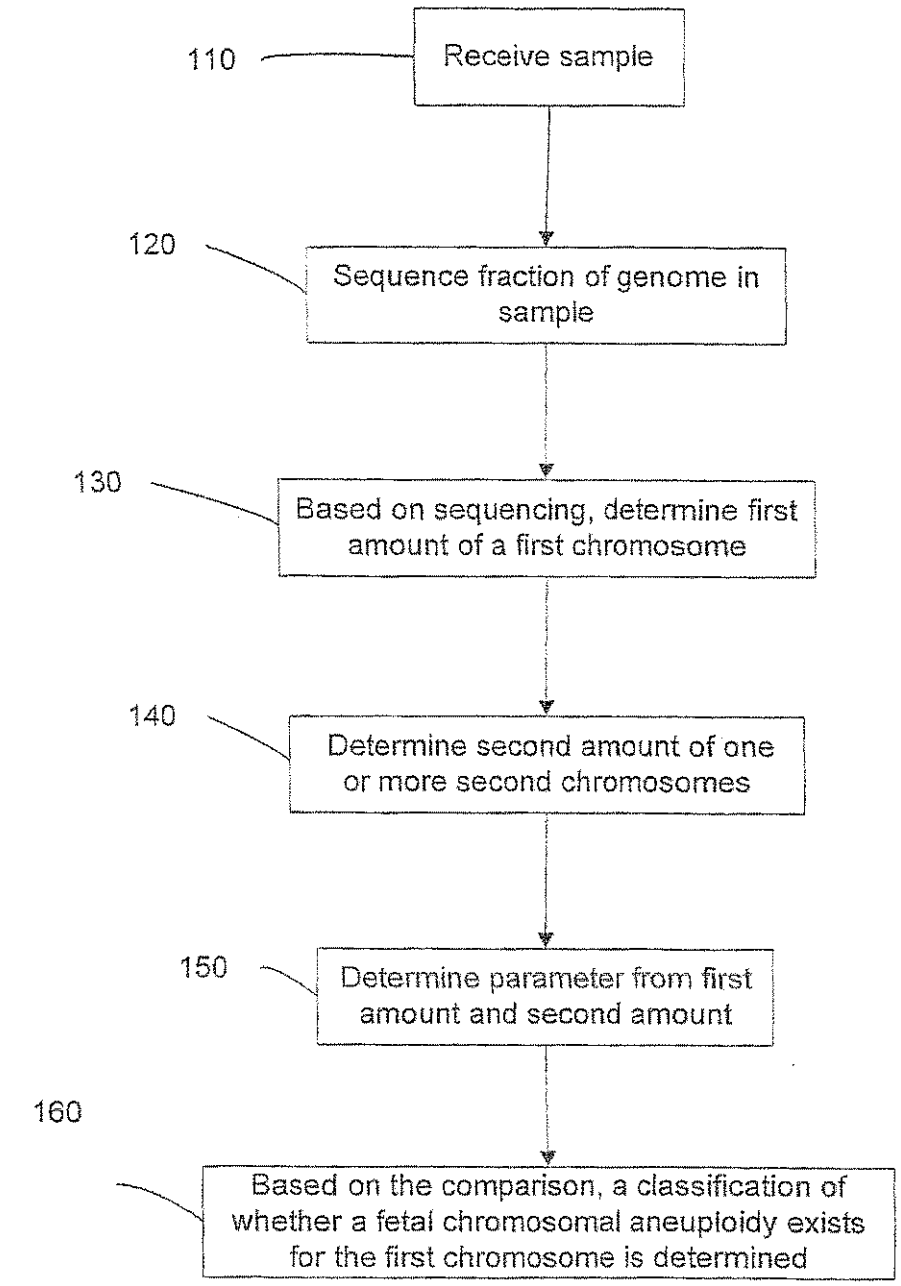
110
Receive sample
120
Sequence fraction of genome in sample
130
Based on sequencing, determine first amount of a first chromosome
140
Determine second amount of one or more second chromosomes
150
Determine parameter from first amount and second amount
160
Based on the comparison, a classification of whether a fetal chromosomal aneuploidy exists for the first chromosome is determined
100

FIG. 1

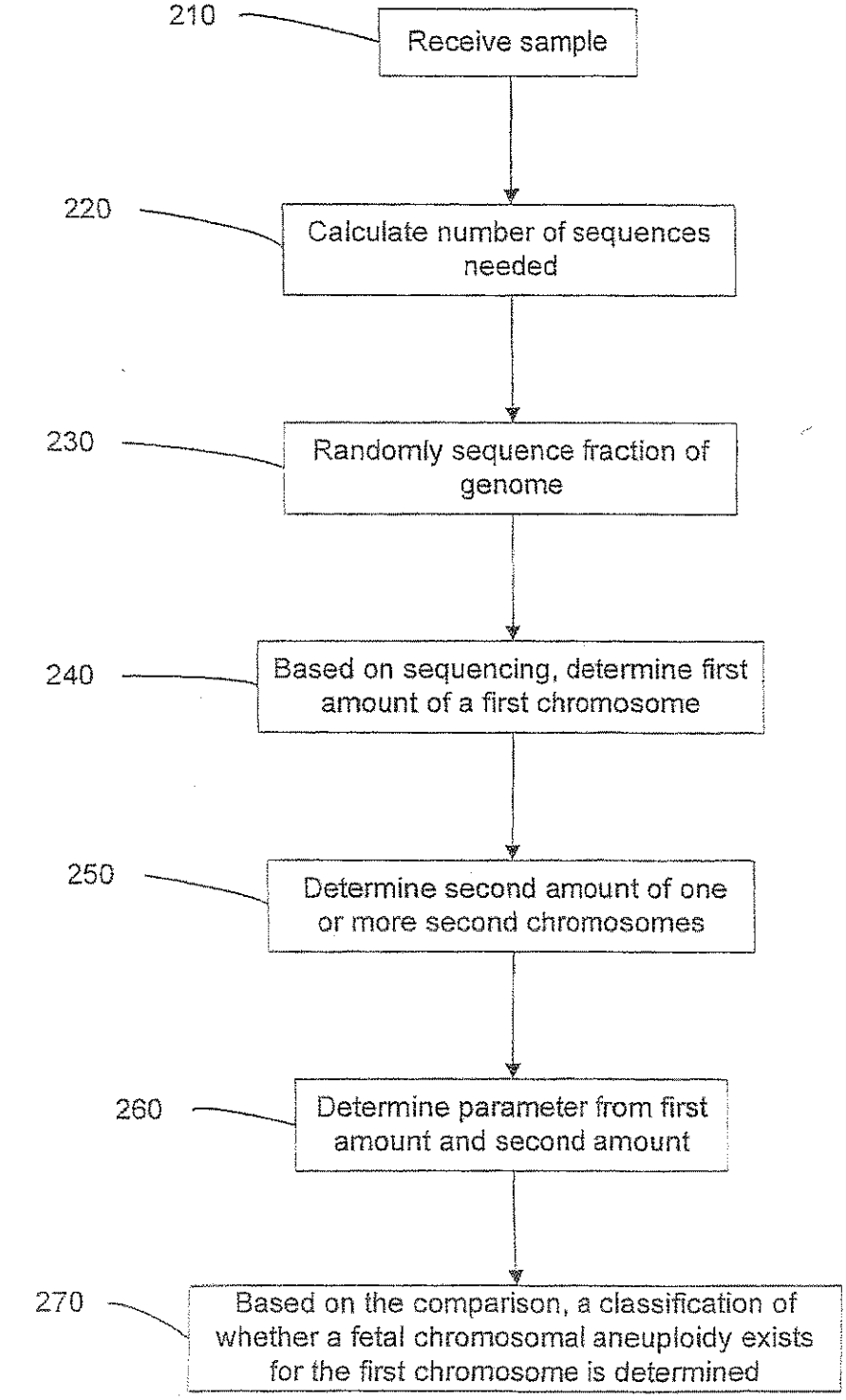
210
Receive sample
220
Calculate number of sequences needed
230
Randomly sequence fraction of genome
240
Based on sequencing, determine first amount of a first chromosome
250
Determine second amount of one or more second chromosomes
260
Determine parameter from first amount and second amount
270
Based on the comparison, a classification of whether a fetal chromosomal aneuploidy exists for the first chromosome is determined
200

FIG. 2

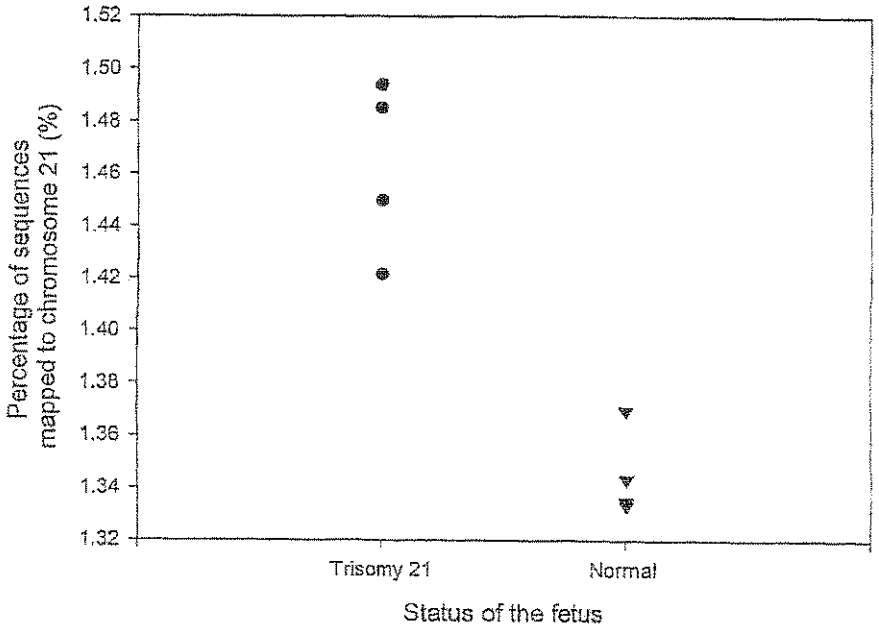
1.52
1.50
1.48
1.46
1.44
1.42
1.40
1.38
1.36
1.34
1.32
Percentage of sequences mapped to chromosome 21 (%)
Trisomy 21
Normal
Status of the fetus

FIG. 3A

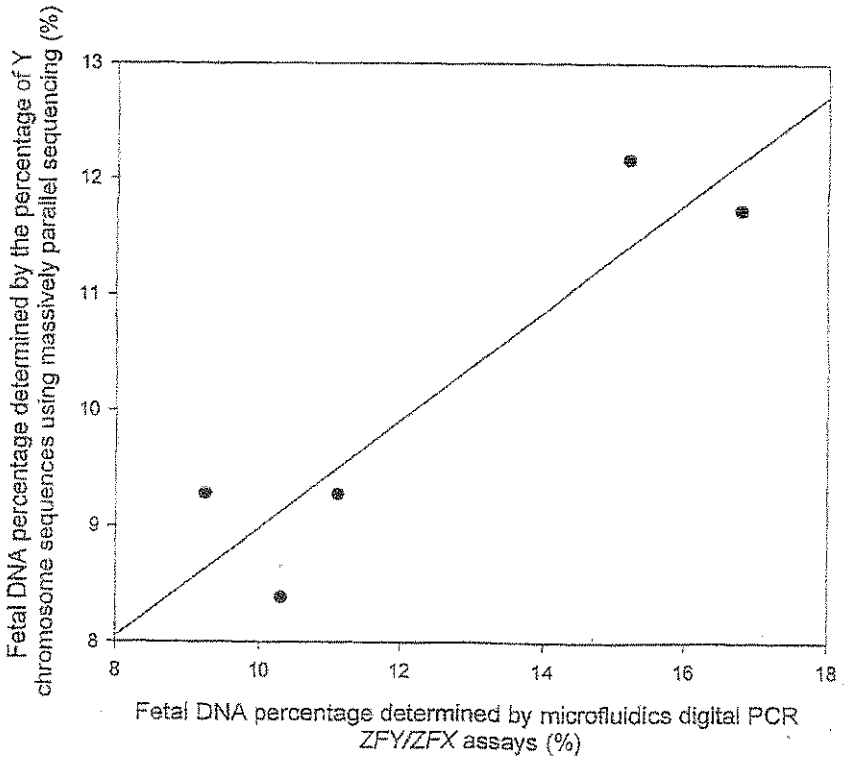
13
12
11
10
9
8
8
10
12
14
16
18
Fetal DNA percentage determined by the percentage of Y chromosome sequences using massively parallel sequencing (%)
Fetal DNA percentage determined by microfluidics digital PCR *ZFY/ZFX* assays (%)

FIG. 3B

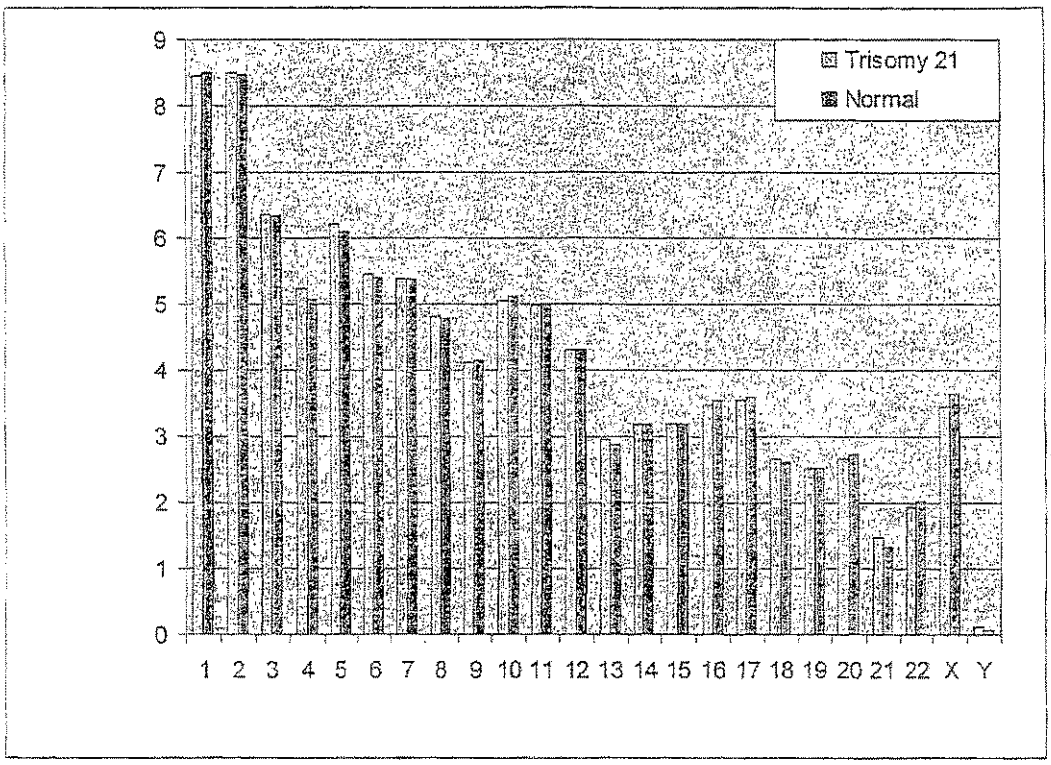
Trisomy 21
Normal
9
8
7
6
5
4
3
2
1
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

FIG. 4A

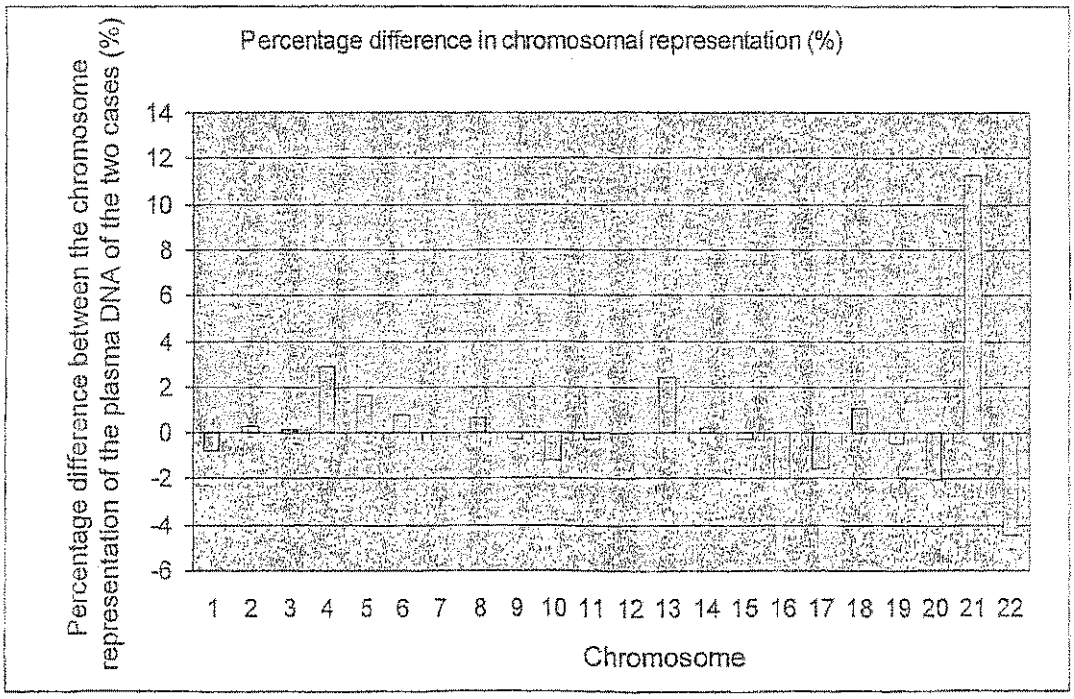
Percentage difference in chromosomal representation (%)
Percentage difference between the chromosome representation of the plasma DNA of the two cases (%)
14
12
10
8
6
4
2
0
-2
-4
-6
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Chromosome

FIG. 4B

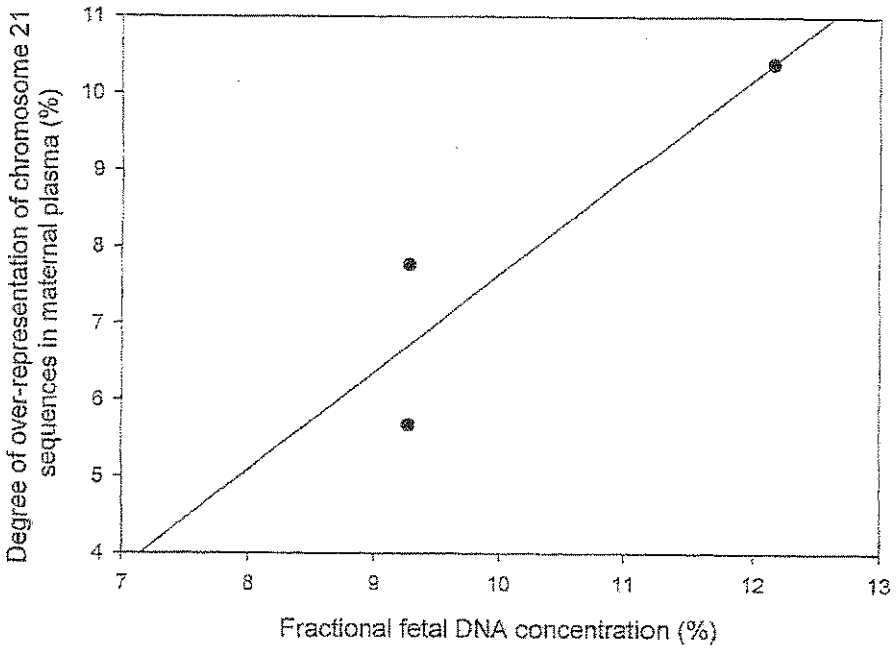
Degree of over-representation of chromosome 21 sequences in maternal plasma (%)
11
10
9
8
7
6
5
4
7
8
9
10
11
12
13
Fractional fetal DNA concentration (%)

FIG. 5

Sample	Total no. of sequenced tags	Total no. of sequenced basepairs	Proportion of the human genome (%)	U0 count	U0 count / total count (%)	No. of U0 sequenced basepairs	U0 Proportion of the human genome (%)
Sample 1 T21	1.12E+07	4.02E+08	13.4	1.93E+06	17.3	6.94E+07	2.31
Sample 2 T21	1.04E+07	3.73E+08	12.4	1.80E+06	17.4	6.50E+07	2.17
Sample 3 T21	8.90E+06	3.20E+08	10.7	2.09E+06	23.4	7.51E+07	2.50
Sample 4 T21	1.02E+07	3.69E+08	12.3	2.23E+06	21.7	8.02E+07	2.67
Sample 5 euploid	1.06E+07	3.83E+08	12.8	2.12E+06	19.9	7.62E+07	2.54
Sample 6 euploid	9.58E+06	3.45E+08	11.5	1.91E+06	20.0	6.88E+07	2.29
Sample 7 euploid	9.55E+06	3.44E+08	11.5	2.01E+06	21.0	7.22E+07	2.41
Sample 8 euploid	9.09E+06	3.27E+08	10.9	2.09E+06	23.0	7.53E+07	2.51

FIG. 6

	Euploid				T21 (5%)				T21 (10%)				T21 (20%)			
No. of sequences in each subset	*Mean*	*SD*	*5 percentile*	*95 percentile*	*Mean*	*5 percentile*	*95 percentile*	*Successful Differentiation (vs euploid)?*	*Mean*	*5 percentile*	*95 percentile*	*Successful Differentiation (vs euploid)?*	*Mean*	*5 percentile*	*95 percentile*	*Successful Differentiation (vs euploid)?*
60,000	1.322%	0.036%	1.260%	1.385%	1.355%	1.283%	1.428%	*No*	1.368%	1.316%	1.461%	*No*	1.454%	1.382%	1.527%	*No*
120,000	1.322%	0.022%	1.277%	1.367%	1.355%	1.311%	1.400%	*No*	1.368%	1.344%	1.433%	*No*	1.454%	1.410%	1.499%	*Yes*
180,000	1.322%	0.016%	1.291%	1.353%	1.355%	1.324%	1.386%	*No*	1.368%	1.357%	1.420%	*Yes*	1.454%	1.423%	1.486%	*Yes*
240,000	1.322%	0.013%	1.295%	1.348%	1.355%	1.328%	1.382%	*No*	1.368%	1.361%	1.415%	*Yes*	1.454%	1.427%	1.481%	*Yes*
300,000	1.322%	0.011%	1.301%	1.344%	1.355%	1.334%	1.377%	*No*	1.368%	1.367%	1.410%	*Yes*	1.454%	1.433%	1.476%	*Yes*
360,000	1.322%	0.010%	1.302%	1.343%	1.355%	1.335%	1.376%	*No*	1.368%	1.368%	1.409%	*Yes*	1.454%	1.434%	1.475%	*Yes*
420,000	1.322%	0.095%	1.303%	1.341%	1.355%	1.336%	1.374%	*No*	1.368%	1.369%	1.407%	*Yes*	1.454%	1.435%	1.473%	*Yes*
480,000	1.322%	0.009%	1.305%	1.339%	1.355%	1.338%	1.372%	*No*	1.368%	1.371%	1.405%	*Yes*	1.454%	1.437%	1.471%	*Yes*
540,000	1.322%	0.008%	1.306%	1.339%	1.355%	1.339%	1.372%	*Yes*	1.368%	1.372%	1.405%	*Yes*	1.454%	1.438%	1.471%	*Yes*

FIG. 7

Sequenced tag order	Sample 1 T21	Sample 2 T21	Sample 3 T21	Sample 4 T21	Sample 5 Euploid	Sample 6 Euploid	Sample 7 Euploid	Sample 8 Euploid
1	9796394	9798087	9798123	9795700	9797841	9795972	9796536	9795601
2	9797424	9798402	9798250	9797860	9798176	9796549	9796863	9797404
3	9797438	9798708	9798715	9797864	9798835	9797359	9798161	9798117
4	9798112	9799733	9799467	9798106	9800315	9797418	9 798401	9798175
5	9798394	9799852	9799730	9799209	9800385	9797446	9798722	9798387
6	9798729	9800362	9799788	9799440	9800554	9797860	9799752	9798816
7	9798768	9800914	9799834	9799440	9800820	9798062	9800317	9799732
8	9798816	9801528	9800332	9799741	9800829	9798135	9800800	9800144
9	9799421	9801779	9800869	9799812	9800832	9798707	9801380	9800421
10	9799464	9803801	9800881	9799833	9800866	9798715	9801699	9800827

FIG. 8A

Sequenced tag order	Sample 1 T21	Sample 2 T21	Sample 3 T21	Sample 4 T21	Sample 5 Euploid	Sample 6 Euploid	Sample 7 Euploid	Sample 8 Euploid
1	14469232	14510976	14510792	14510867	14434681	14510711	14512069	14510996
2	14503781	14511307	14510807	14511312	14506660	14510835	14512407	14522947
3	14510805	14511512	14510886	14511983	14511219	14511308	14522879	14530478
4	14510824	14511755	14511816	14522914	14511328	14511354	14609732	14565255
5	14510965	14511774	14512410	14522978	14511377	14511703	14628248	14609733
6	14511369	14512067	14522944	14523028	14511432	14511703	14675246	14628261
7	14511702	14512190	14523047	14565245	14511597	14512184	14675250	14668784
8	14511738	14522891	14564769	14628257	14511755	14512204	14680184	14680163
9	14523000	14539630	14565205	14635374	14512204	14524806	14692539	14689547
10	14524823	14541260	14565251	14665101	14512204	14565230	14694114	14689592

FIG. 8B

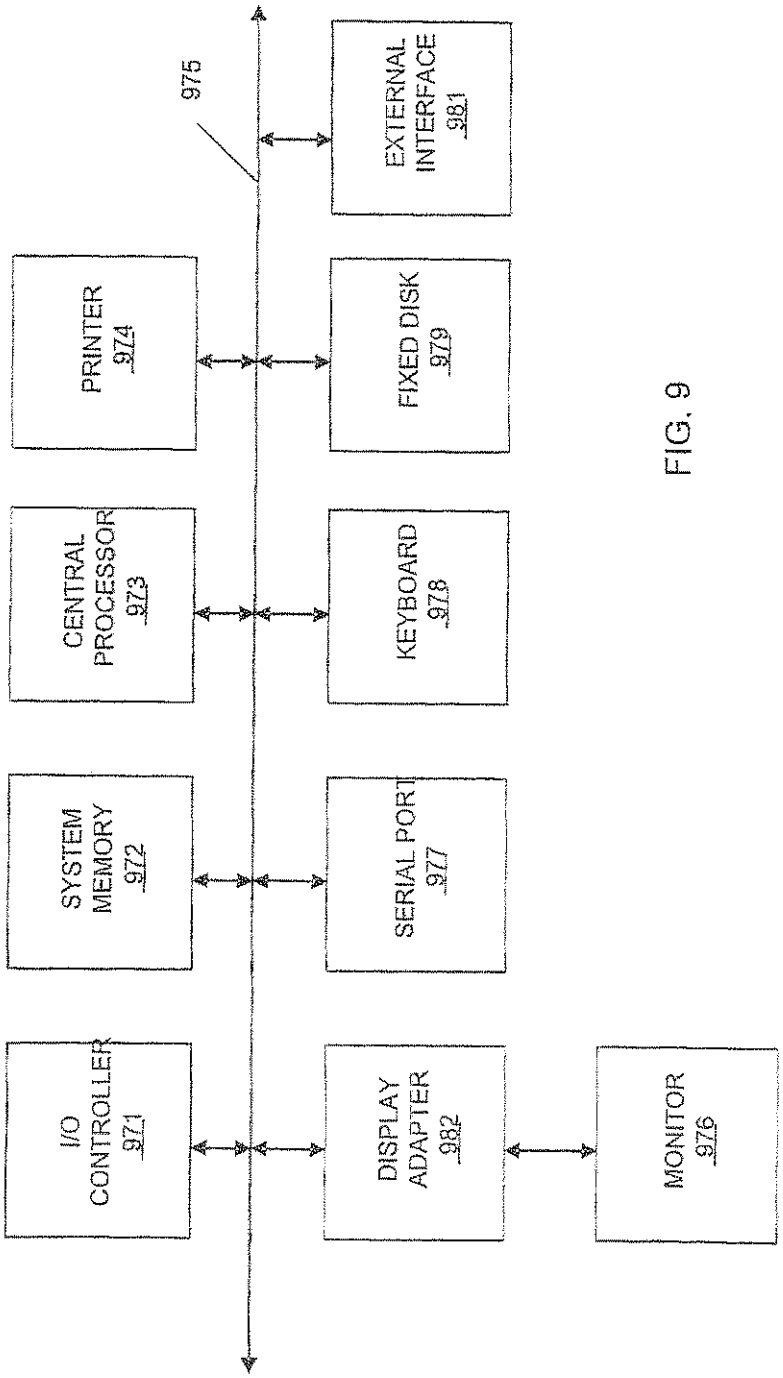
975
I/O CONTROLLER 971
SYSTEM MEMORY 972
CENTRAL PROCESSOR 973
PRINTER 974
DISPLAY ADAPTER 982
SERIAL PORT 977
KEYBOARD 978
FIXED DISK 979
MONITOR 976
EXTERNAL INTERFACE 981

FIG. 9