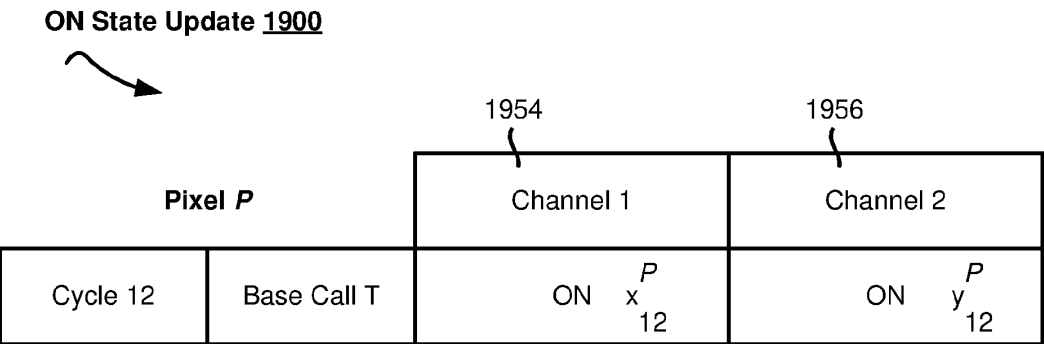


Figure 19A

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

Figure 19B

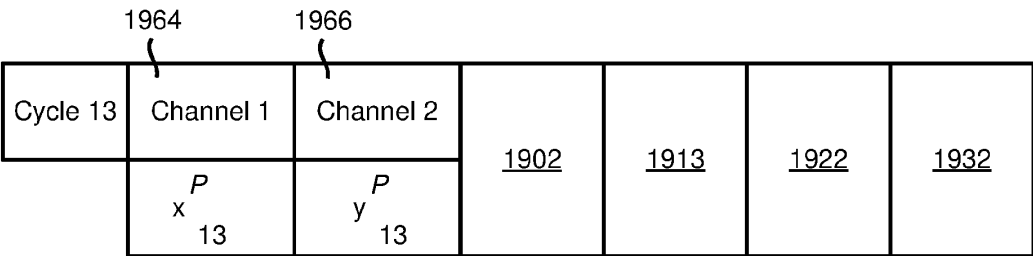


Figure 19C

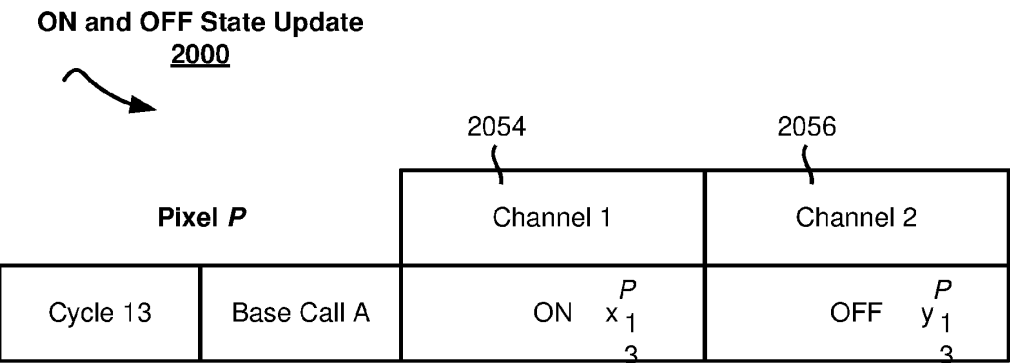


Figure 20A

Per-Channel State Calculation for Cycle 14			$f = \text{AVG, MAX, MIN, EXPWEGAVG, MOVAVG, EXPMOVAVG, STDEV}$
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

	2064	2066				
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

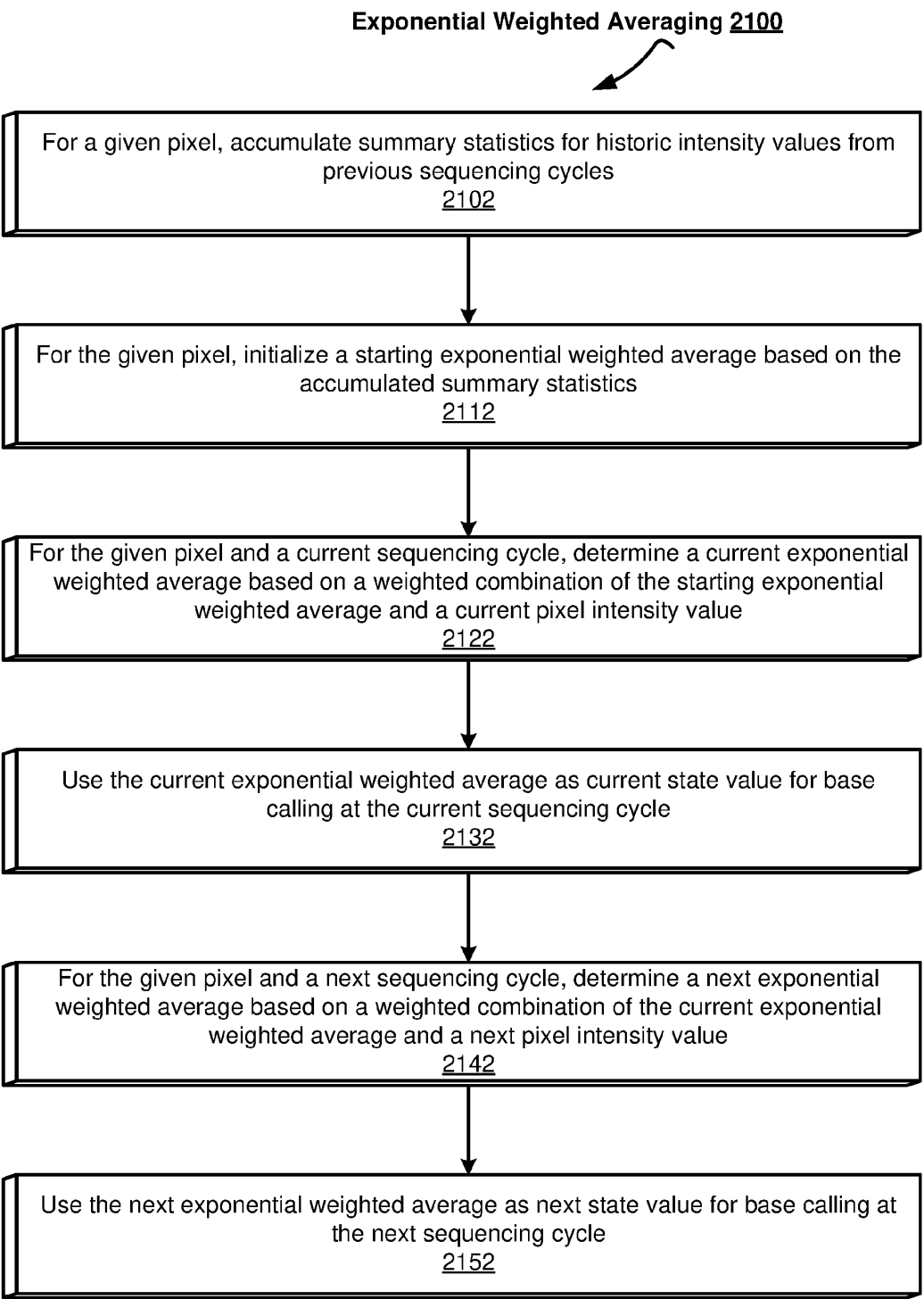


Figure 21

Per-Channel Exponential Weighted Averaging 2200

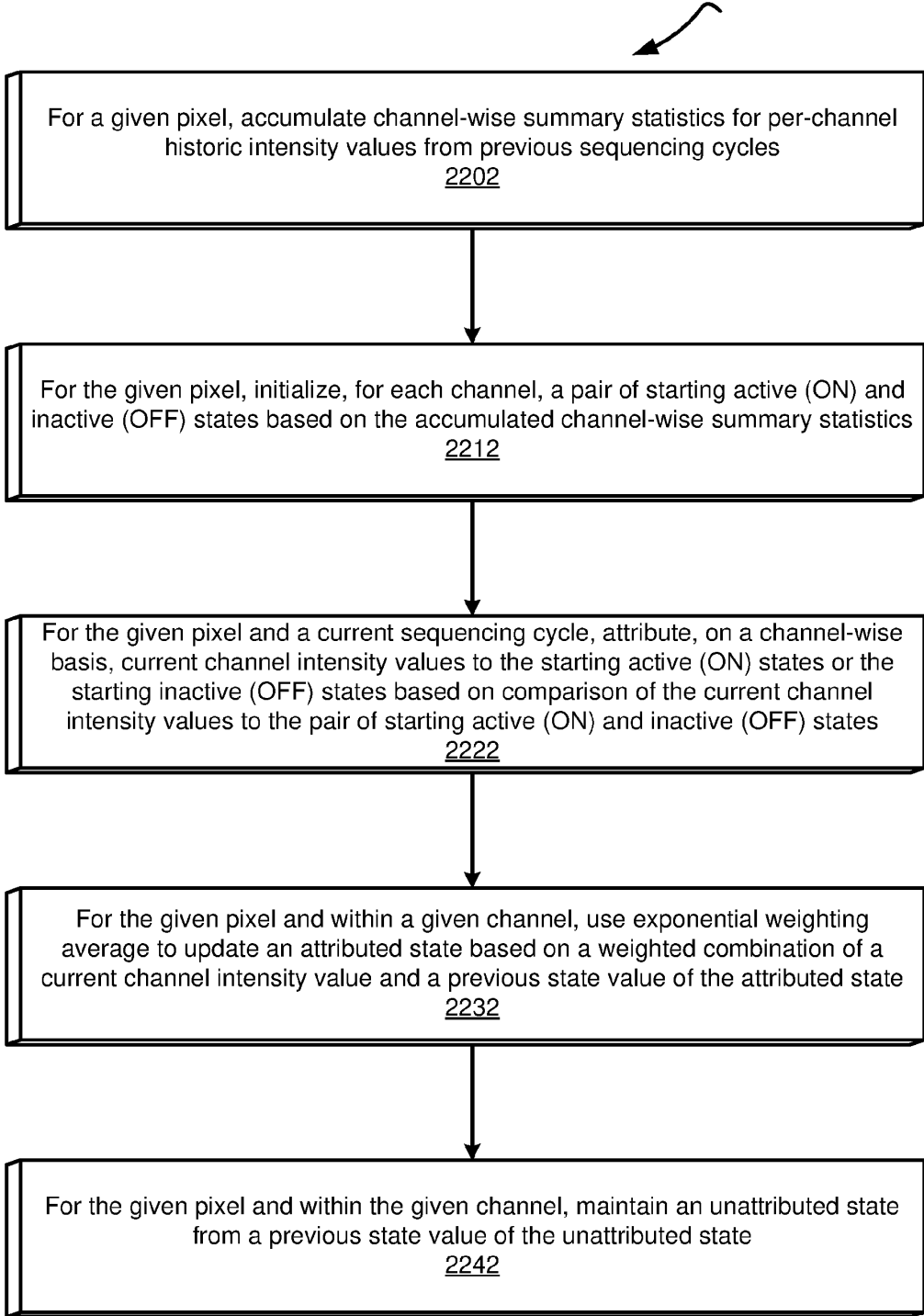


Figure 22

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	821.3	2376
Cycle 4	933.3		540.1	
Cycle 5	-63.8	2314	-16.0	2318
	Global Max = 1345.5	Global Min = -150.2	Global Max = 821.3	Global Min = -16.0
Cycle 6	2322 (attribution to active state)	Inactive state	2326 (attribution to active state)	Inactive state
	Active State	Inactive state	Active State	Inactive state
2332	Exponential Weighted Average [1345.5 * 0.12] + [1768 * 0.88]	2314 Global min = -150.2 (no change)	2316 Global Max = 821.3 (no change)	Exponential Weighted Average [-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)	Inactive state	2356 (attribution to active state)	Inactive state
	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

Figure 23

Base Call-Directed Per-Channel Exponential Weighted Averaging 2400

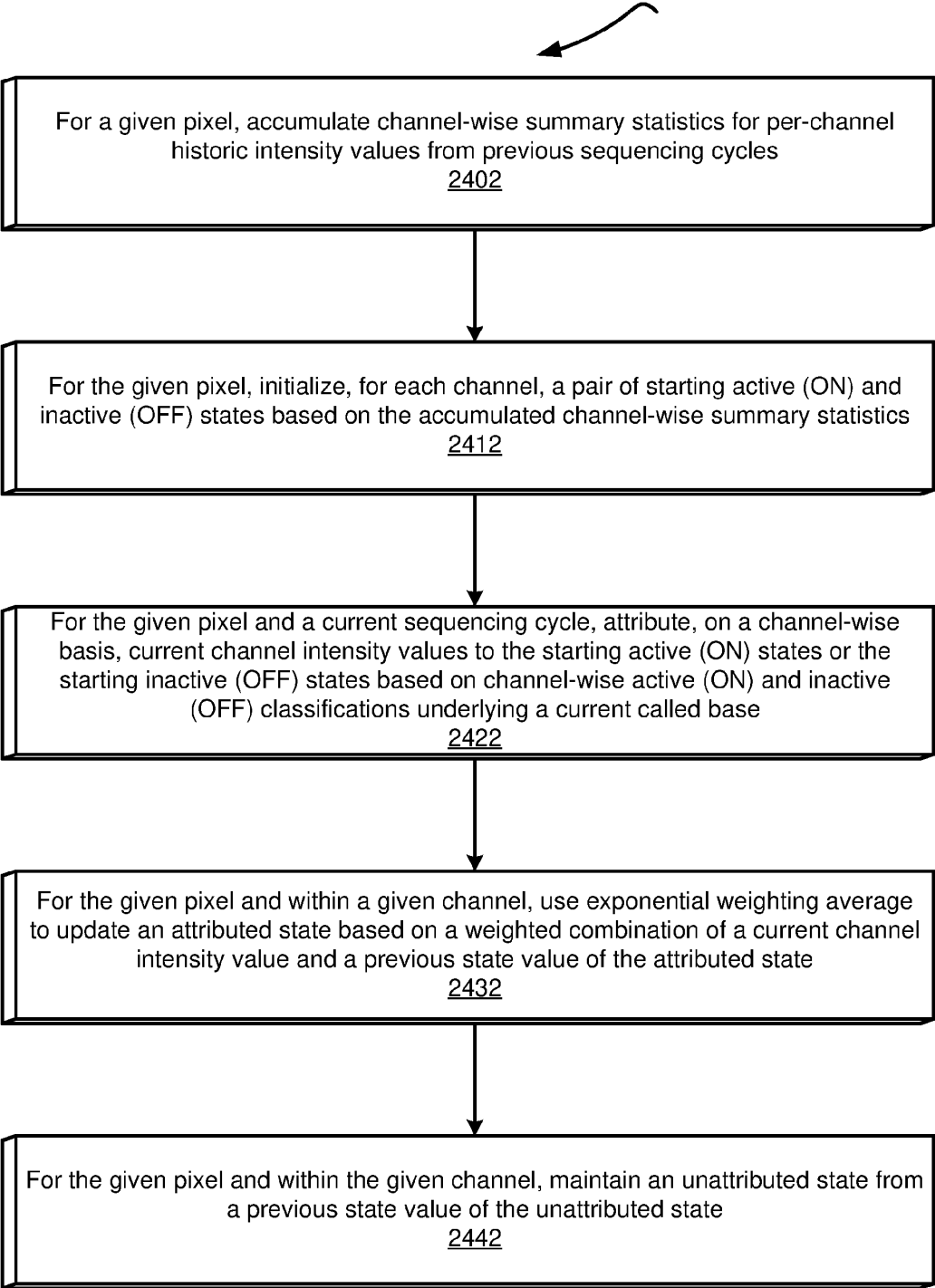


Figure 24

Pixel P		Base Call-Directed Per-Channel ON and OFF StateDetermination using Exponential Weighted Averages 2500	
		Channel 1	Channel 2
Cycle 1		171.4	619.2
Cycle 2		-150.2	5.9
Cycle 3		1345.5	2376
Cycle 4		933.3	540.1
Cycle 5		-63.8	-16.0
Cycle 6		2322 — 1768 (attribution to active state)	2326 — -90.1 (attribution to active state)
Base Call A		2504 — ON	2506 — OFF
2502		Active State	Inactive state
2332	Exponential Weighted Average	2314 Global min = -150.2 (no change)	2338 Exponential Weighted Average [-16.0 * 0.12] + [-90.1 * 0.88]
	[1345.5 * 0.12] + [1768 * 0.88]	2344	
2342	EWA 6 = 1717.3	EWA 6 = -150.2	EWA 6 = -81.208
	2352 — 5.9 (attribution to active state)		2348
Cycle 7		2356 — 151.5 (attribution to active state)	
Base Call A		2514 — OFF	2516 — ON
2512		Active State	Inactive state
2342	EWA 6 = 1717.3 (no change)	2374 Exponential Weighted Average [-150.2 * 0.12] + [5.9 * 0.88]	2348 EWA 6 = -81.208 (no change)
2372	EWA 7 = 1717.3	EWA 7 = -12832	EWA 7 = -81.208
			2378

Figure 25

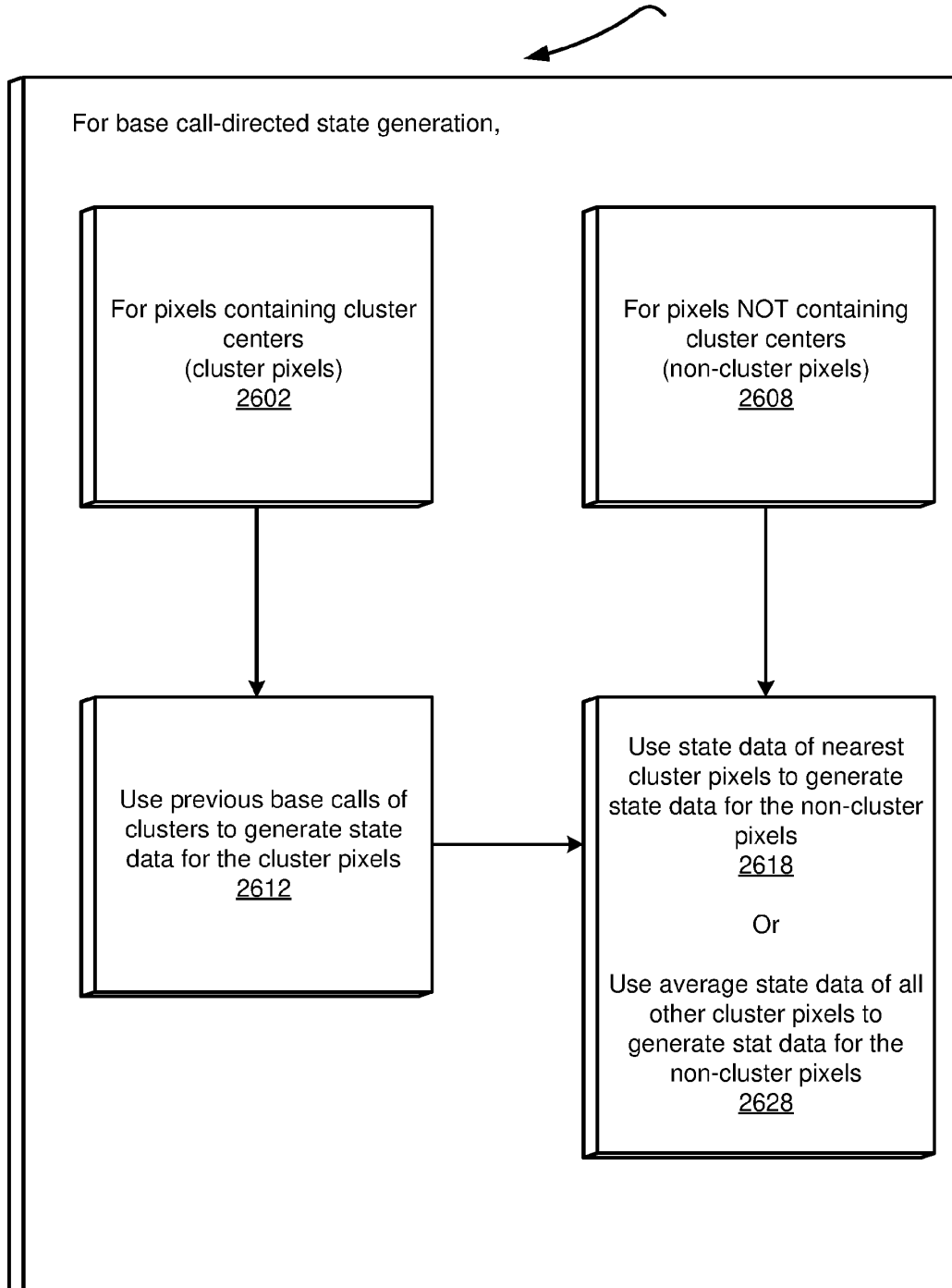
2376

2366

2374

2364

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

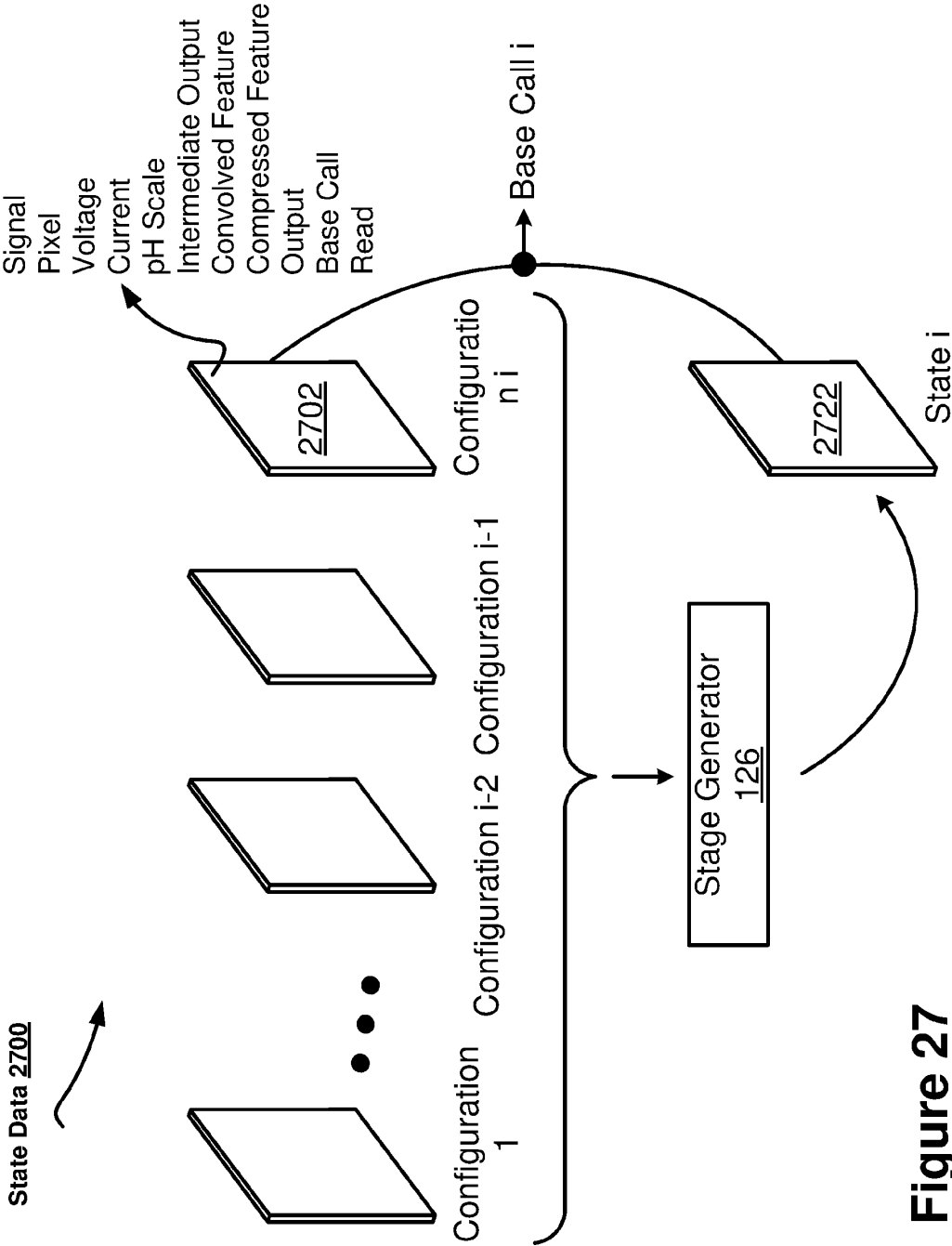


Figure 27

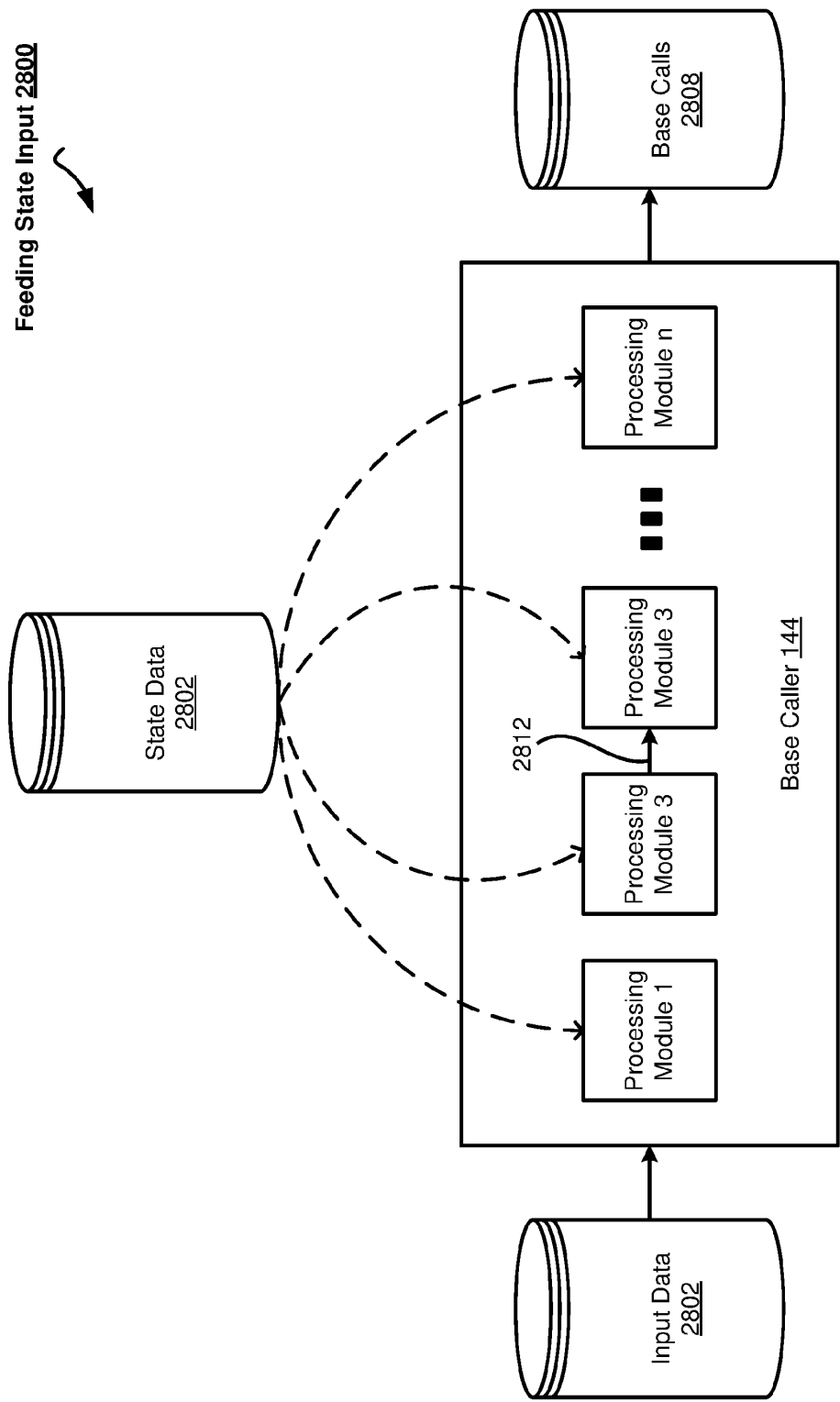


Figure 28

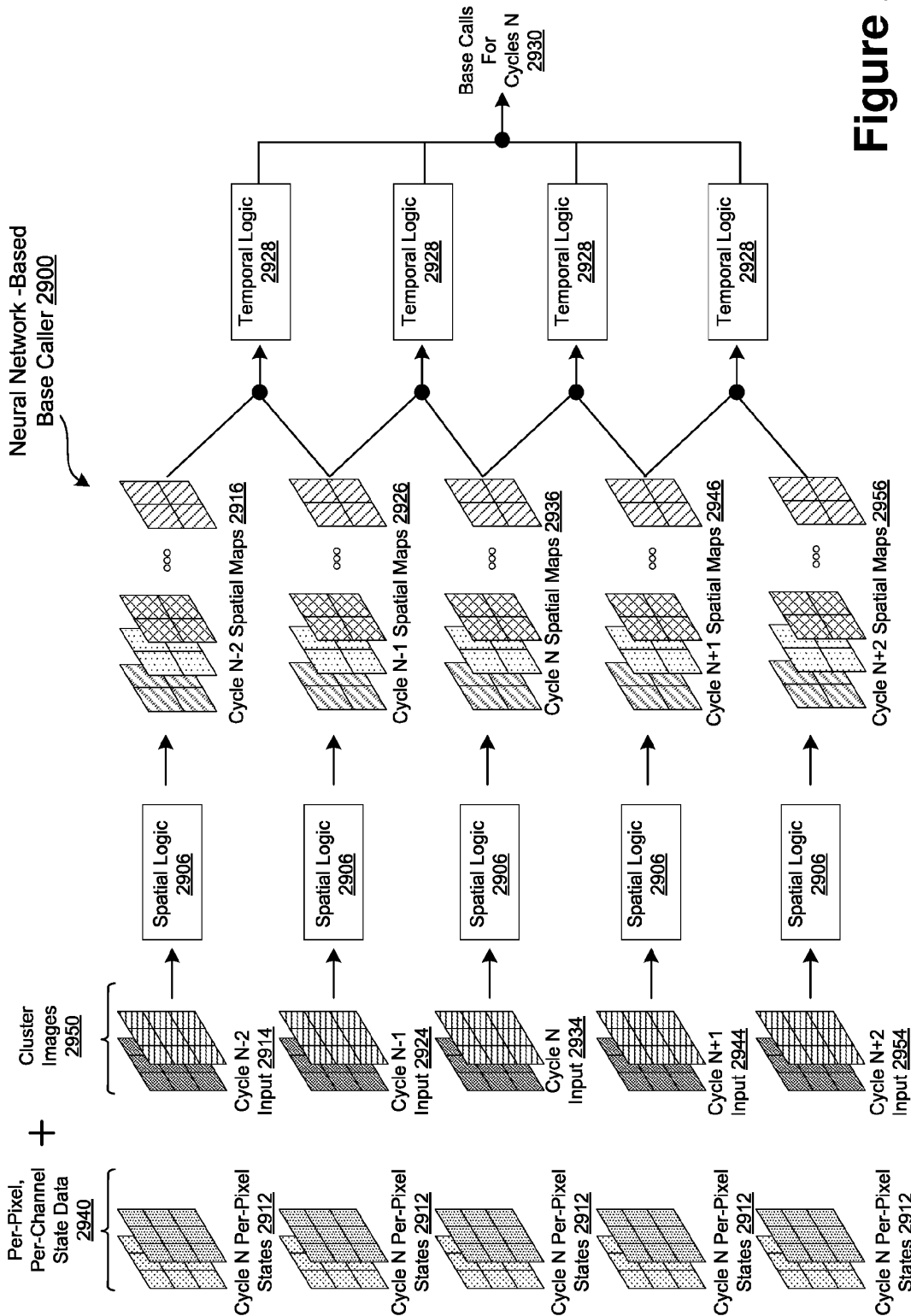


Figure 29

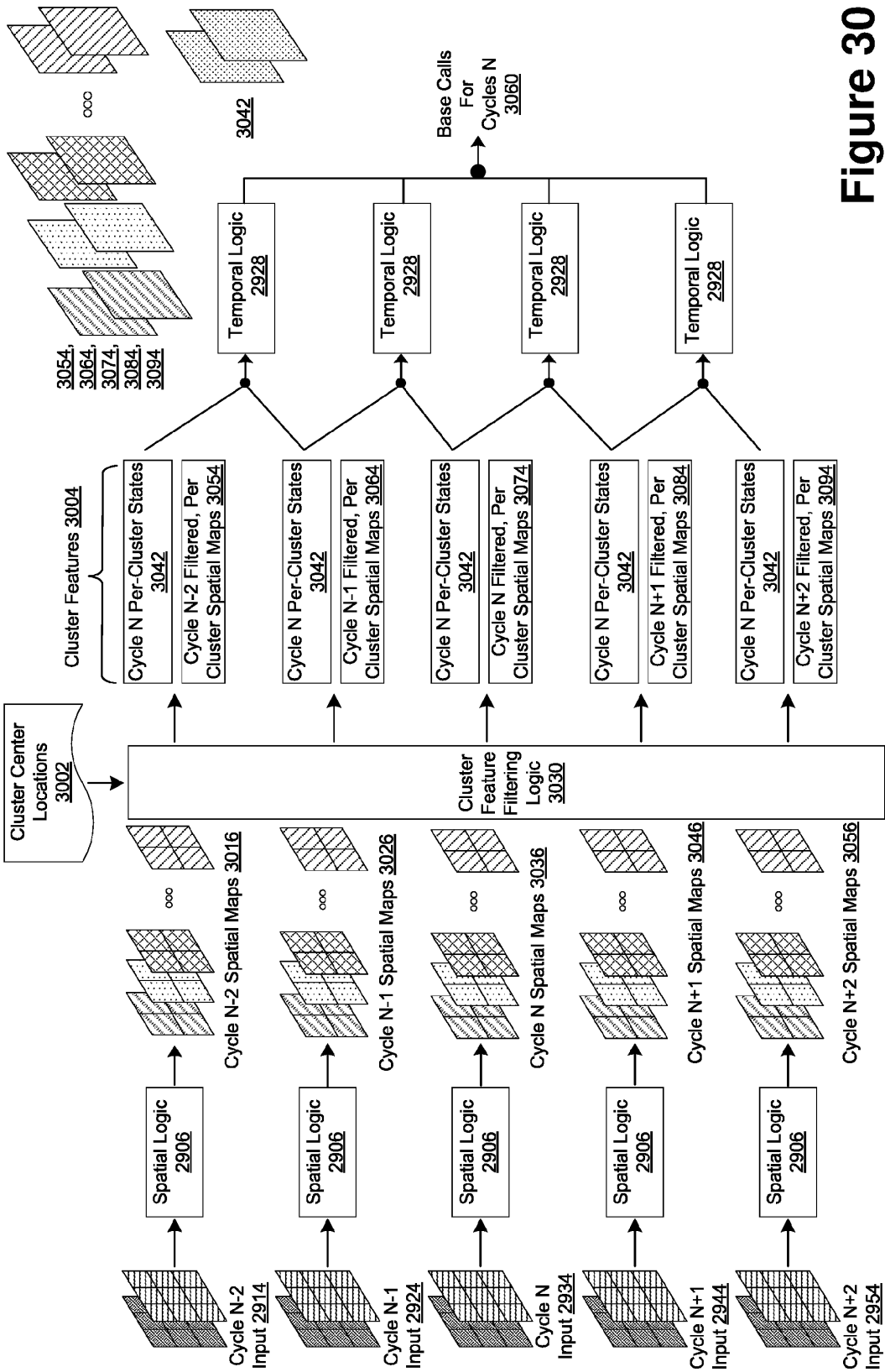
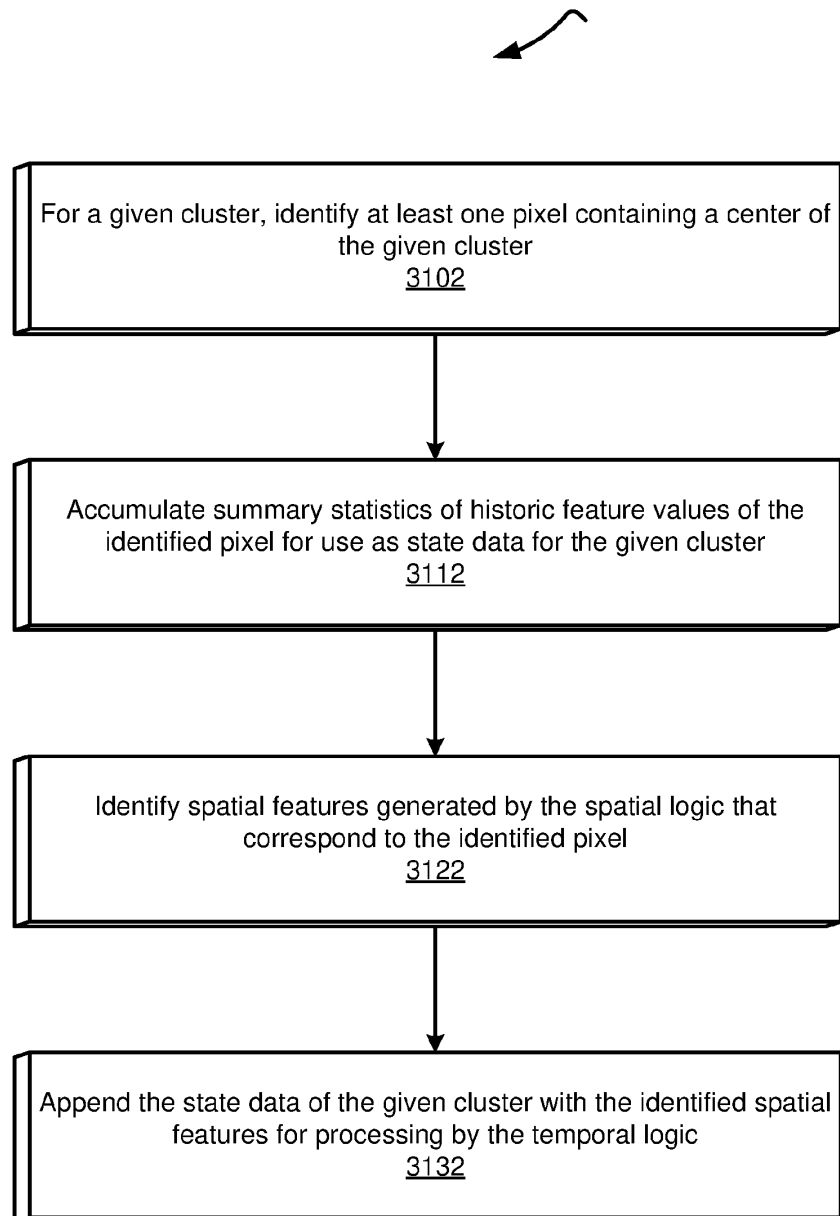


Figure 30

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

Per-Cluster Spatial Features-Based State Generation 3200

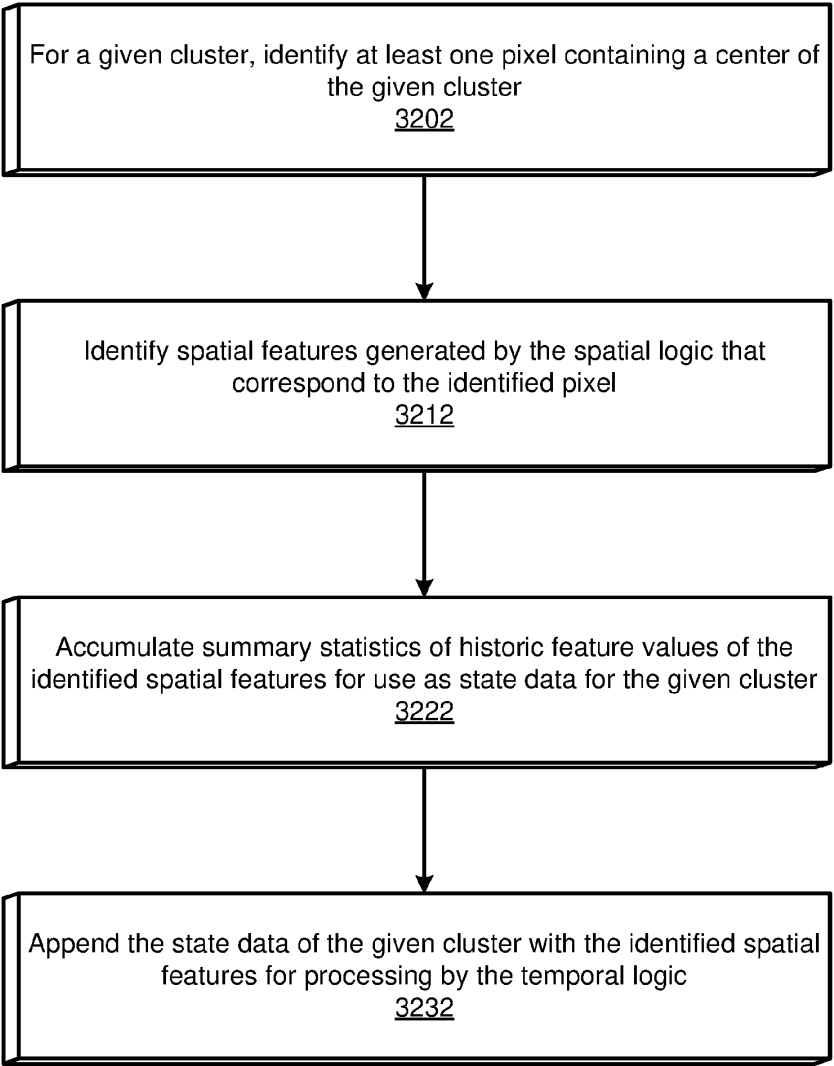
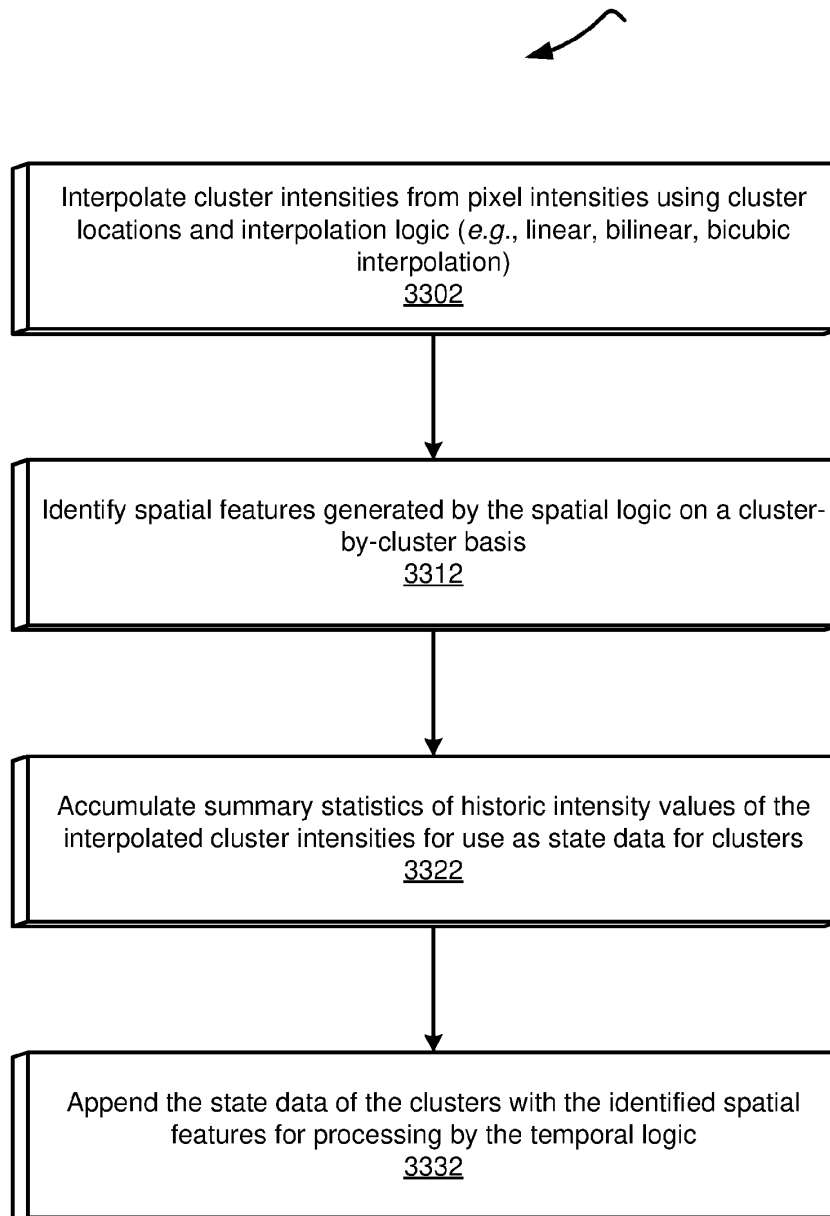
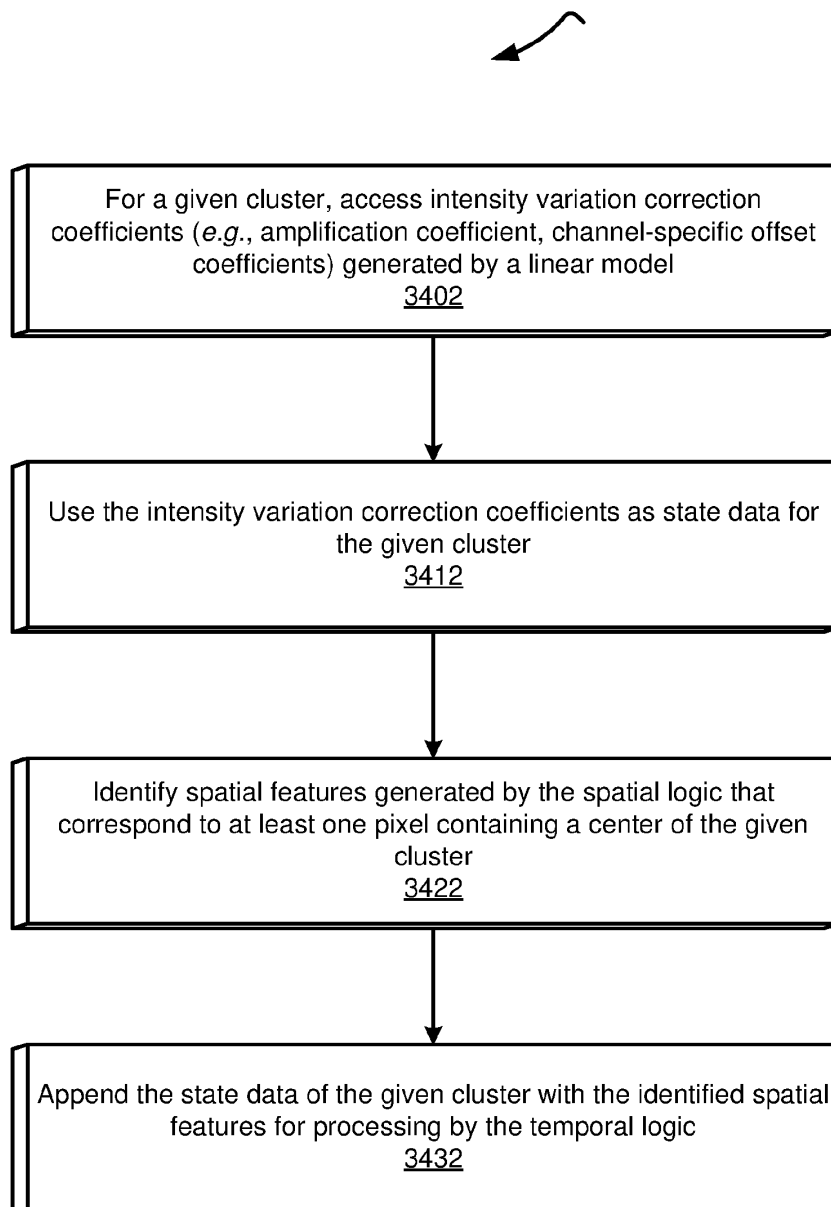


Figure 32

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

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

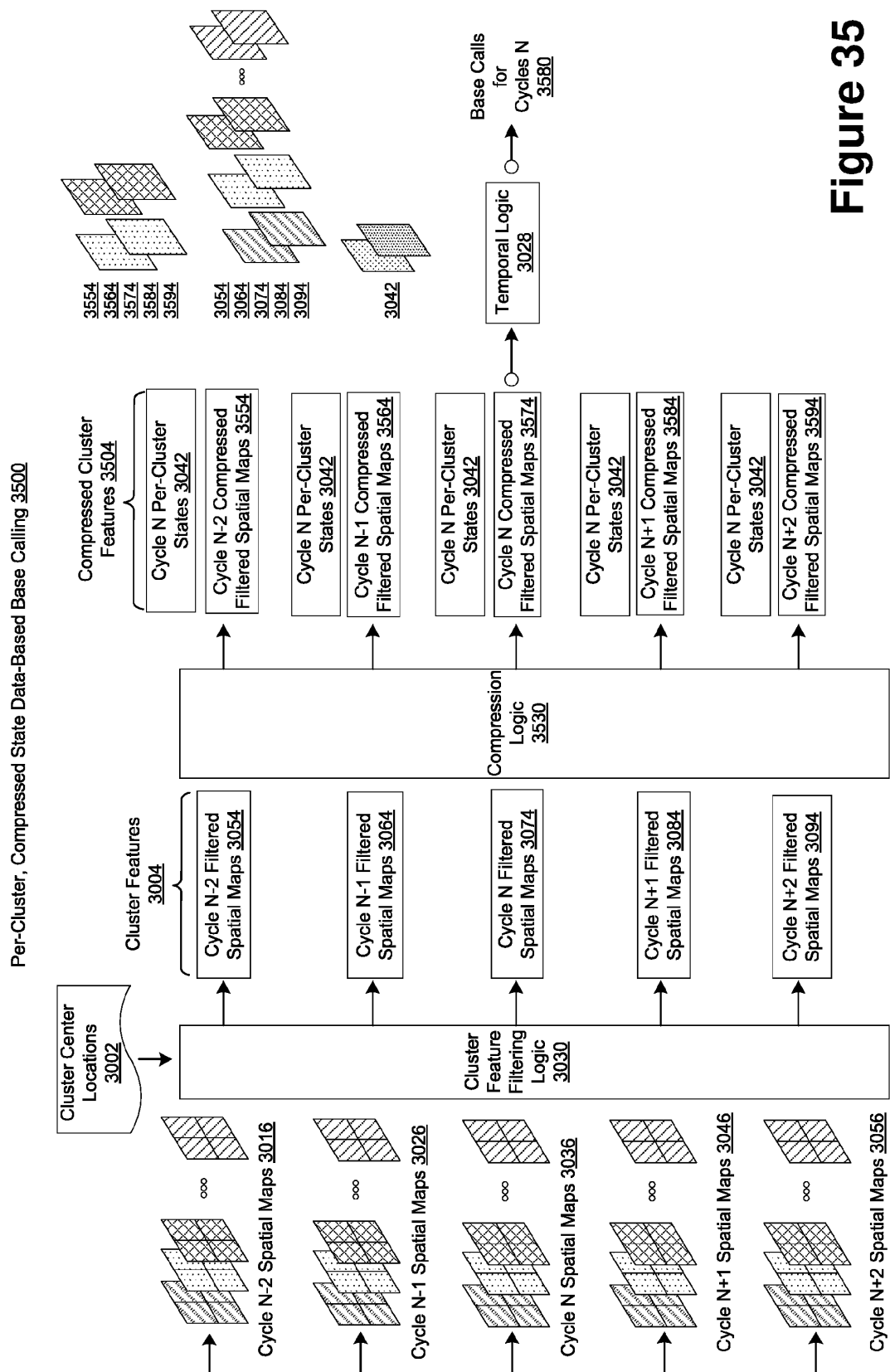


Figure 35

Per-Cluster Compressed Spatial Features-Based State Generation 3600

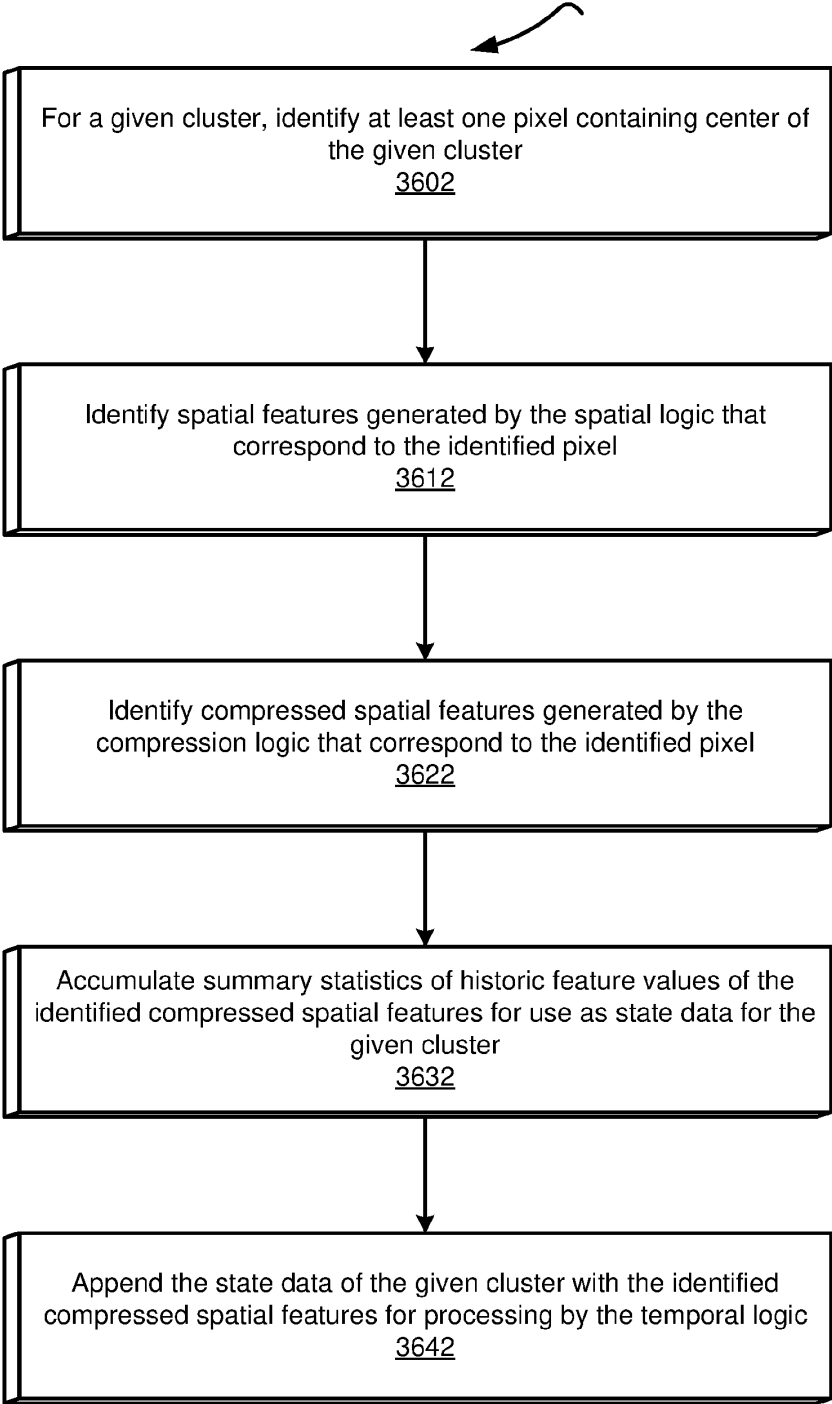


Figure 36

Per-Cluster RTA Compressed Features-Based State Generation 3700

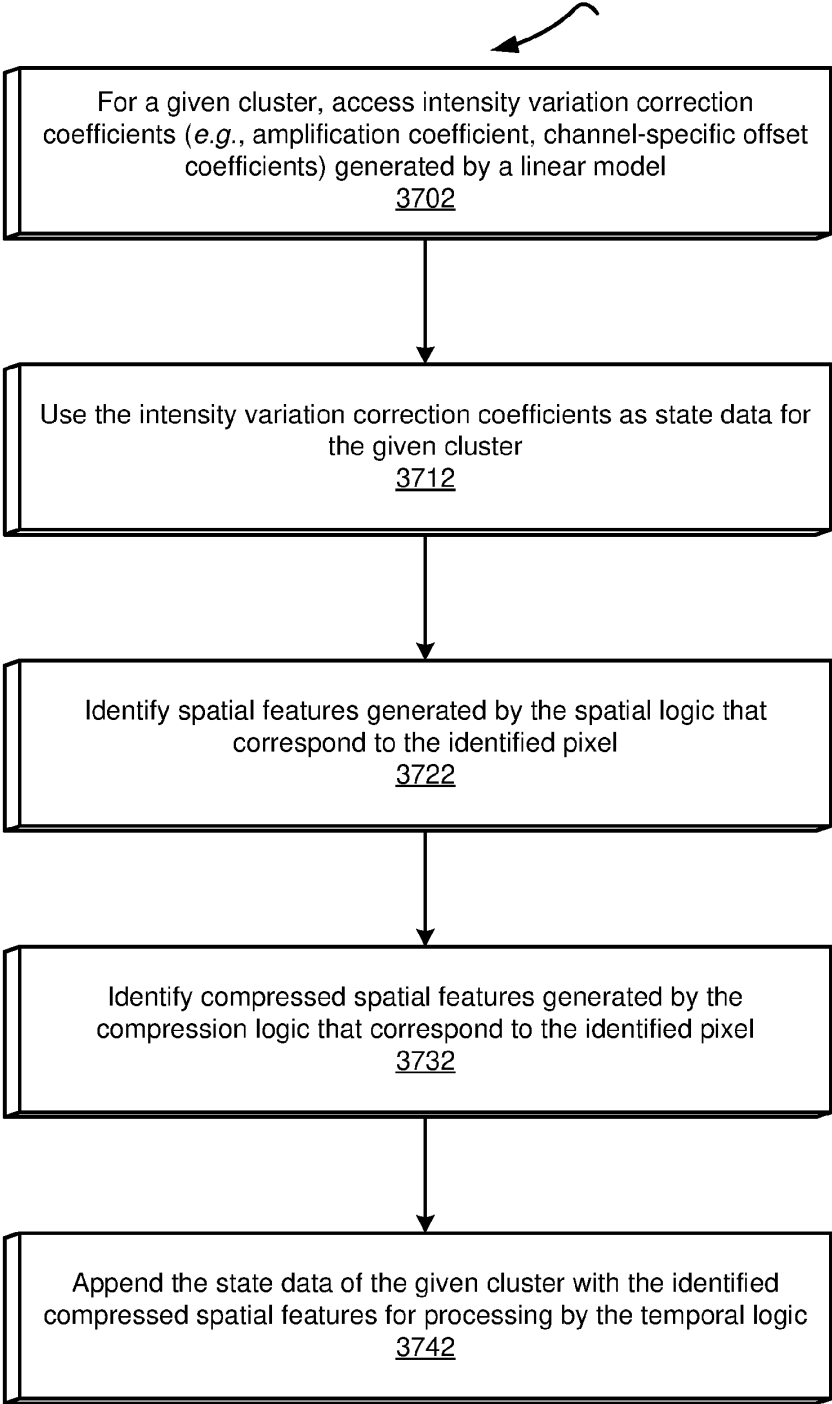


Figure 37

Per-Cluster Compressed Pixel-Based State Generation 3800

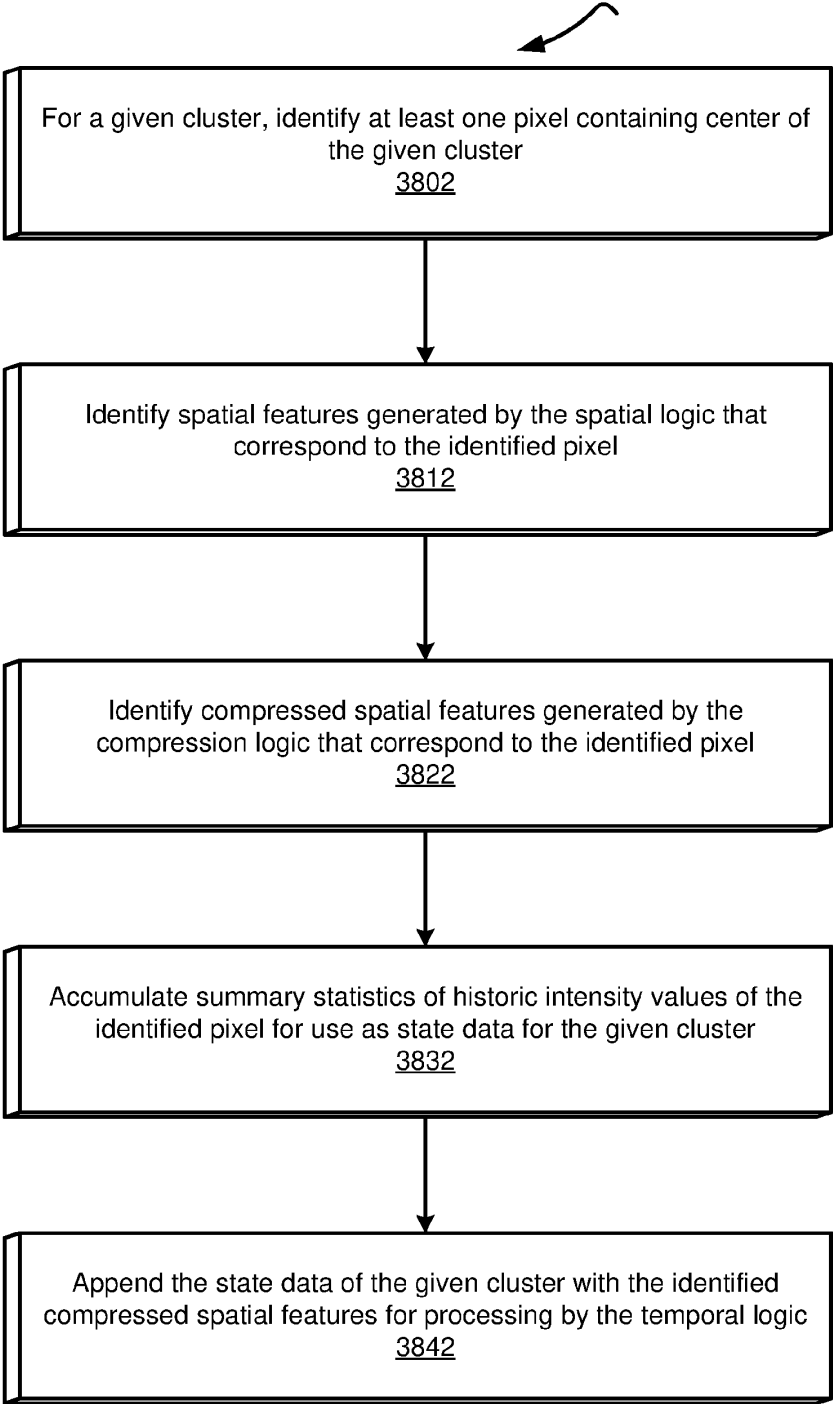


Figure 38

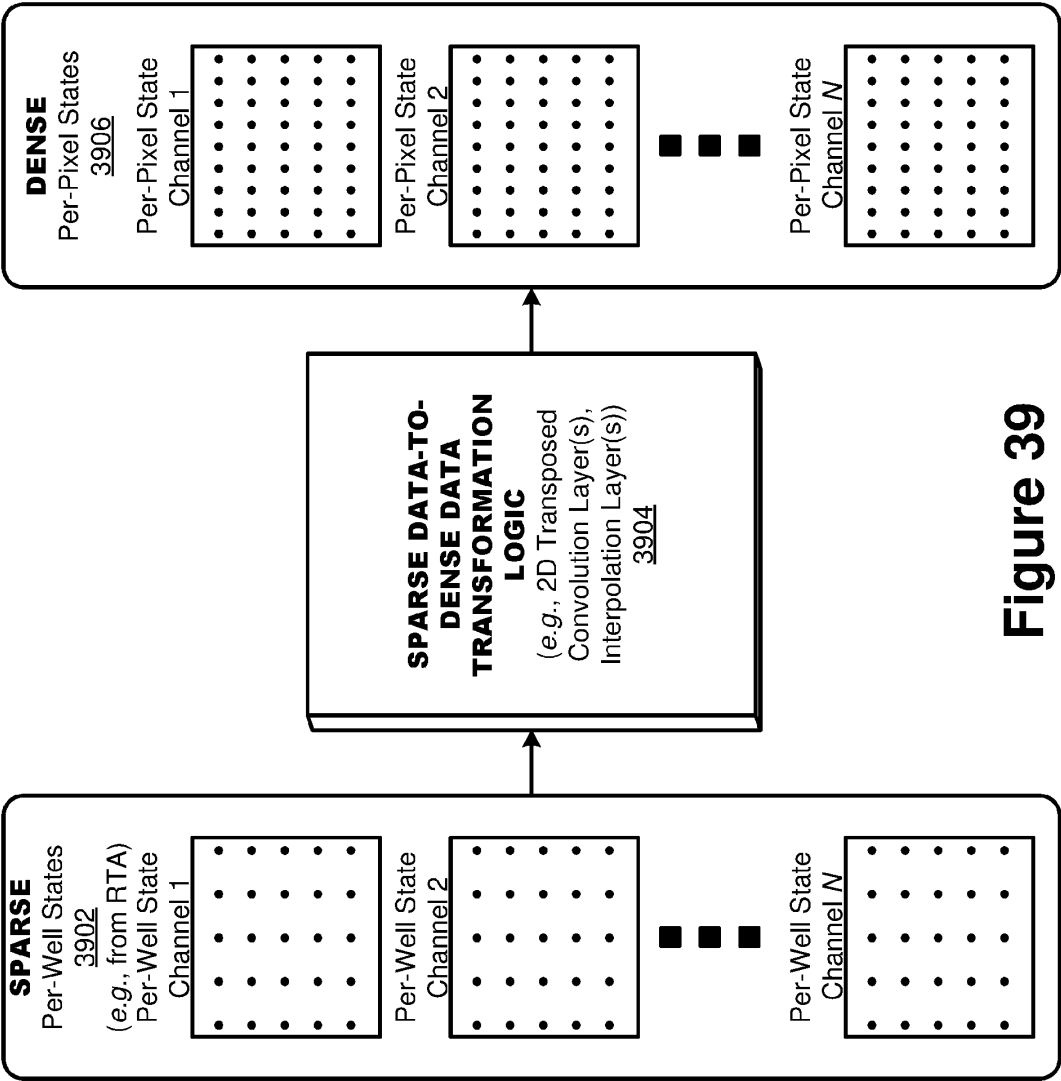


Figure 39

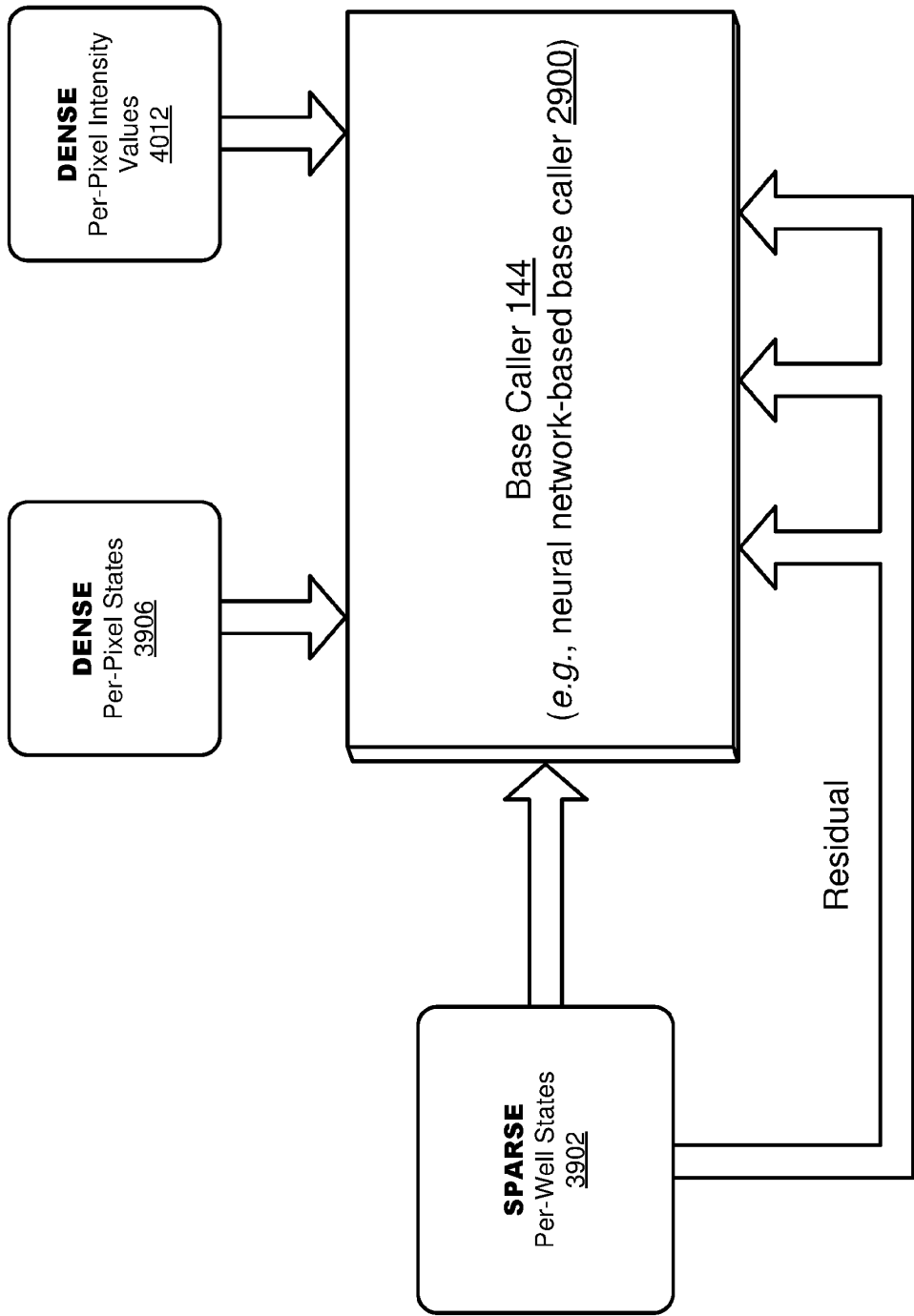


Figure 40

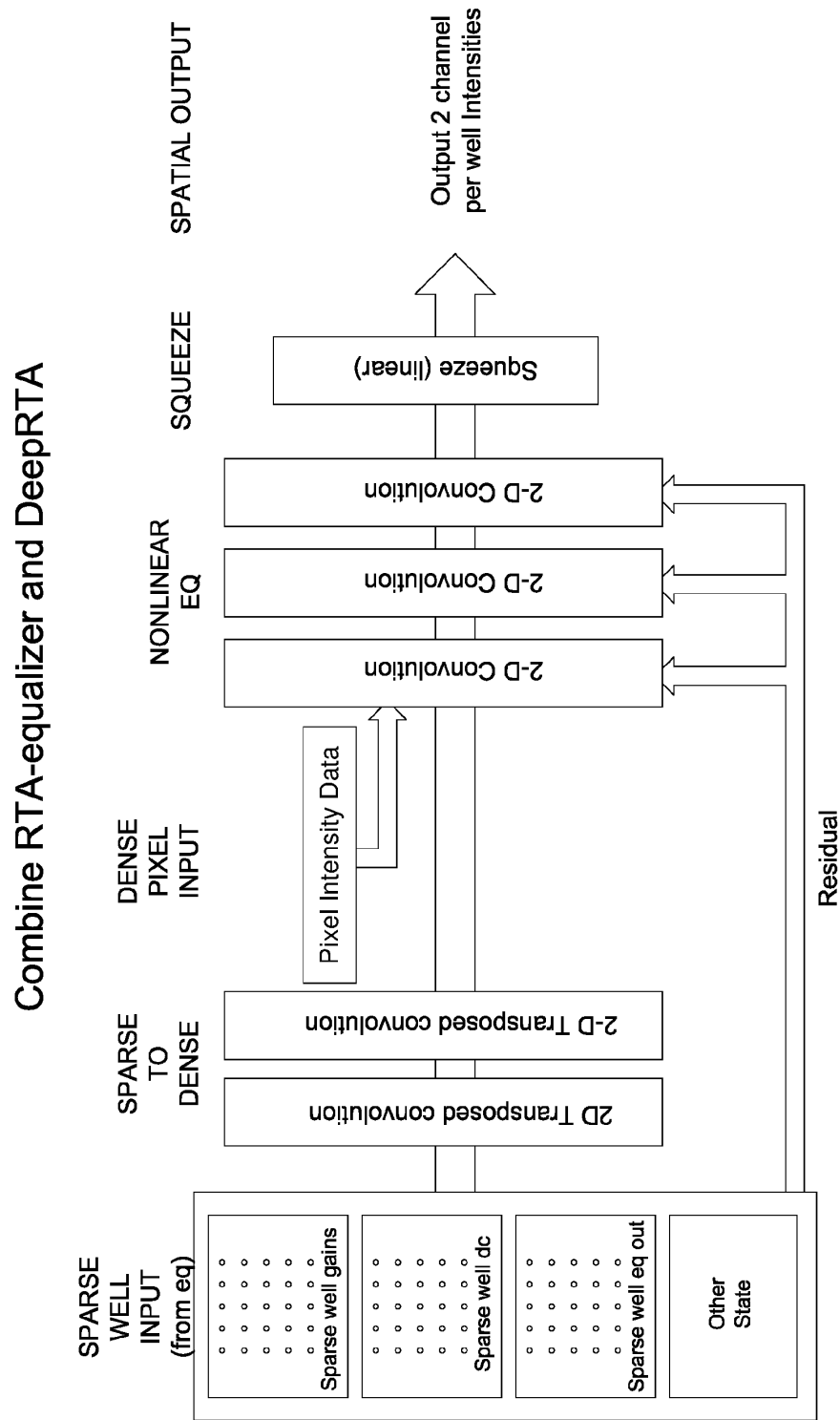


Figure 41

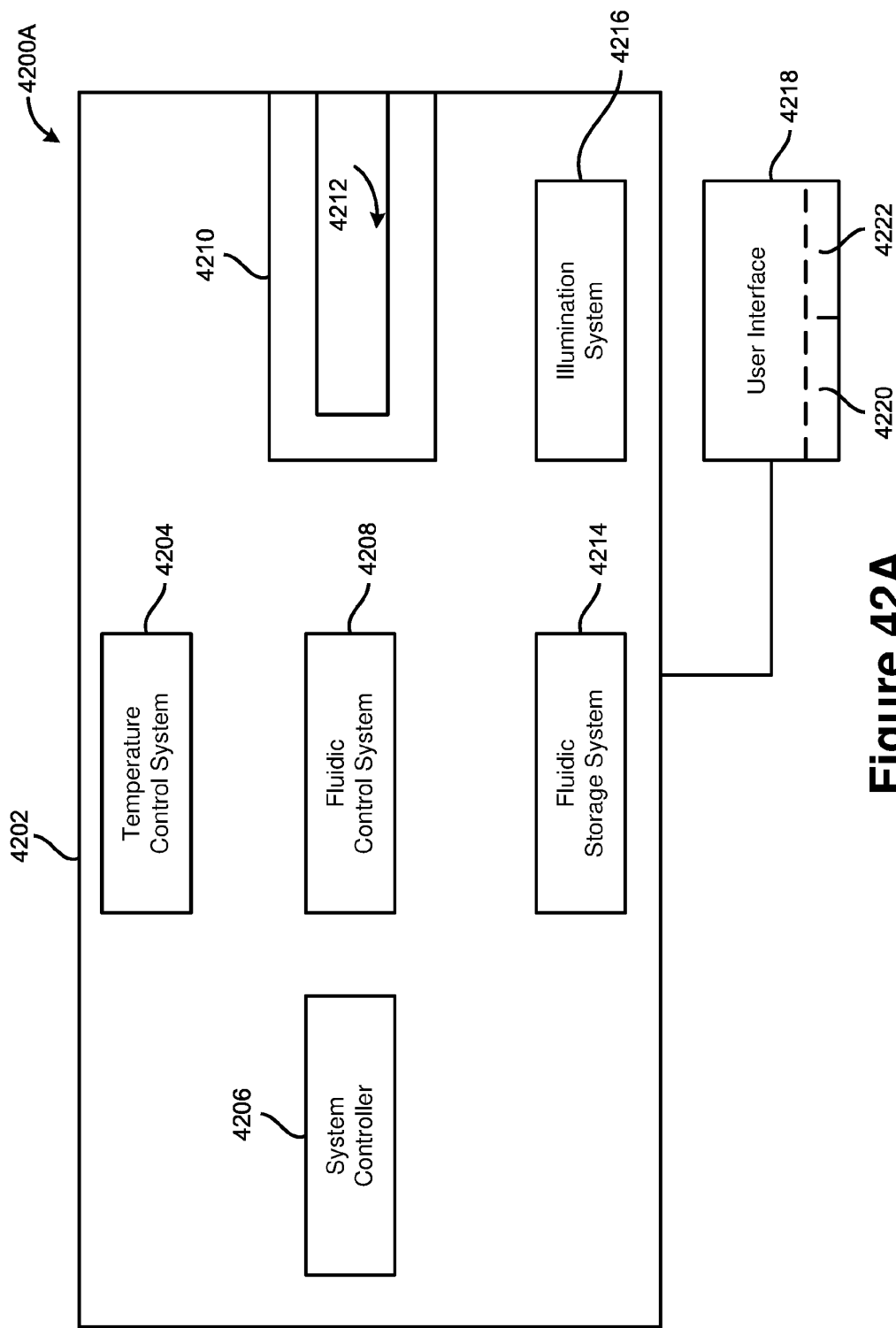


Figure 42A

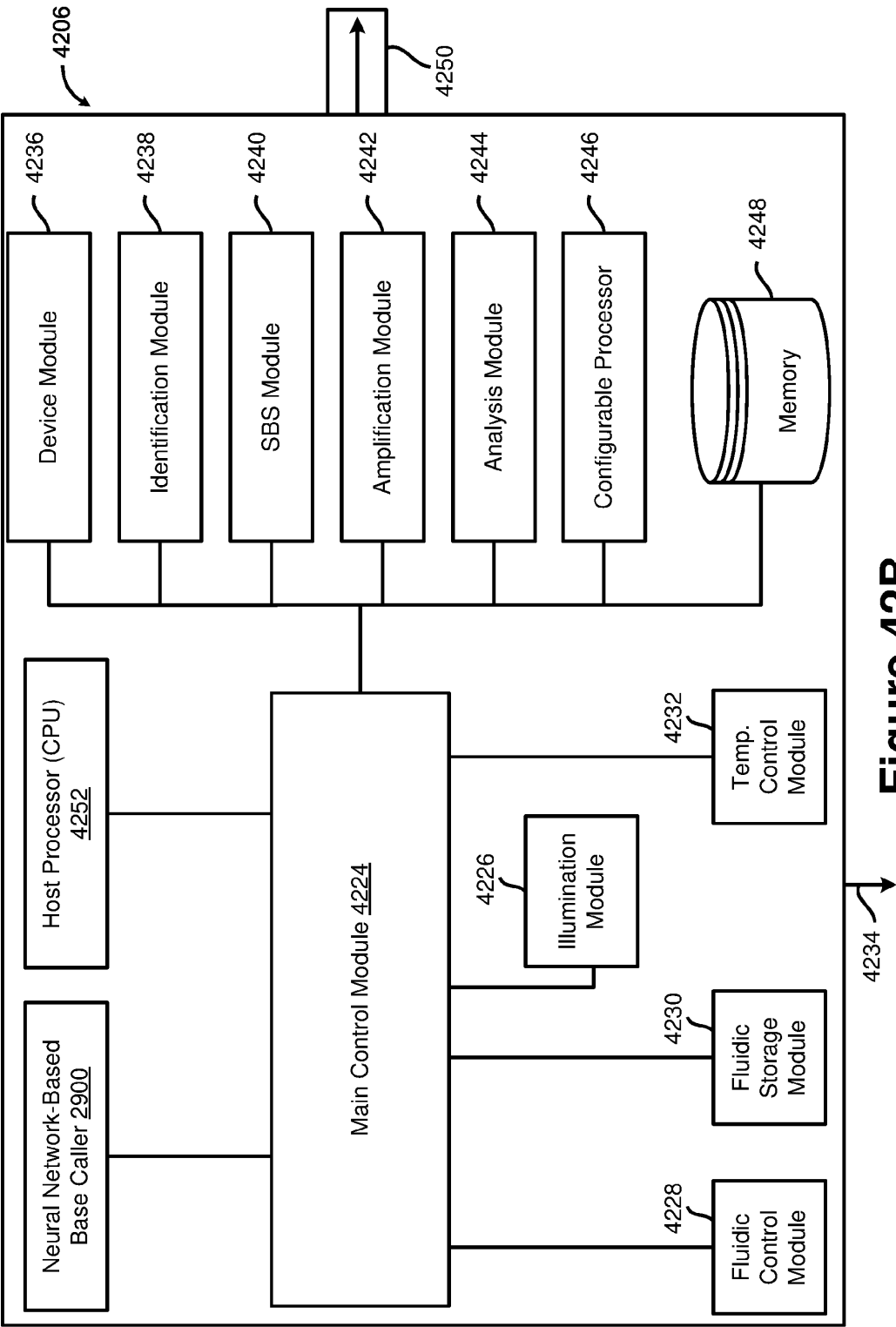


Figure 42B

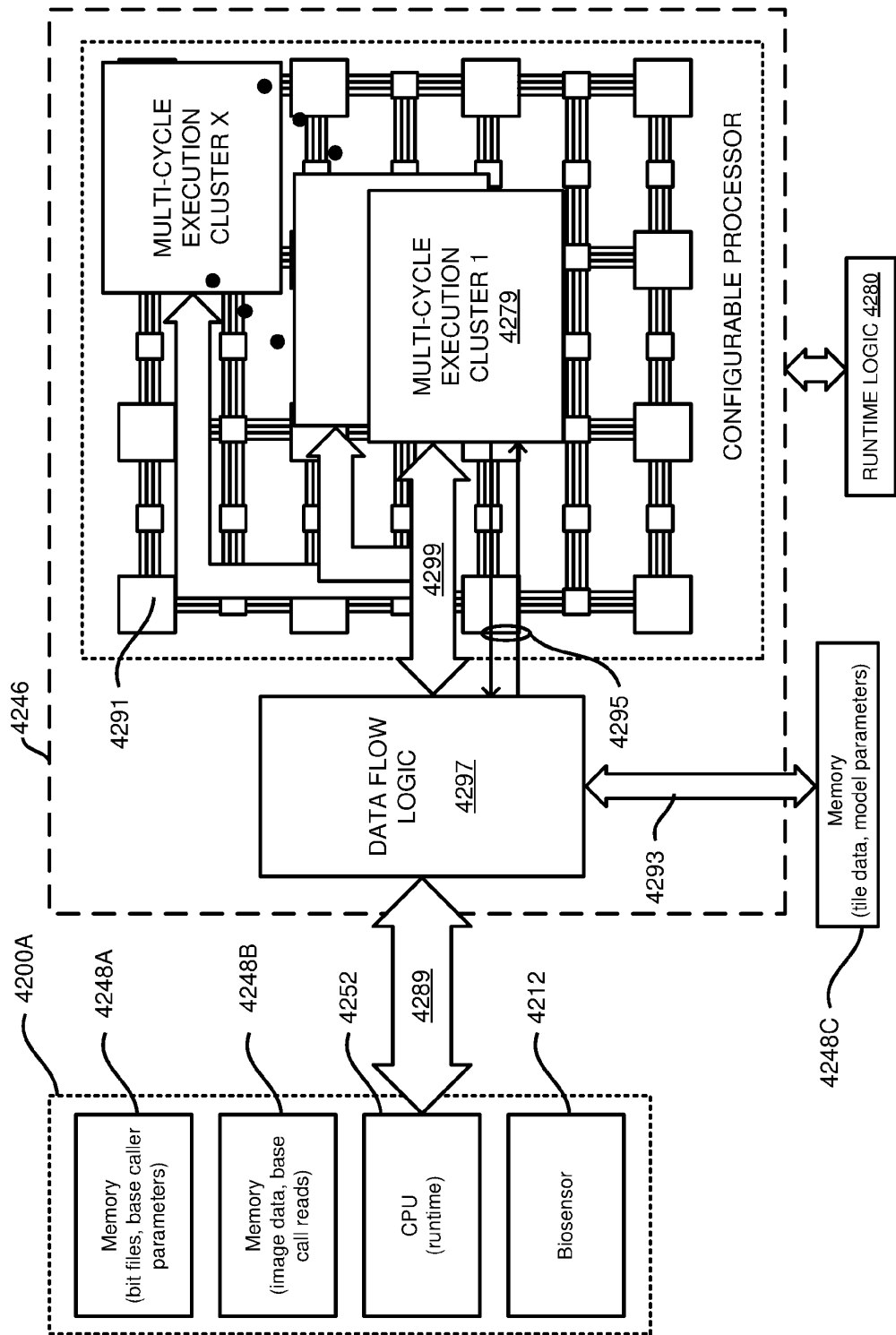


Figure 42C

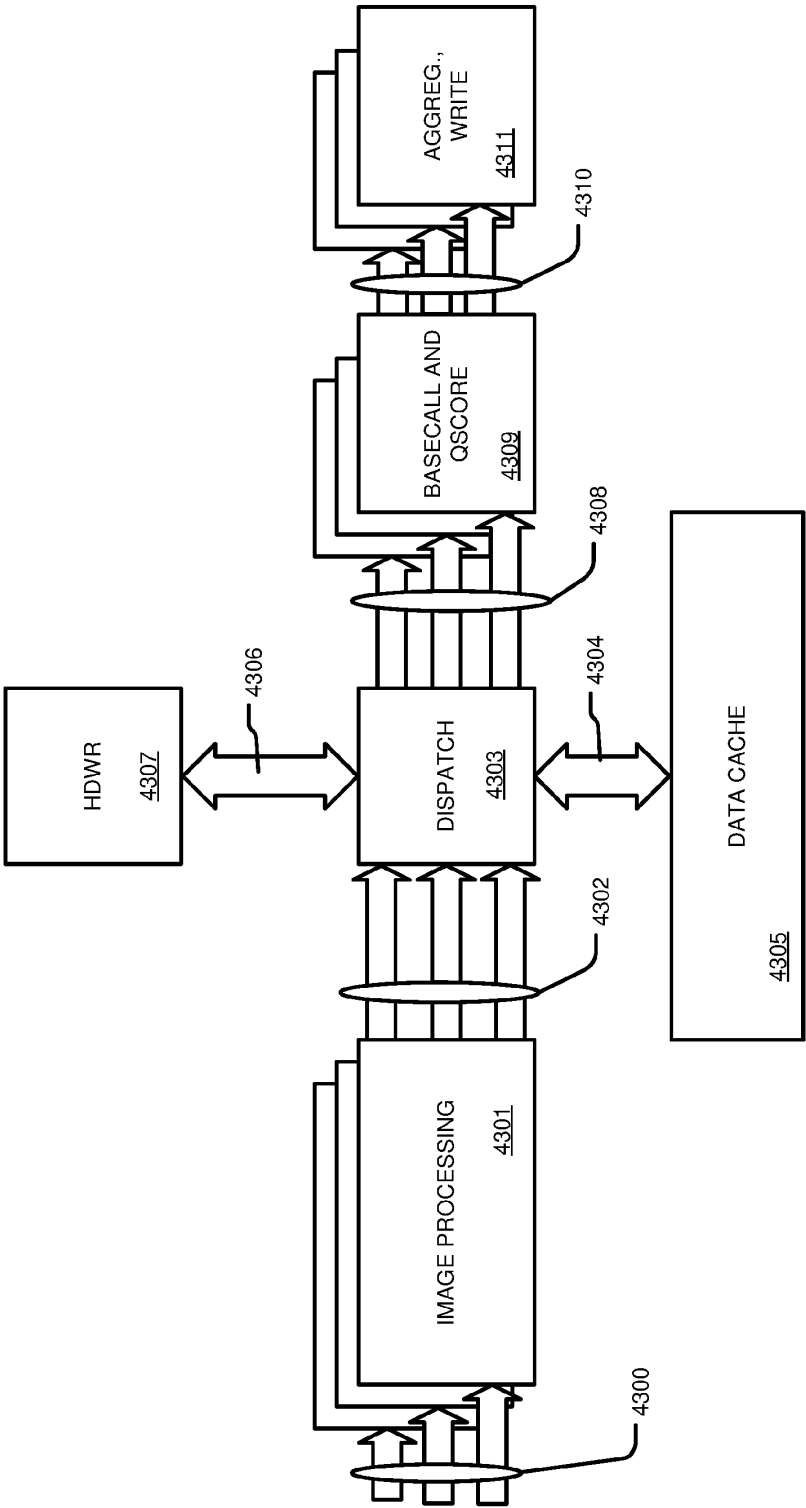


Figure 43A

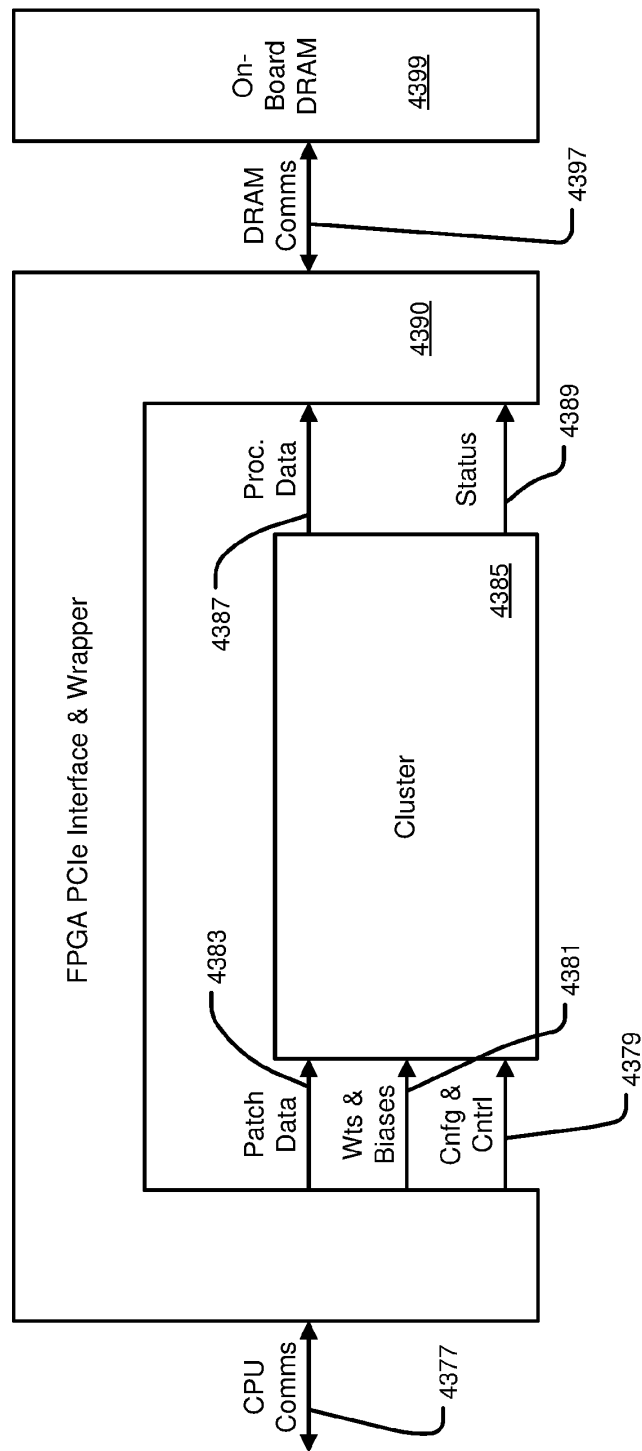


Figure 43B

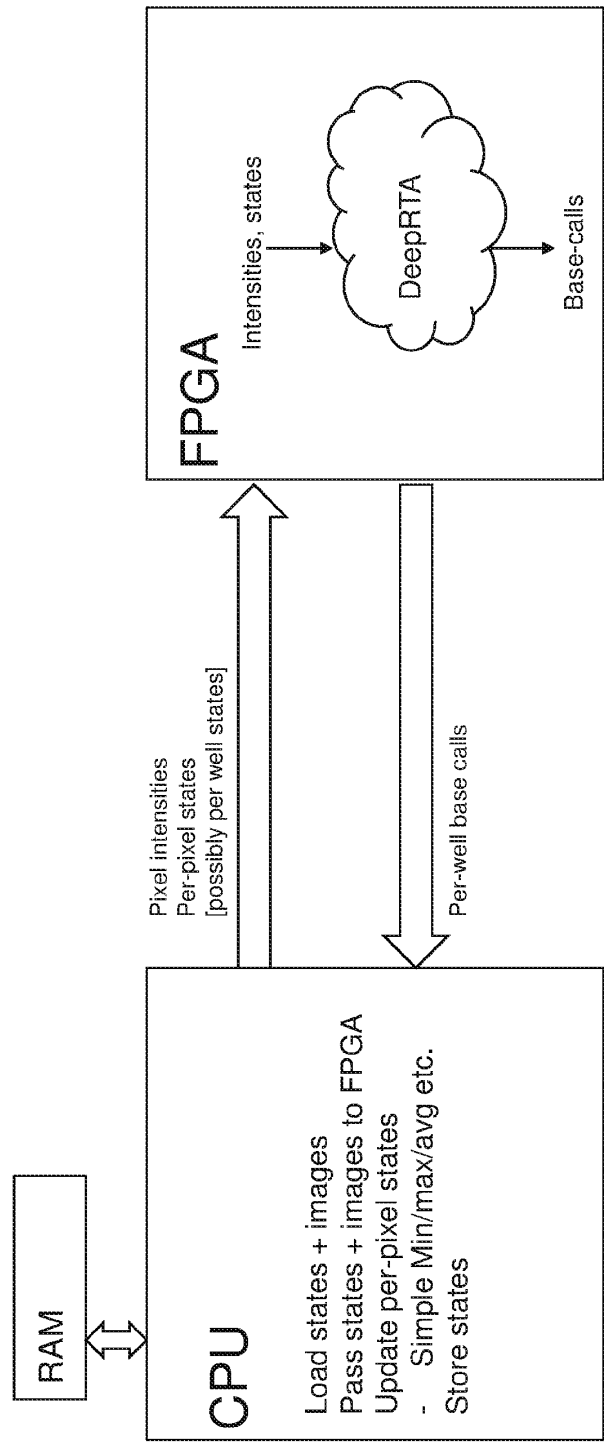


Figure 44

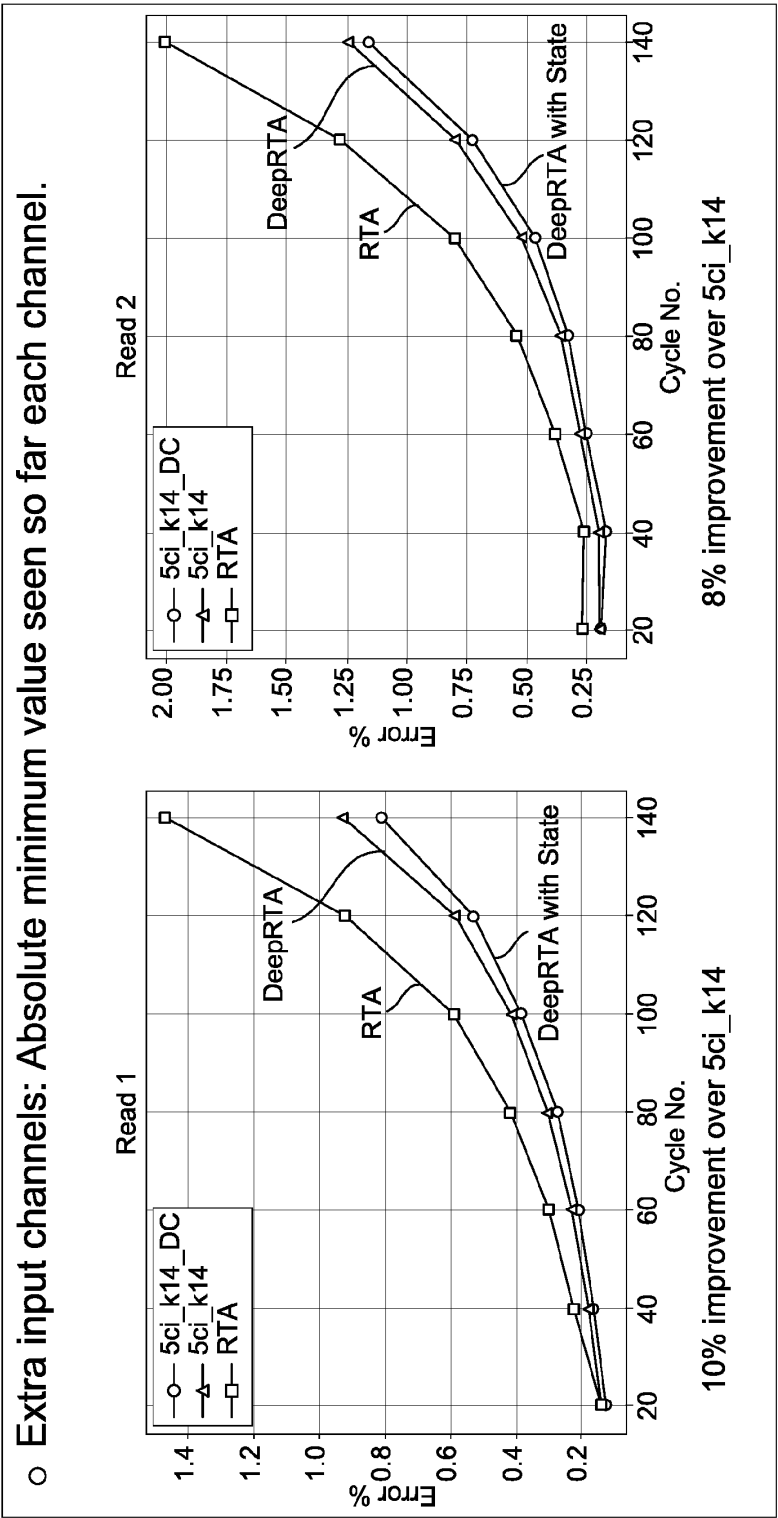


Figure 45

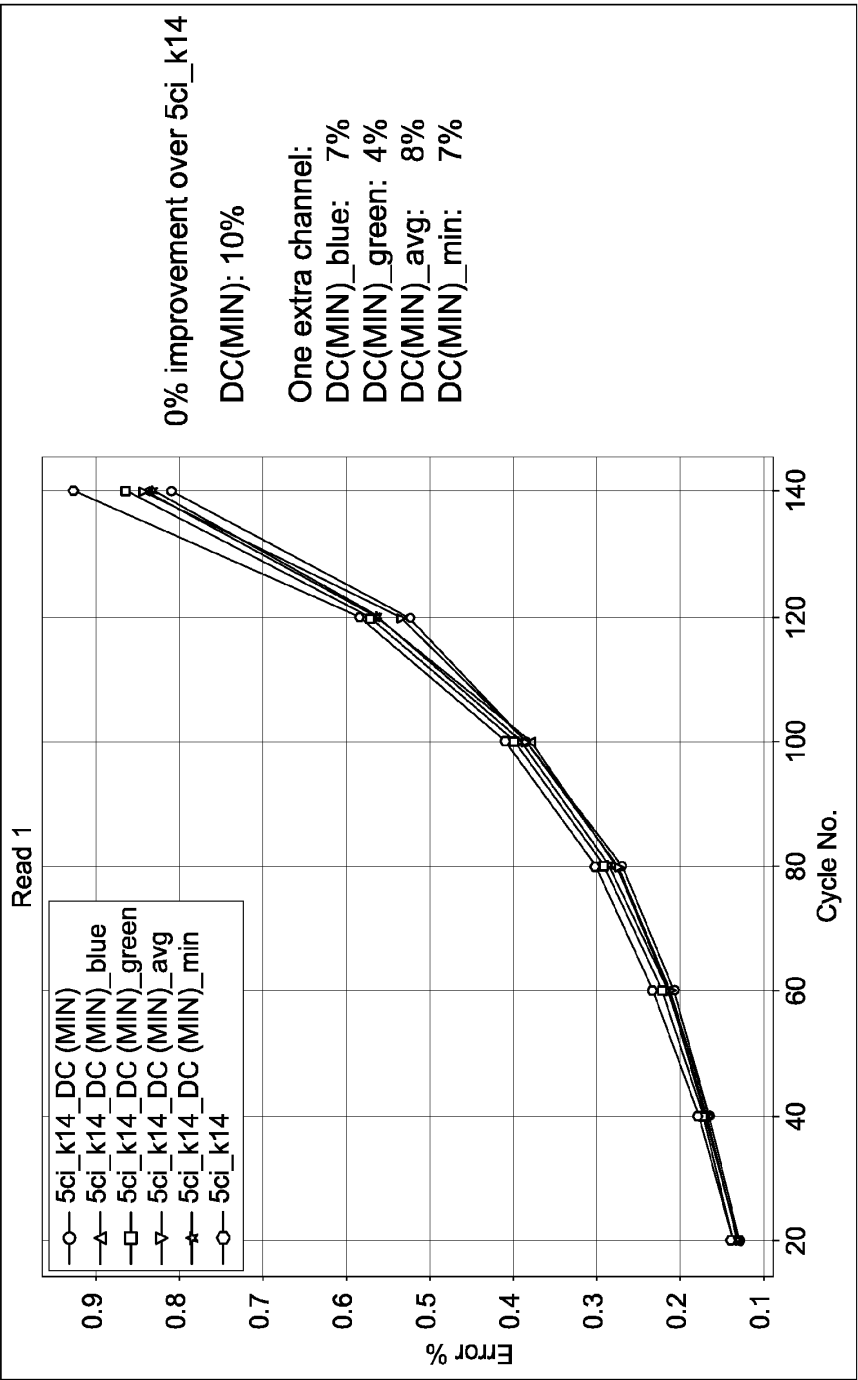


Figure 46

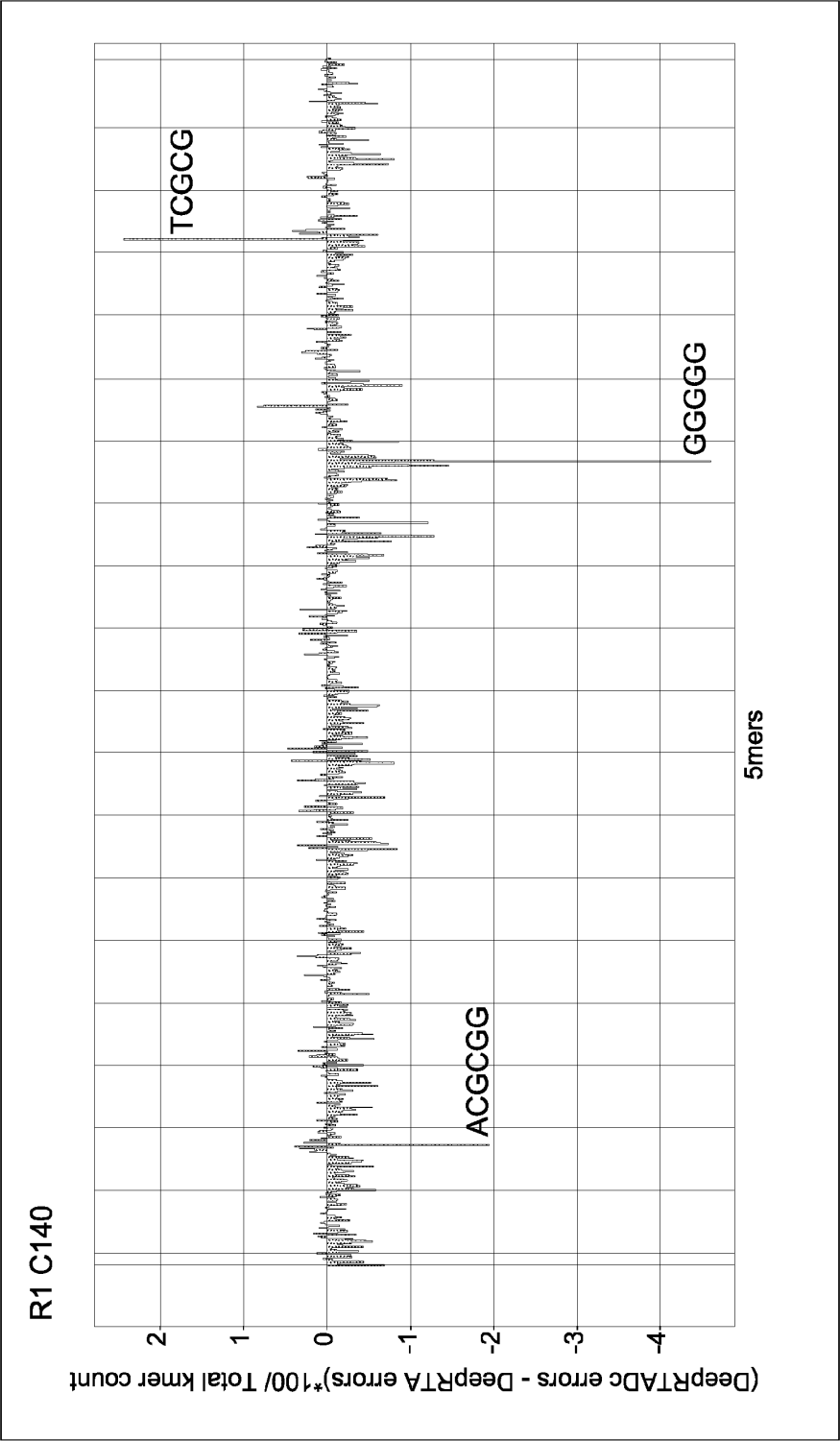
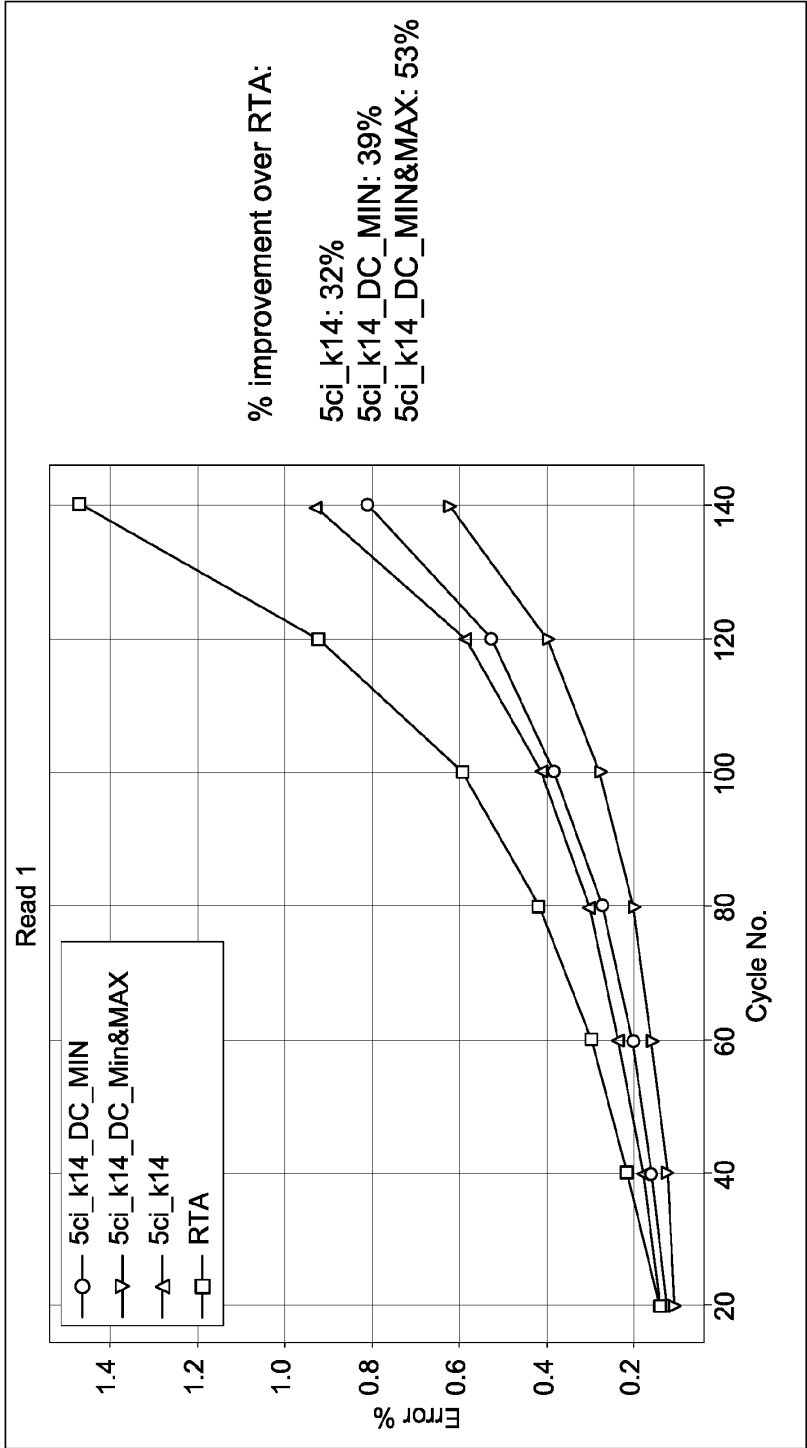


Figure 47



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

- 'compute' cost is negligible
- Hardware compatible

Figure 48

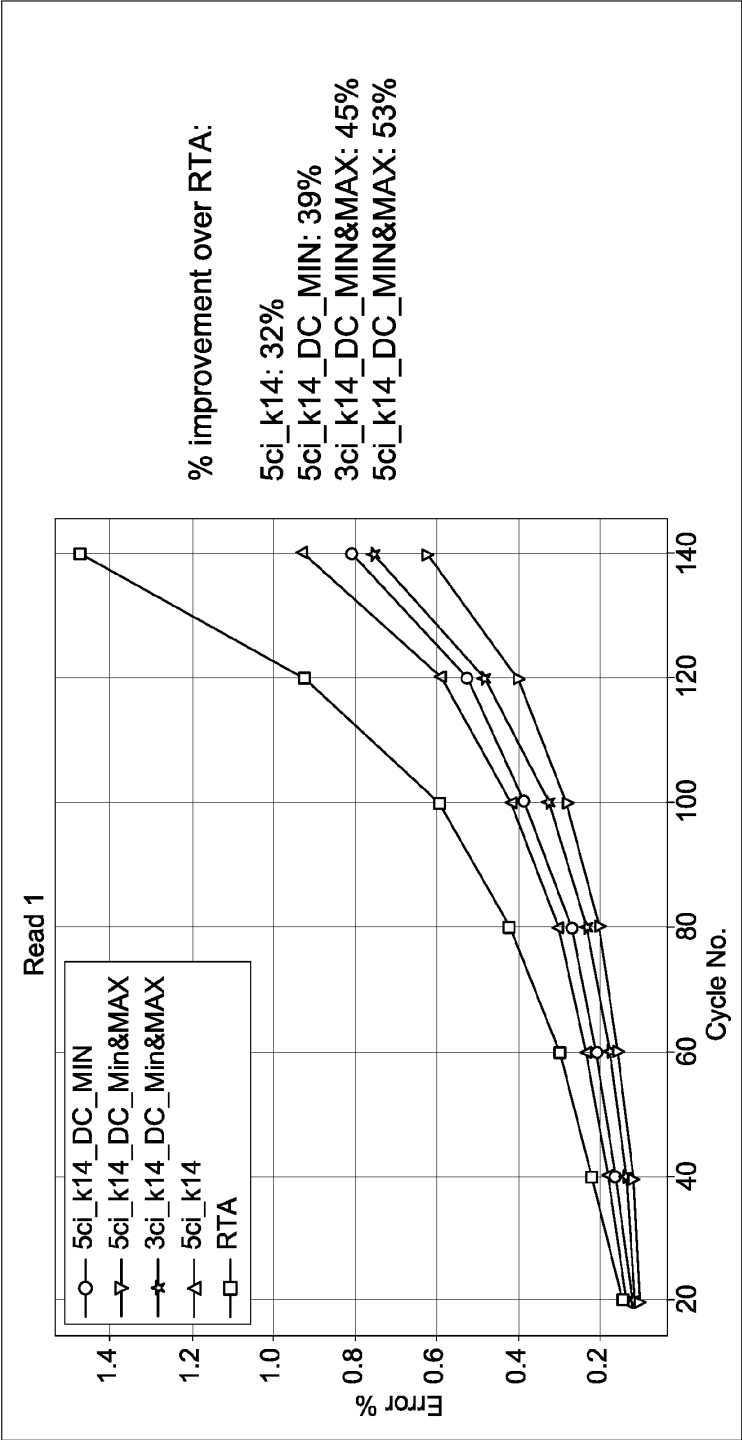


Figure 49

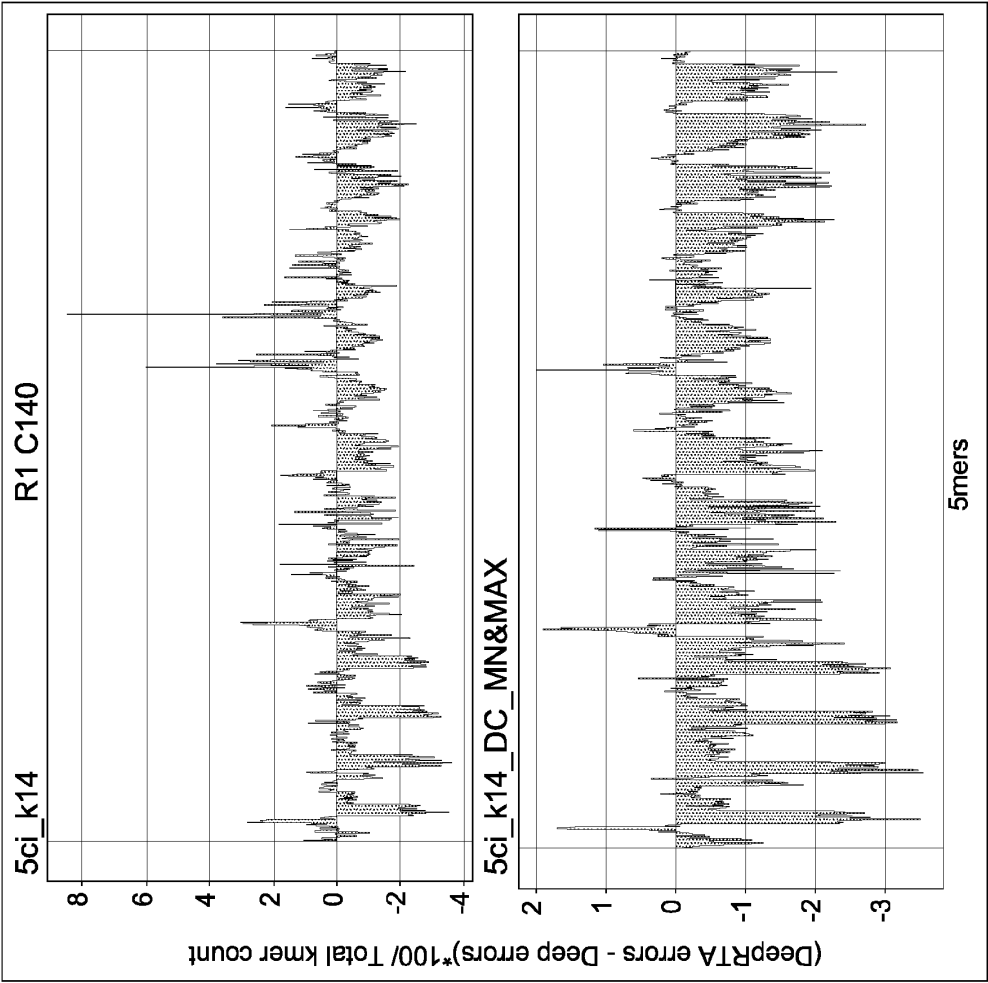


Figure 50

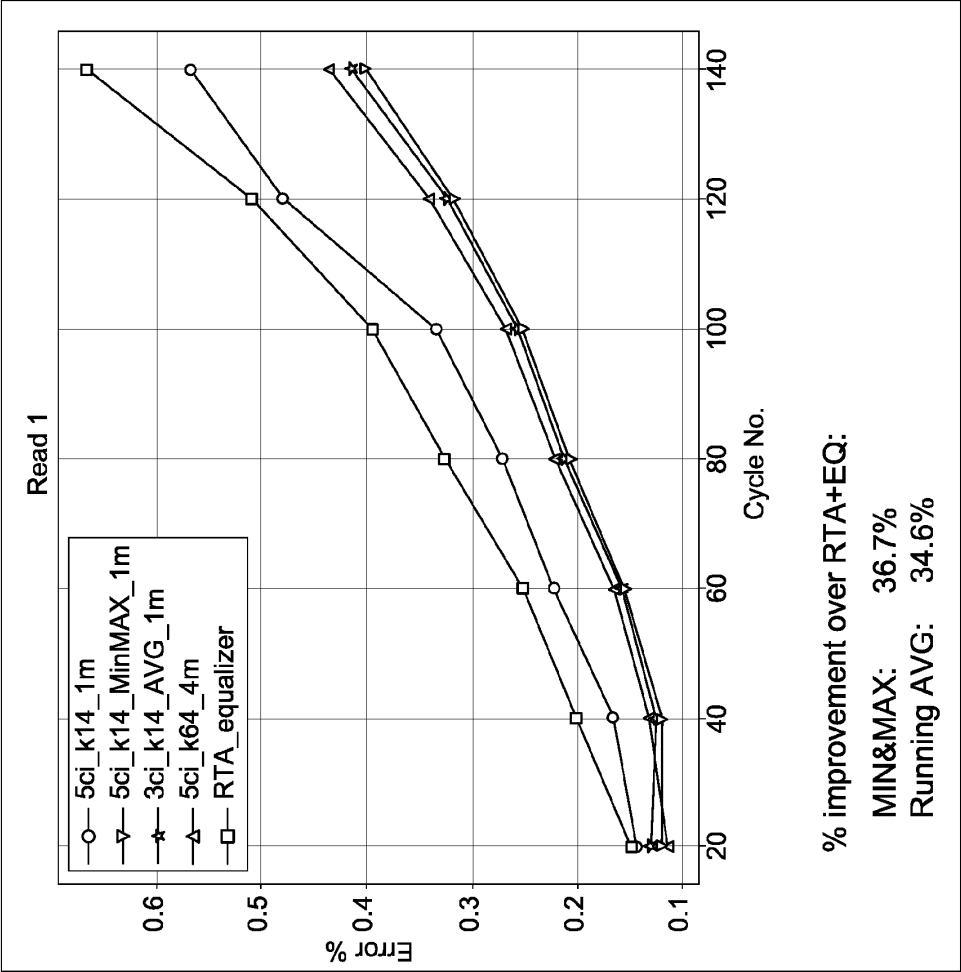


Figure 51

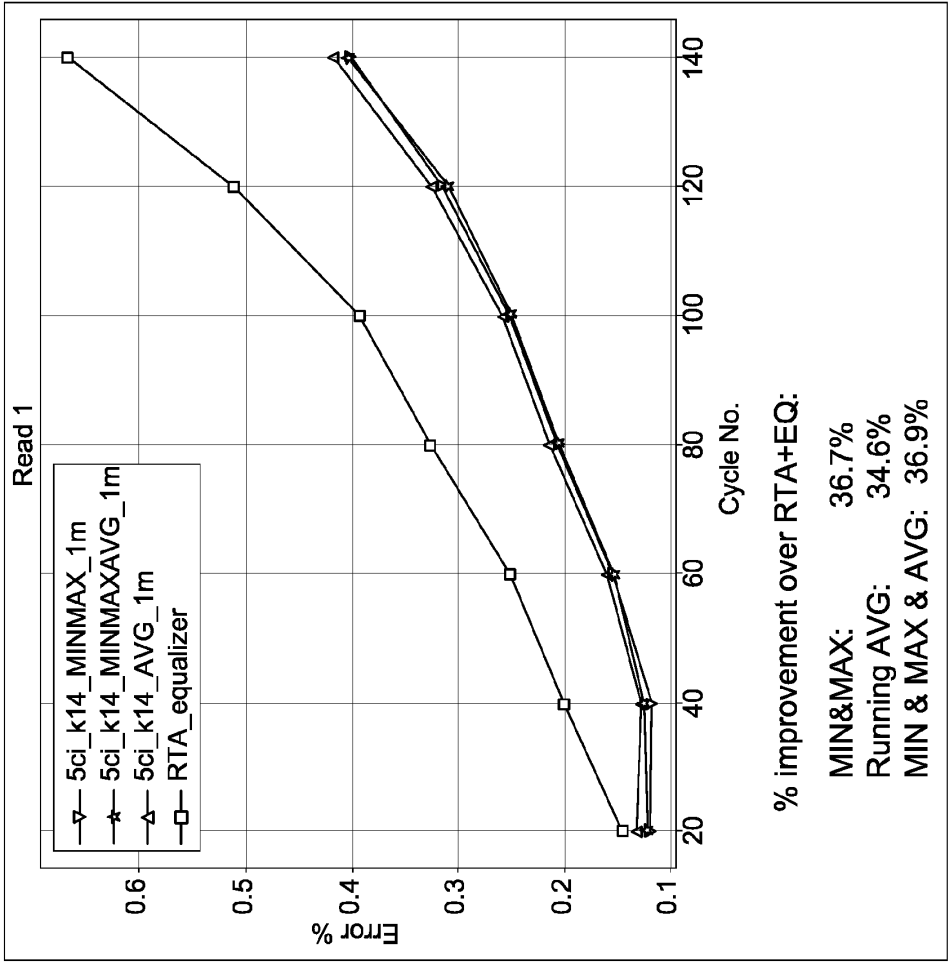


Figure 52

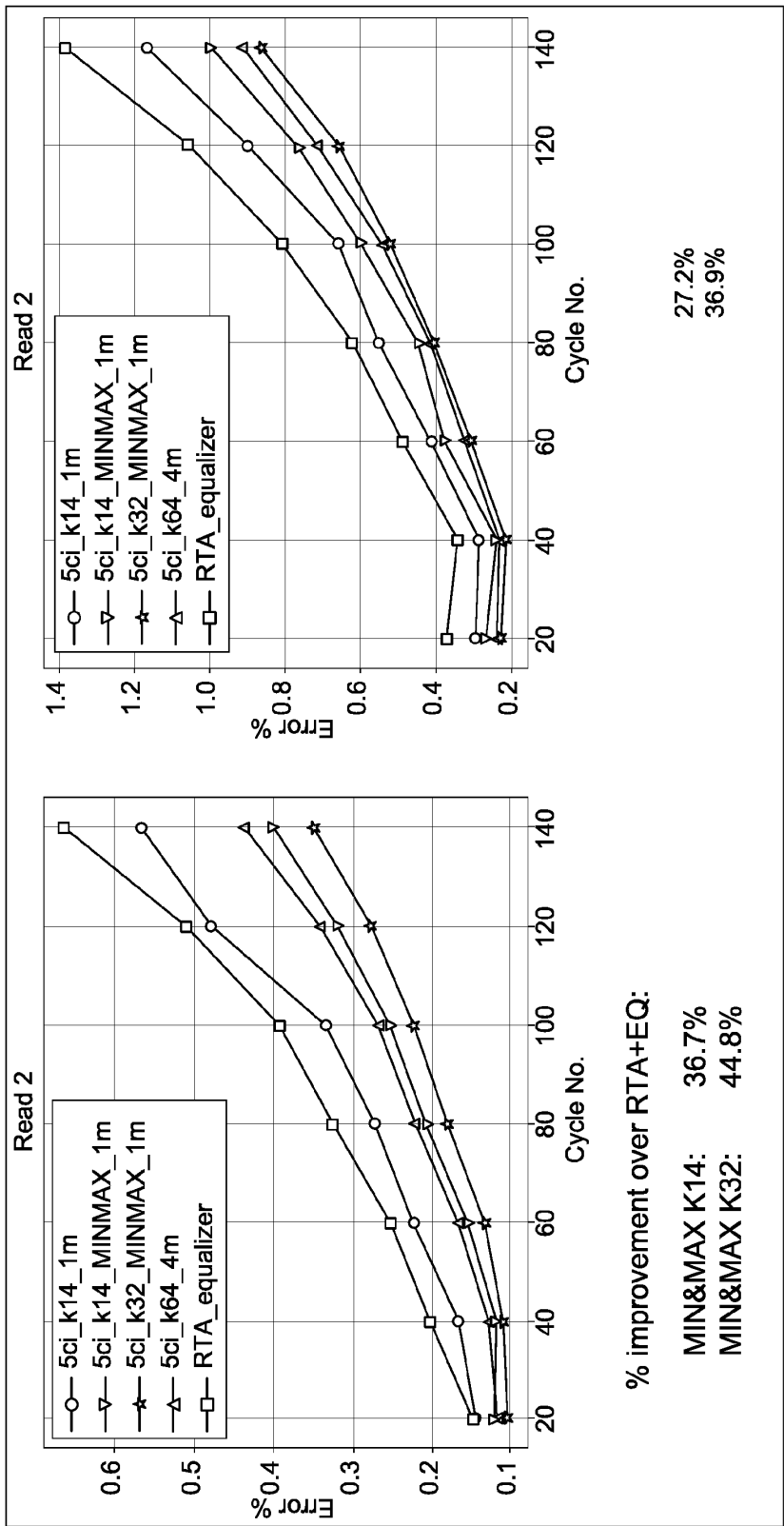


Figure 53

Using Per-Cluster Information

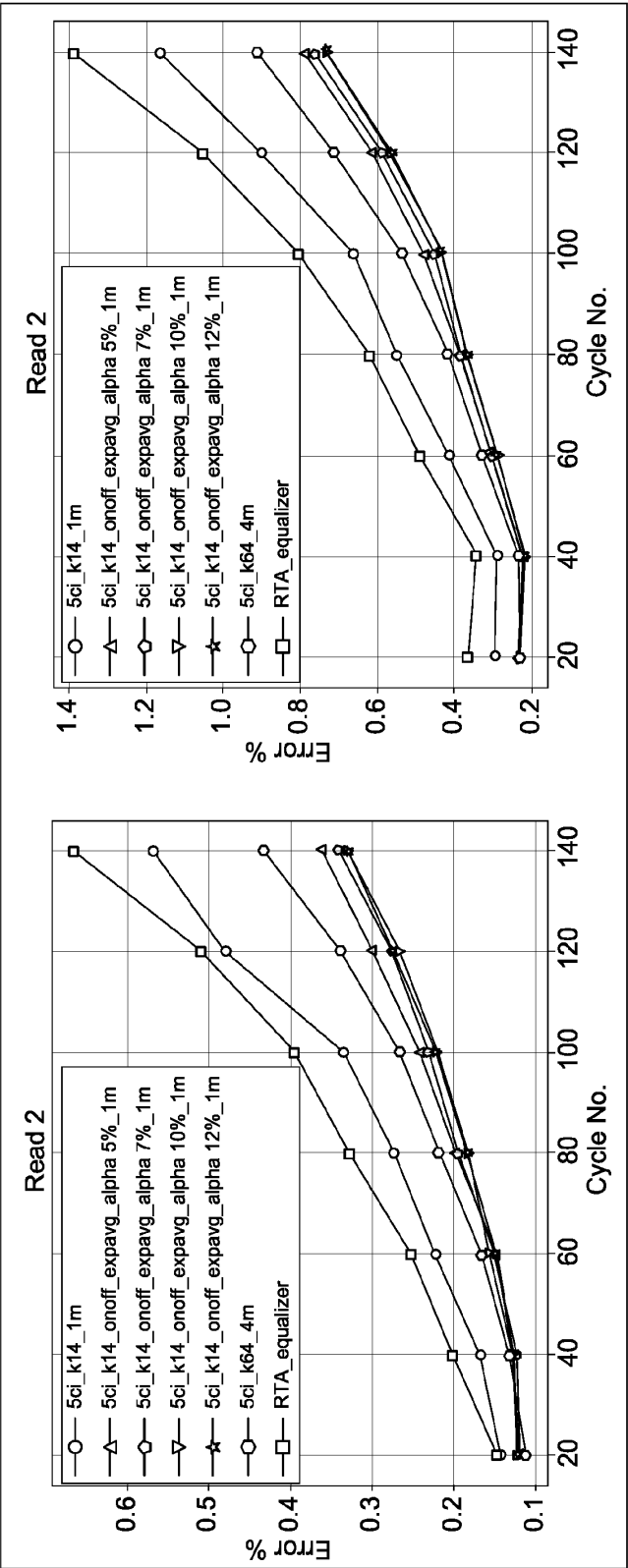


Figure 54

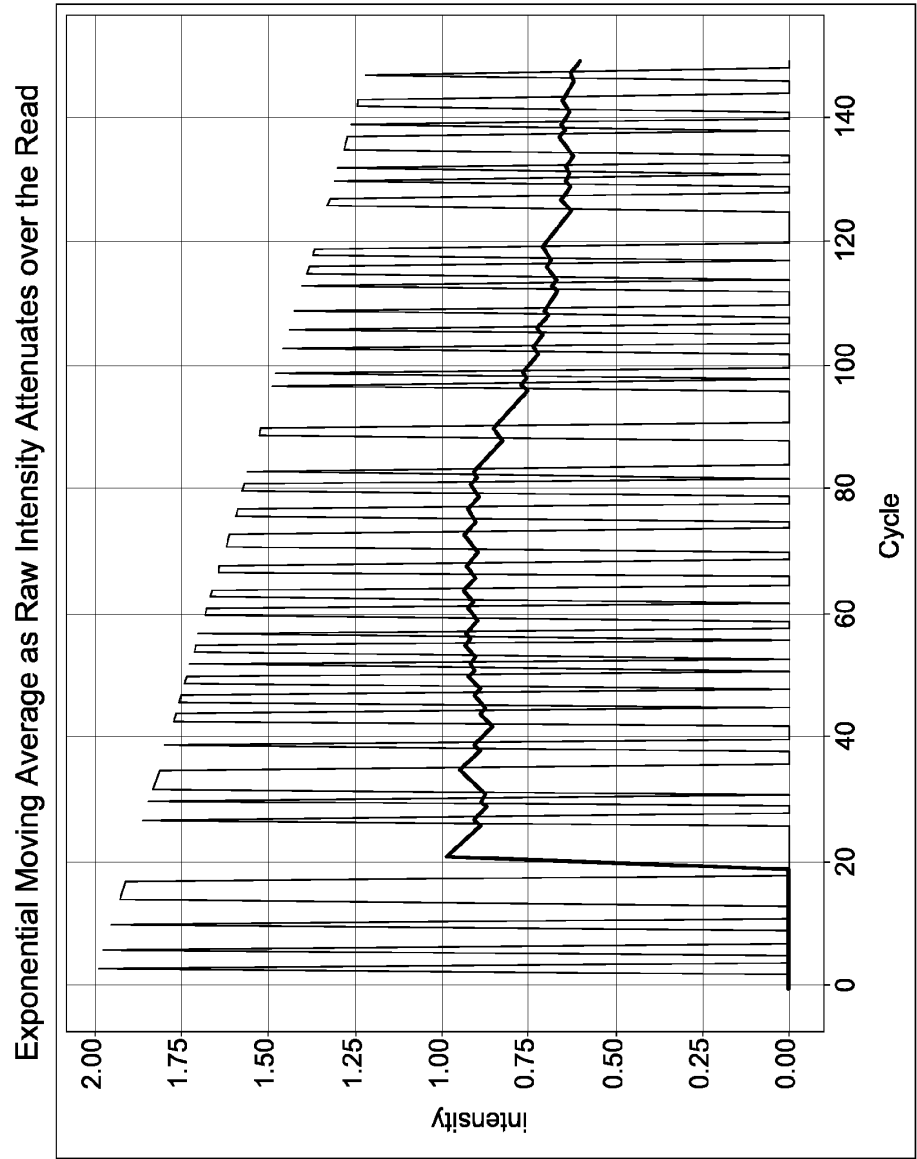


Figure 55

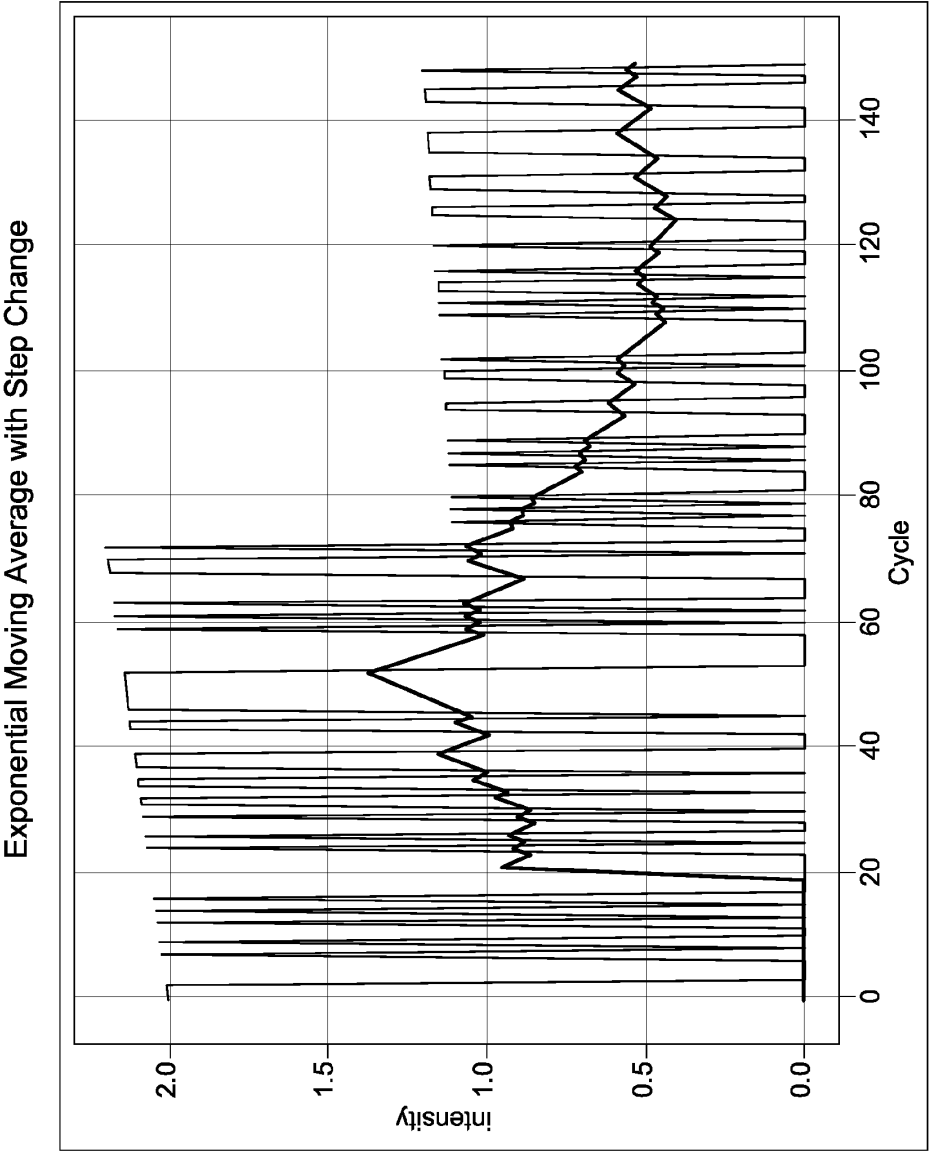


Figure 56

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