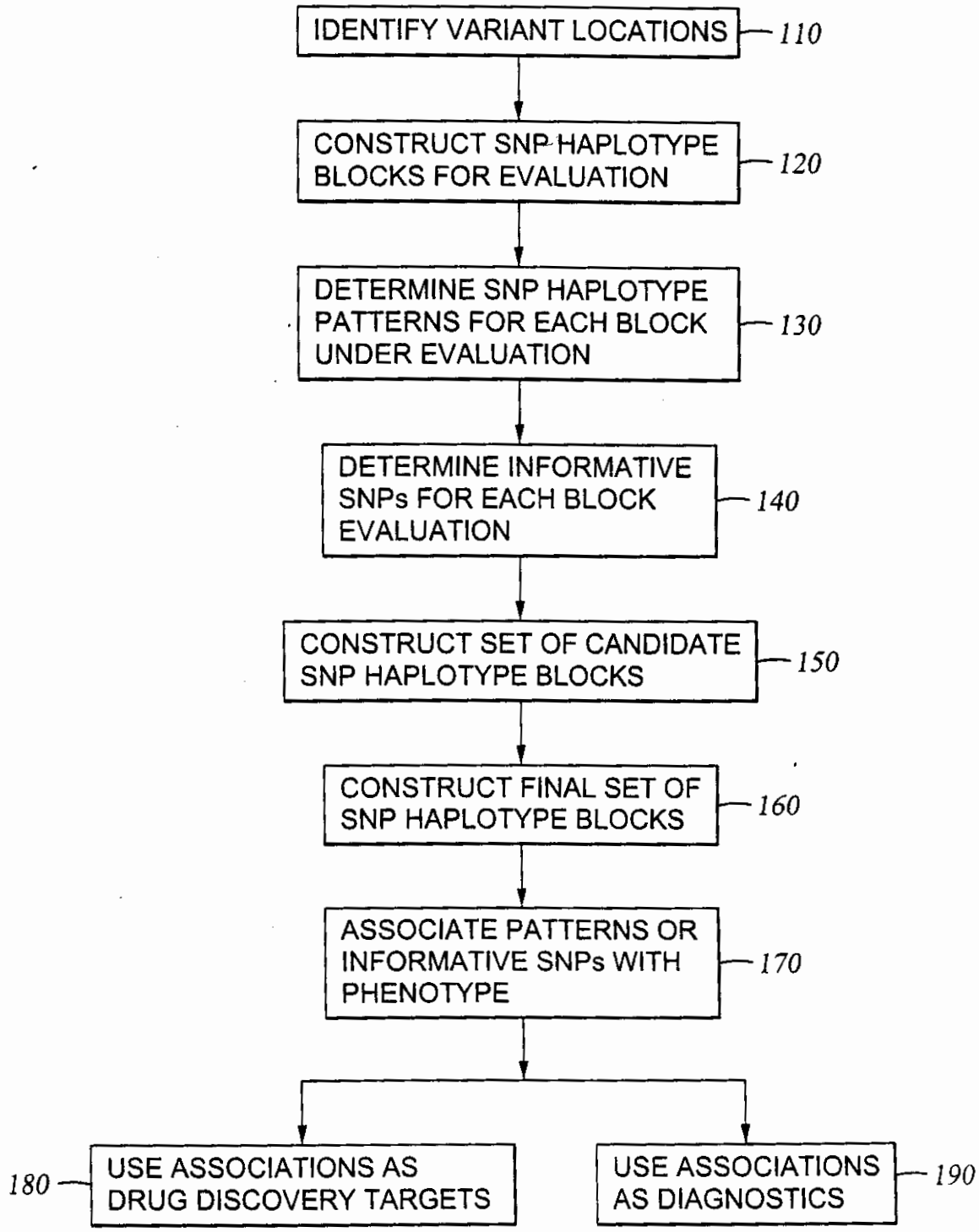

IDENTIFY VARIANT LOCATIONS
110
CONSTRUCT SNP HAPLOTYPE BLOCKS FOR EVALUATION
120
DETERMINE SNP HAPLOTYPE PATTERNS FOR EACH BLOCK UNDER EVALUATION
130
DETERMINE INFORMATIVE SNPs FOR EACH BLOCK EVALUATION
140
CONSTRUCT SET OF CANDIDATE SNP HAPLOTYPE BLOCKS
150
CONSTRUCT FINAL SET OF SNP HAPLOTYPE BLOCKS
160
ASSOCIATE PATTERNS OR INFORMATIVE SNPs WITH PHENOTYPE
170
180
USE ASSOCIATIONS AS DRUG DISCOVERY TARGETS
USE ASSOCIATIONS AS DIAGNOSTICS
190

Fig. 1

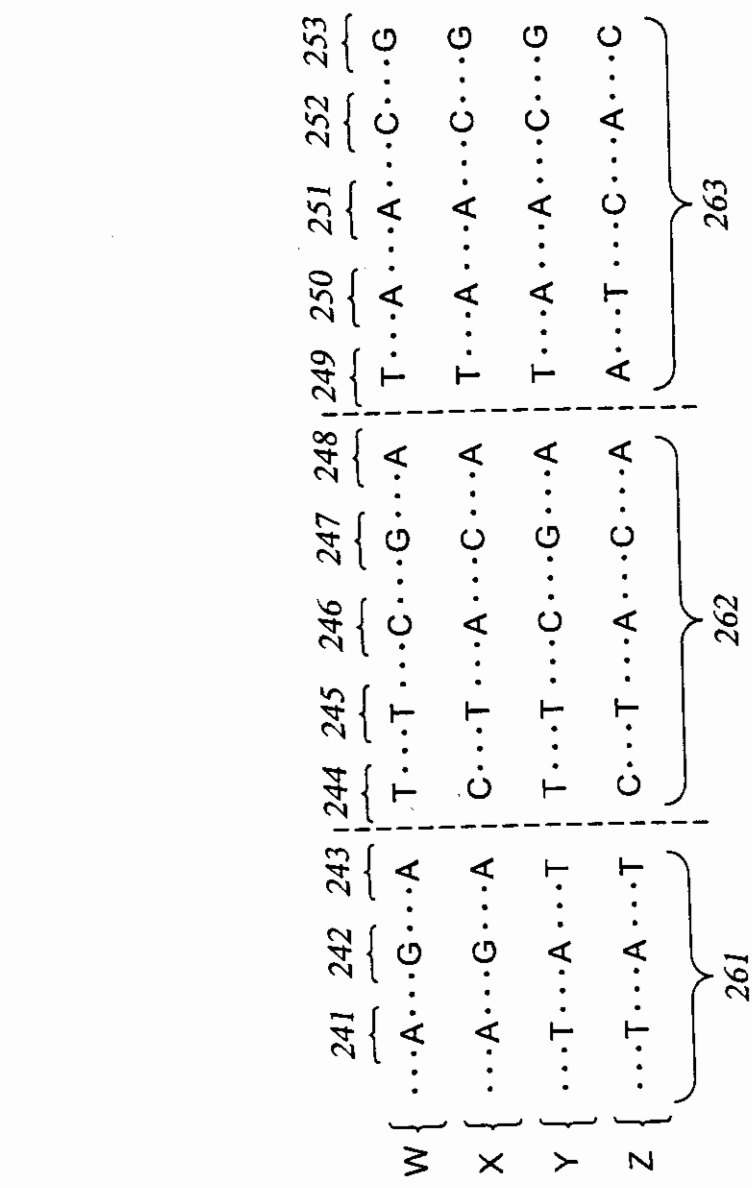

241 242 243 244 245 246 247 248 249 250 251 252 253
W ...A...G...A T...T...C...G...A T...A...A...C...G
X ...A...G...A C...T...A...C...A T...A...A...C...G
Y ...T...A...T T...T...C...G...A T...A...A...C...G
Z ...T...A...T C...T...A...C...A A...T...C...A...C
261
262
263

Fig. 2

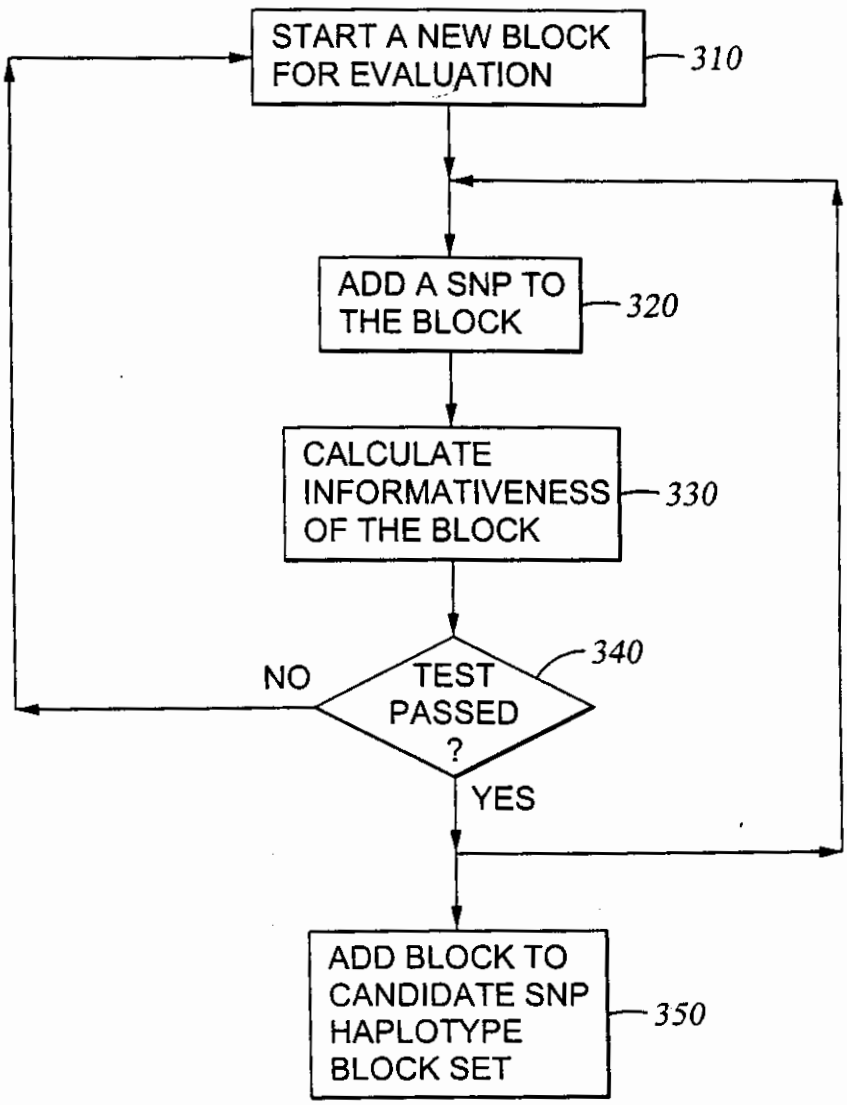

START A NEW BLOCK FOR EVALUATION
310
ADD A SNP TO THE BLOCK
320
CALCULATE INFORMATIVENESS OF THE BLOCK
330
TEST PASSED ?
340
NO
YES
ADD BLOCK TO CANDIDATE SNP HAPLOTYPE BLOCK SET
350

Fig. 3

Fig. 4

BLOCK EVALUATED	SNP POSITIONS 1	2	3	4	5	6	MEET INFORMATIVENESS ?
A	*1*						YES
B	*1*	*2*					YES
C	*1*	*2*	*3*				YES
D	*1*	*2*	*3*	*4*			NO
E		*2*					YES
F		*2*	*3*				YES
G		*2*	*3*	*4*			YES
H		*2*	*3*	*4*	*5*		NO
I			*3*				YES
J			*3*	*4*			NO
K				*4*			YES
L				*4*	*5*		YES
M				*4*	*5*	*6*	YES

BLOCKS SELECTED FOR CANDIDATE SET: A B C E F G I K L M

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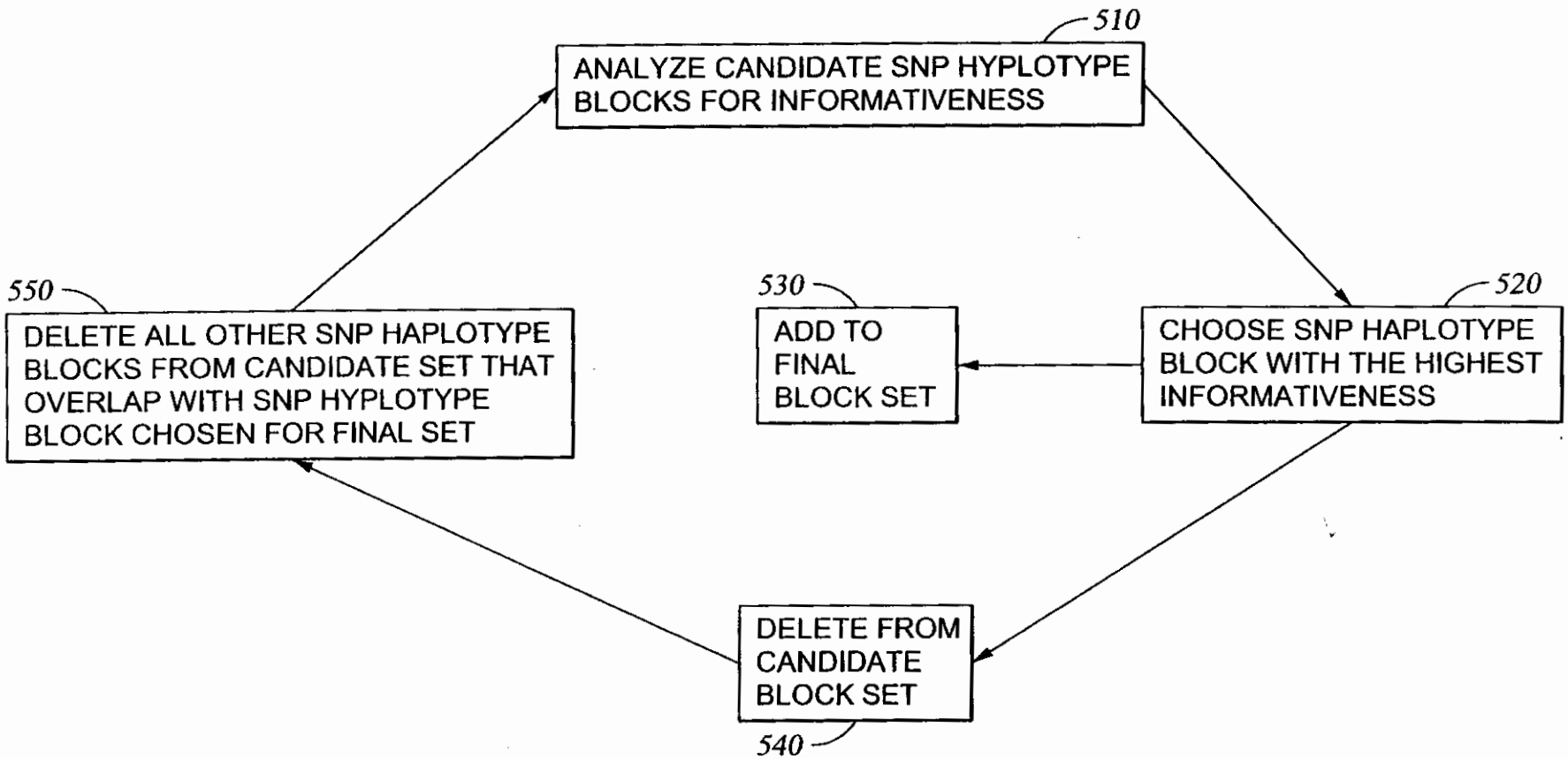
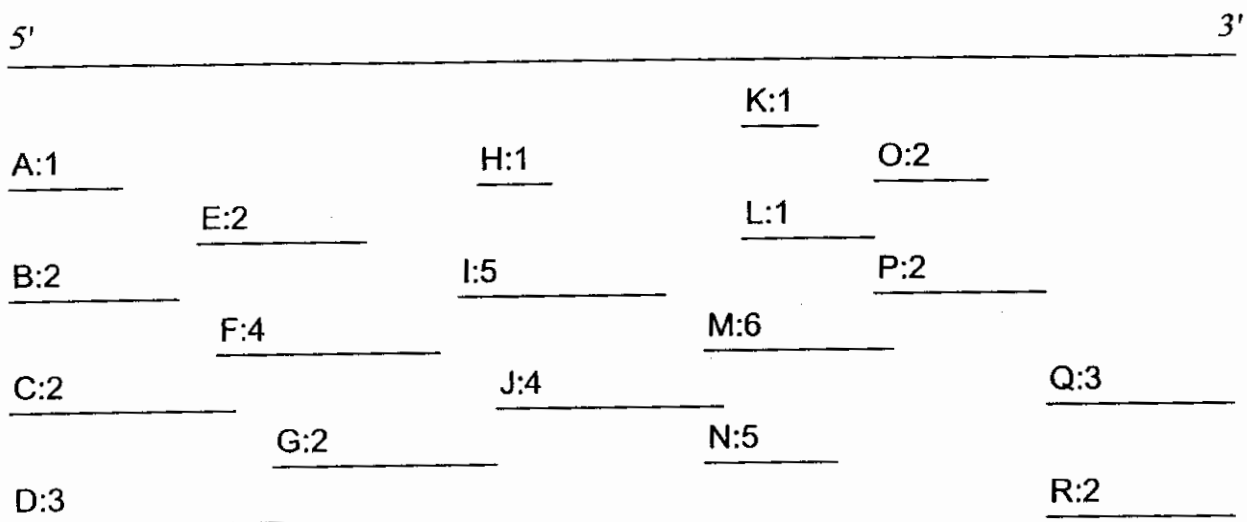


Fig. 5A

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M	DISCARD	J,N,K,L,O & P
I	DISCARD	H
F	DISCARD	E,G,C & D
Q	DISCARD	R
B	DISCARD	A

Fig. 5B

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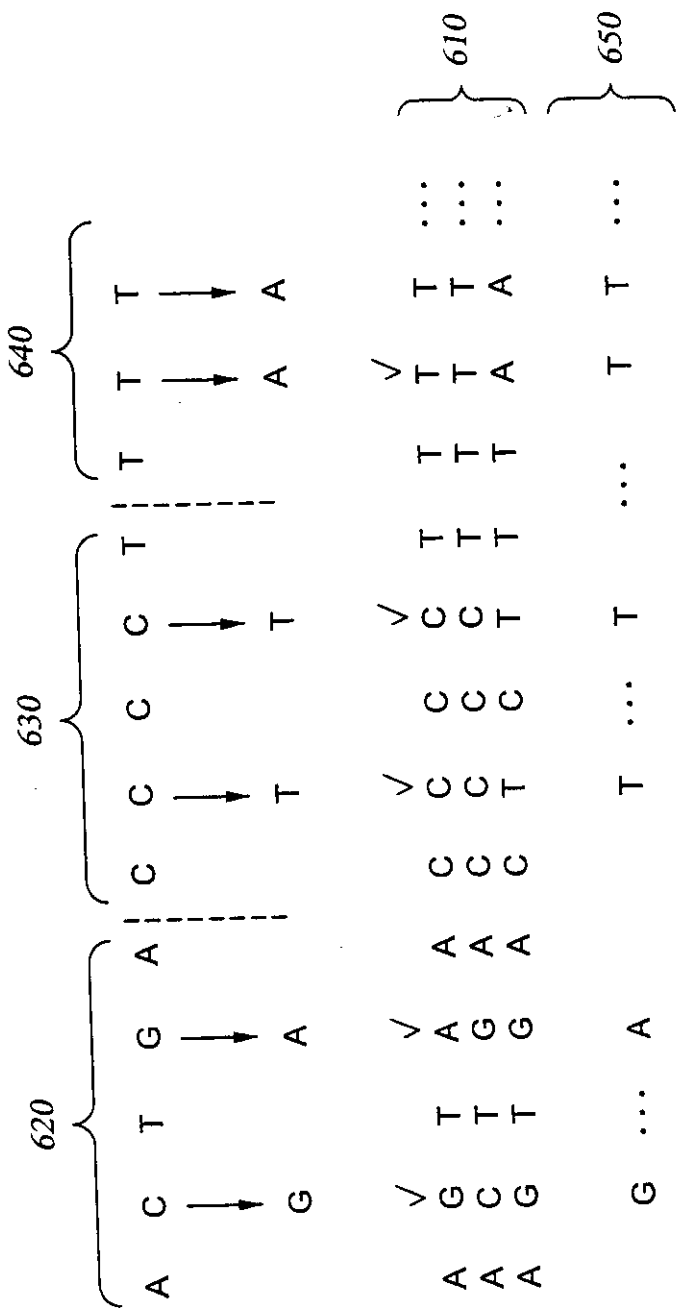


Fig. 6

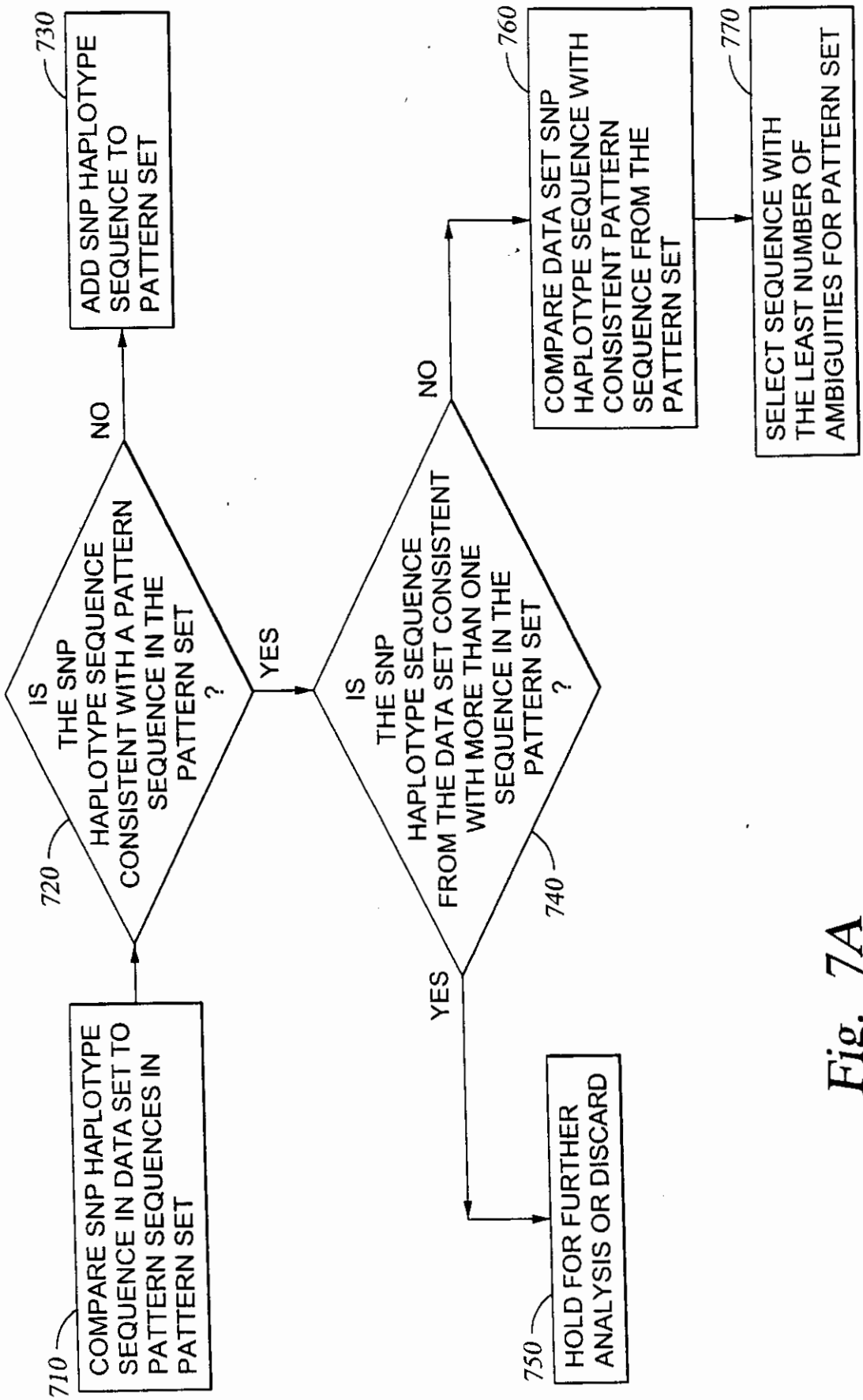

710
COMPARE SNP HAPLOTYPE SEQUENCE IN DATA SET TO PATTERN SEQUENCES IN PATTERN SET
720
IS THE SNP HAPLOTYPE SEQUENCE CONSISTENT WITH A PATTERN SEQUENCE IN THE PATTERN SET ?
NO
730
ADD SNP HAPLOTYPE SEQUENCE TO PATTERN SET
YES
740
IS THE SNP HAPLOTYPE SEQUENCE FROM THE DATA SET CONSISTENT WITH MORE THAN ONE SEQUENCE IN THE PATTERN SET ?
YES
750
HOLD FOR FURTHER ANALYSIS OR DISCARD
NO
760
COMPARE DATA SET SNP HAPLOTYPE SEQUENCE WITH CONSISTENT PATTERN SEQUENCE FROM THE PATTERN SET
770
SELECT SEQUENCE WITH THE LEAST NUMBER OF AMBIGUITIES FOR PATTERN SET

Fig. 7A

DATA SET SEQUENCE TO EVALUATE		PATTERN SET
1) TTCGA	COMPARE →	
NOT CONSISTENT, SO ADD		TTCGA
2) T?C??	COMPARE →	TTCGA
CONSISTENT WITH ONE PATTERN SET SEQUENCE, RETAIN SEQUENCE WITH FEWEST AMBIGUITIES		
3) C????	COMPARE →	TTCGA
NOT CONSISTENT, SO ADD		C????
4) CTACA	COMPARE →	TTCGA, C????
CONSISTENT WITH ONE PATTERN SET SEQUENCE, RETAIN SEQUENCE WITH FEWEST AMBIGUITIES		TTCGA, CTACA
5) ?T???	COMPARE →	TTCGA, CTACA
CONSISTENT WITH TWO PATTERN SET SEQUENCES, HOLD FOR FURTHER ANALYSIS		

Fig. 7B

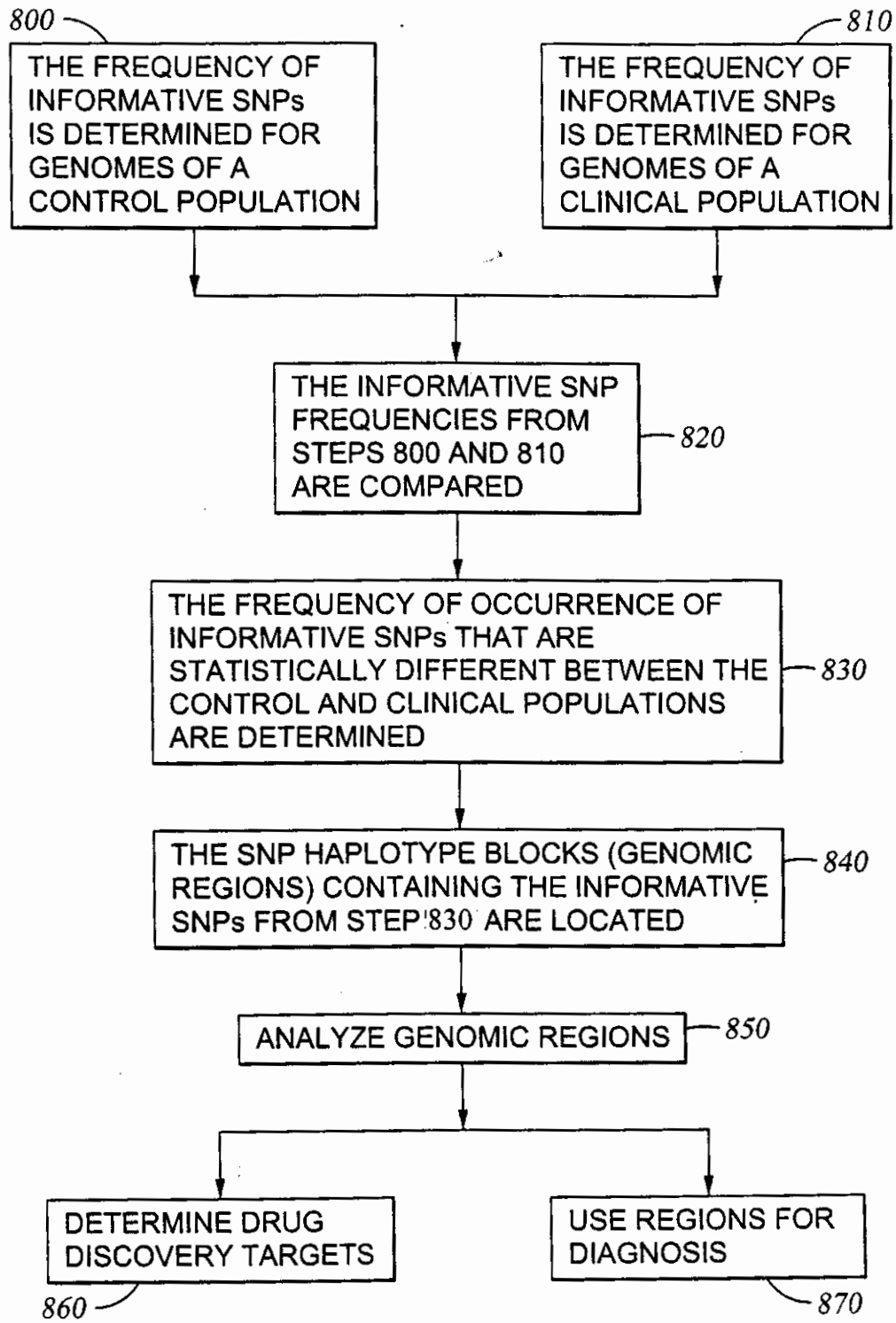
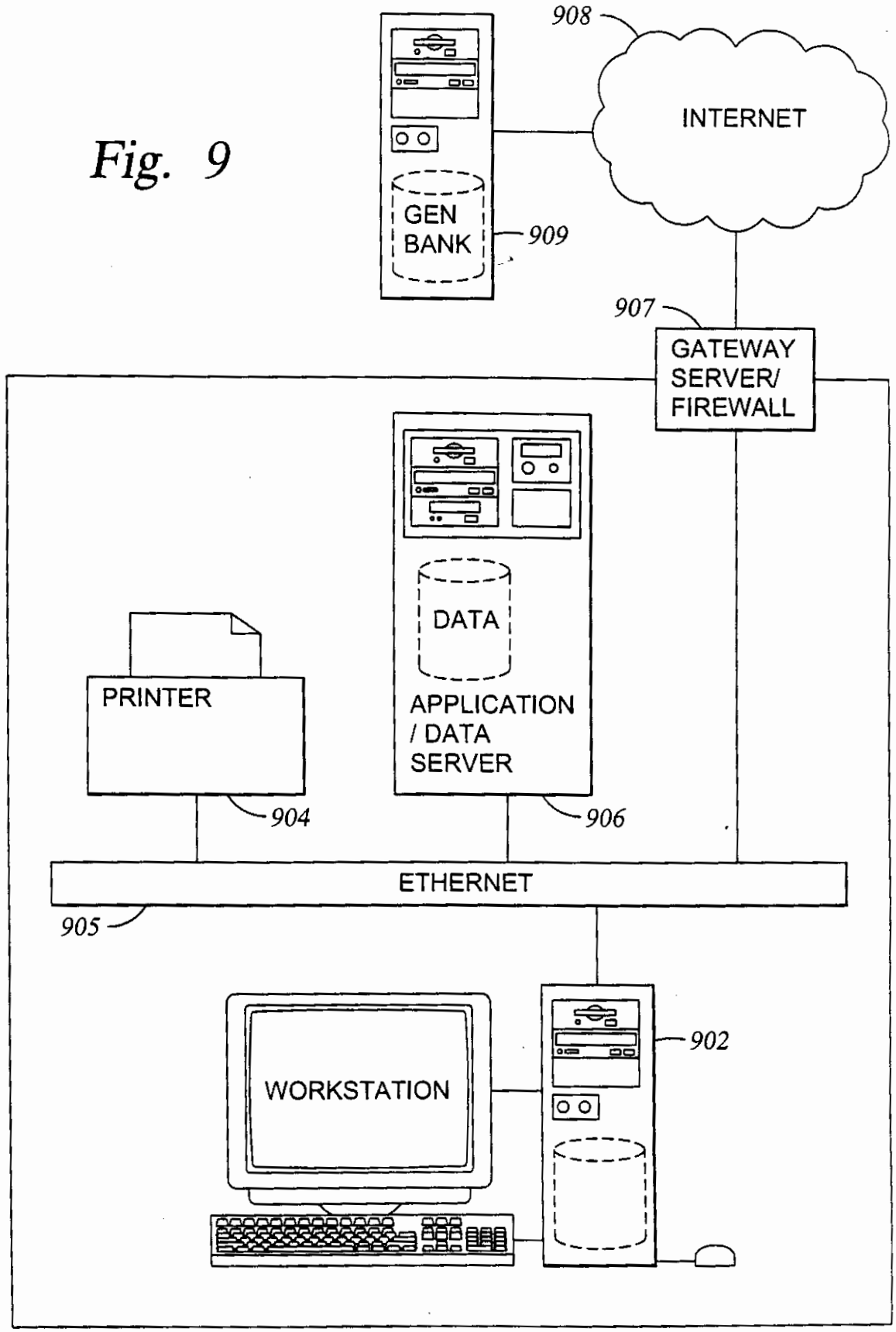

800
THE FREQUENCY OF INFORMATIVE SNPs IS DETERMINED FOR GENOMES OF A CONTROL POPULATION
810
THE FREQUENCY OF INFORMATIVE SNPs IS DETERMINED FOR GENOMES OF A CLINICAL POPULATION
THE INFORMATIVE SNP FREQUENCIES FROM STEPS 800 AND 810 ARE COMPARED
820
THE FREQUENCY OF OCCURRENCE OF INFORMATIVE SNPs THAT ARE STATISTICALLY DIFFERENT BETWEEN THE CONTROL AND CLINICAL POPULATIONS ARE DETERMINED
830
THE SNP HAPLOTYPE BLOCKS (GENOMIC REGIONS) CONTAINING THE INFORMATIVE SNPs FROM STEP 830 ARE LOCATED
840
ANALYZE GENOMIC REGIONS
850
DETERMINE DRUG DISCOVERY TARGETS
860
USE REGIONS FOR DIAGNOSIS
870

Fig. 8

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Fig. 9



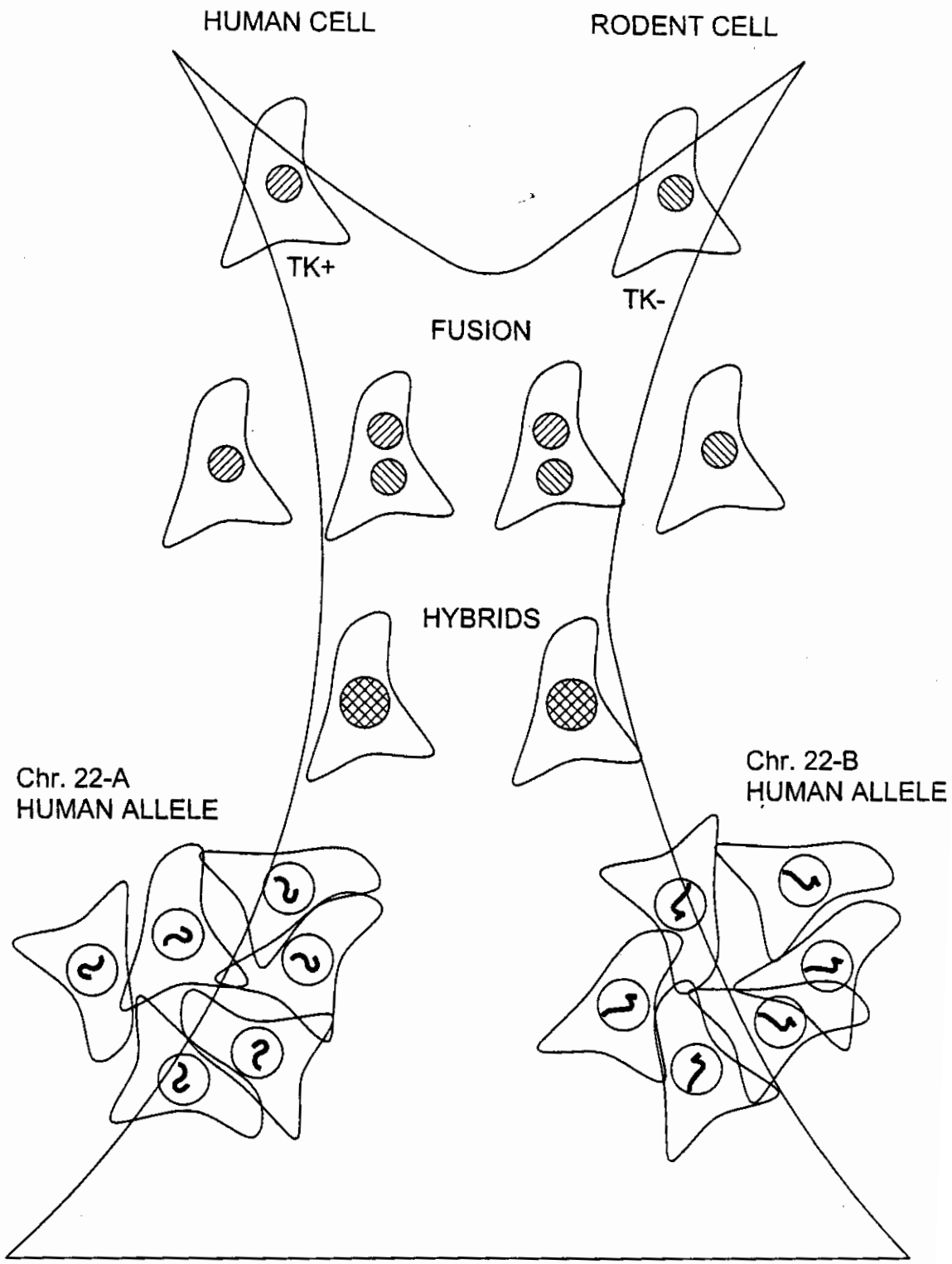

HUMAN CELL
RODENT CELL
TK+
TK-
FUSION
HYBRIDS
Chr. 22-A
HUMAN ALLELE
Chr. 22-B
HUMAN ALLELE

Fig. 10

Chr21 HuSNP MARKERS	HAMSTER	CPD17	HYBRID 1	HYBRID 2
WIAF-3497	NO SIGNAL	A	A	A
WIAF-3498	NO SIGNAL	AB	A	B
WIAF-599	NO SIGNAL	A	A	A
WIAF-3562	NO SIGNAL	NO SIGNAL	A	B
WIAF-559	NO SIGNAL	AB	B	A
WIAF-4546	NO SIGNAL	AB	B	A
WIAF-3508	NO SIGNAL	B	B	B
WIAF-624	NO SIGNAL	B	B	B
WIAF-1500	NO SIGNAL	A	A	A
WIAF-3496	NO SIGNAL	AB	A	B
WIAF-1943	NO SIGNAL	A	A	A
WIAF-2477	NO SIGNAL	NO SIGNAL	NO SIGNAL	A
WIAF-1538	NO SIGNAL	B	NO SIGNAL	B
WIAF-3479	NO SIGNAL	A	A	NO SIGNAL
WIAF-2436	NO SIGNAL	A	A	A
WIAF-1857	NO SIGNAL	AB	B	A
WIAF-899	NO SIGNAL	AB	A	B
WIAF-1682	NO SIGNAL	B	B	B
WIAF-2214	NO SIGNAL	AB	A	B
WIAF-2643	NO SIGNAL	NO SIGNAL	A	NO SIGNAL
WIAF-4514	NO SIGNAL	B	B	B

Fig. 11

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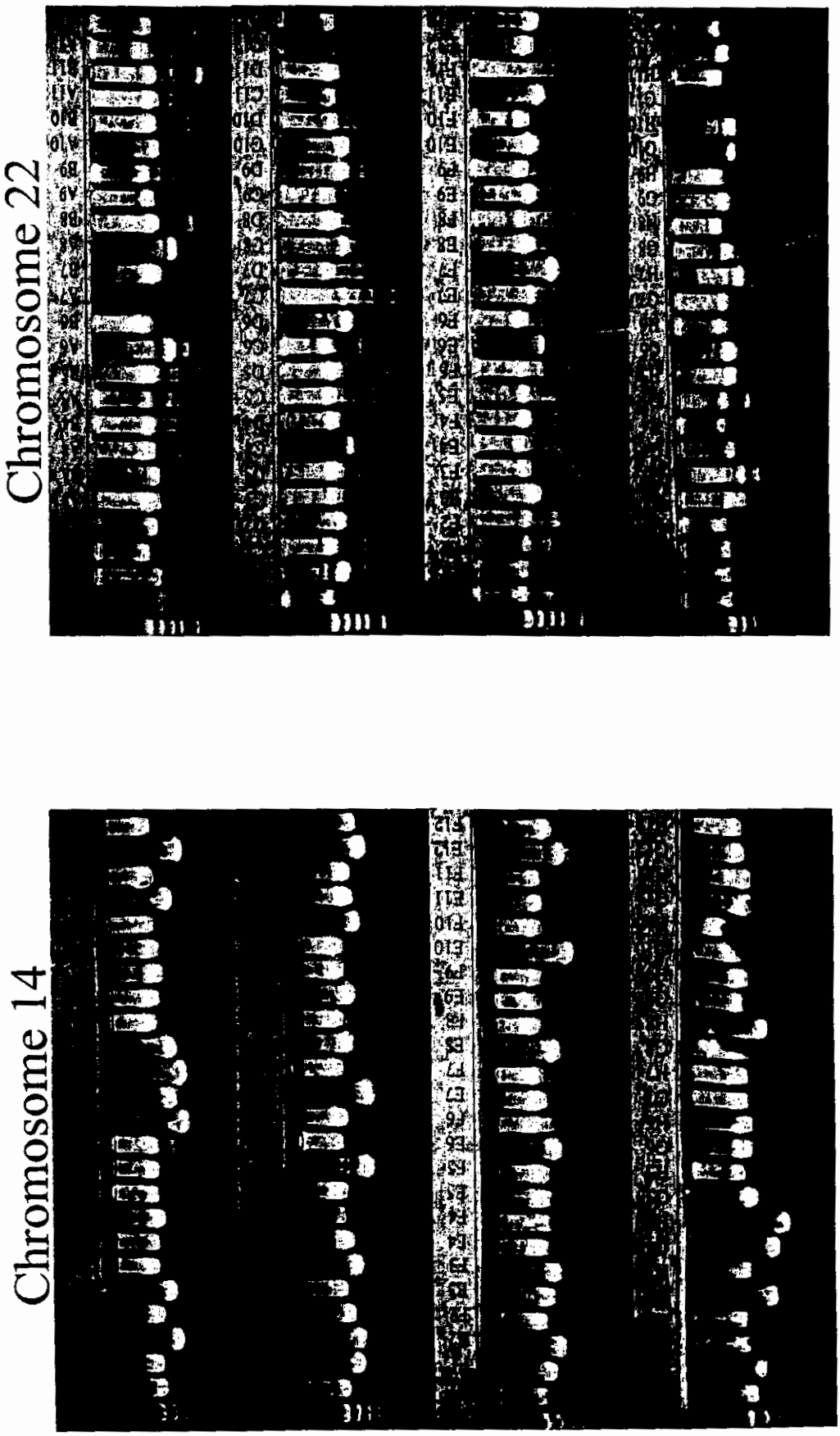


Fig. 12

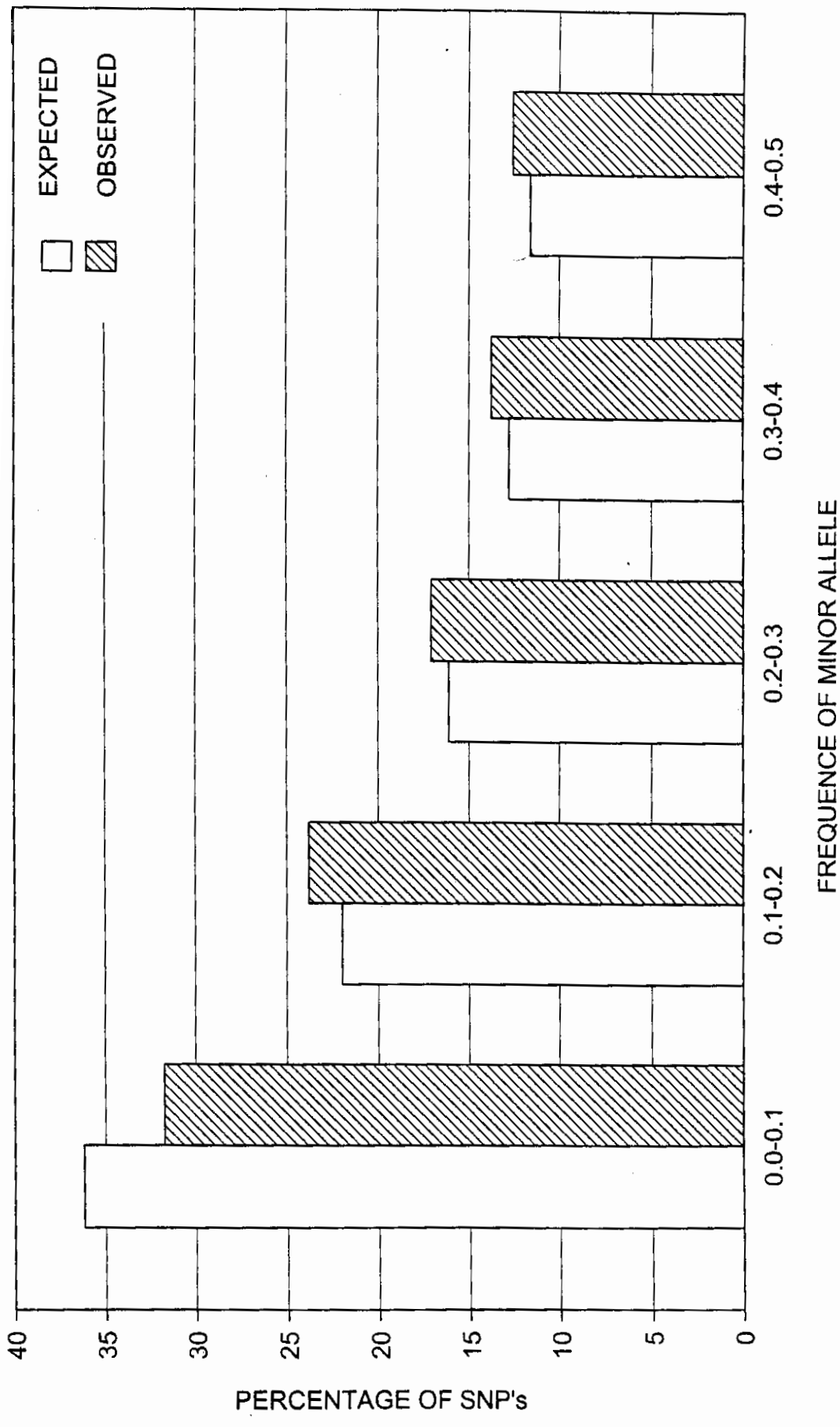

EXPECTED
OBSERVED
40
35
30
25
20
15
10
5
0
PERCENTAGE OF SNP's
0.0-0.1
0.1-0.2
0.2-0.3
0.3-0.4
0.4-0.5
FREQUENCE OF MINOR ALLELE

Fig. 13A

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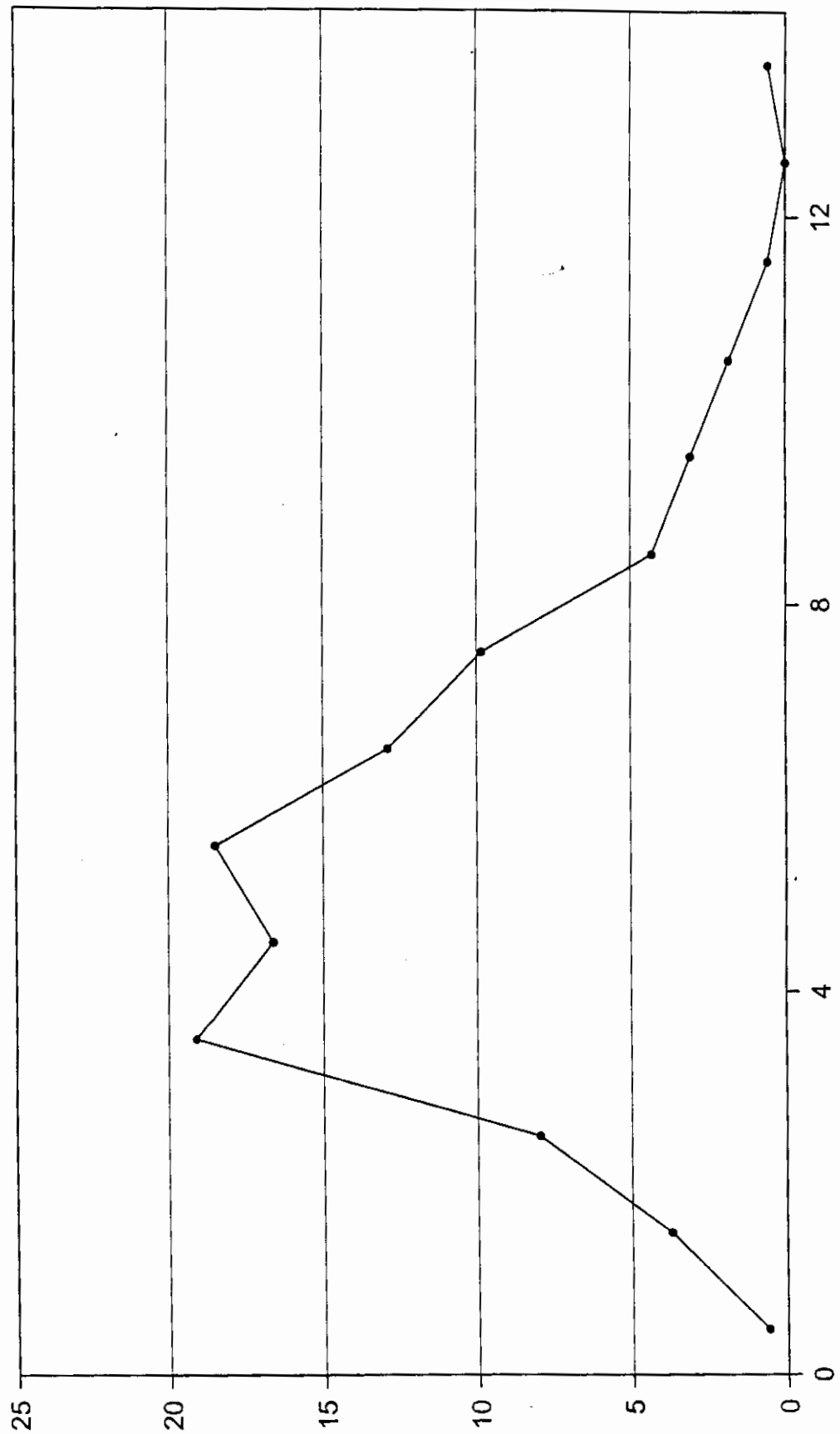


Fig. 13B

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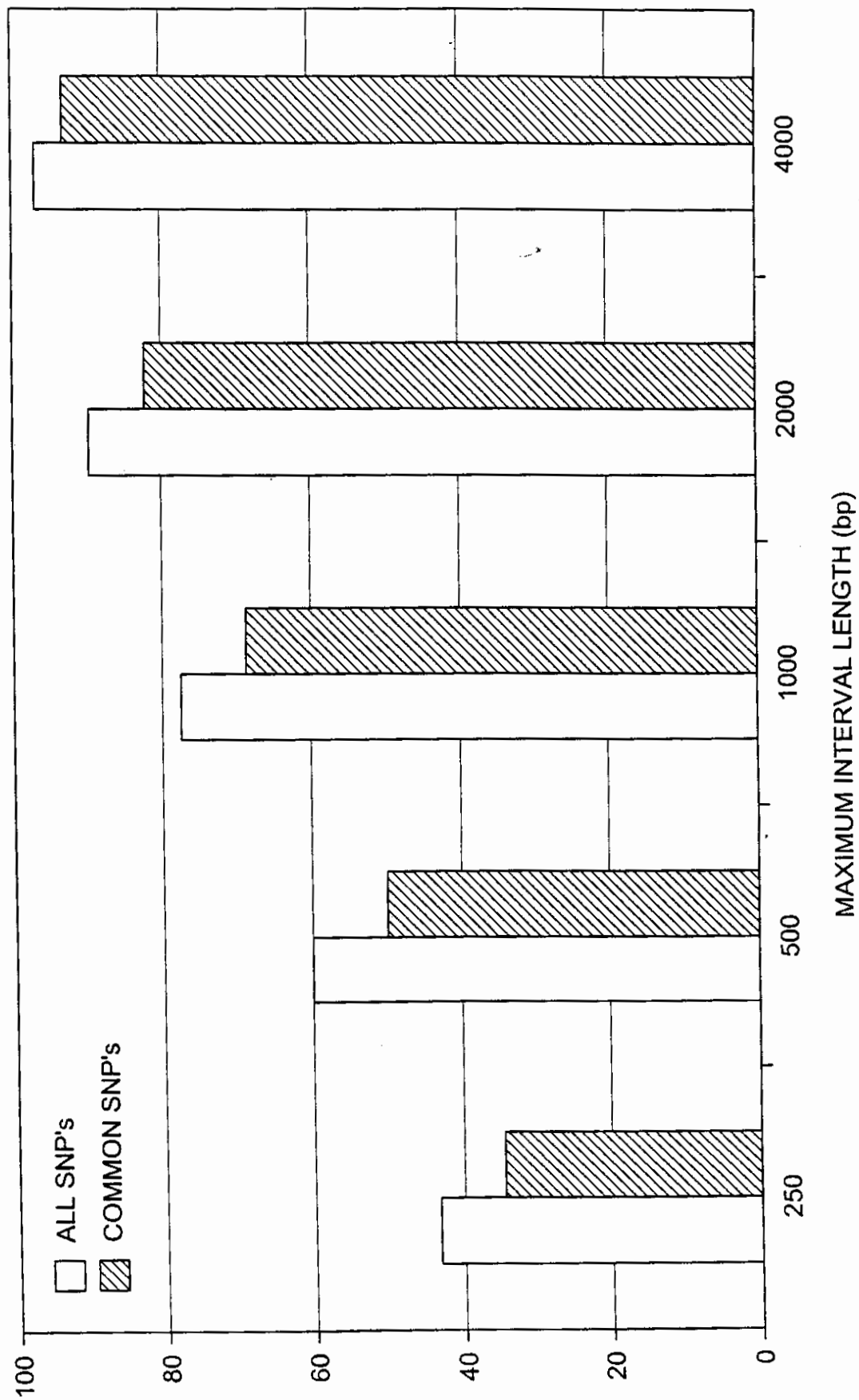


Fig. 13C

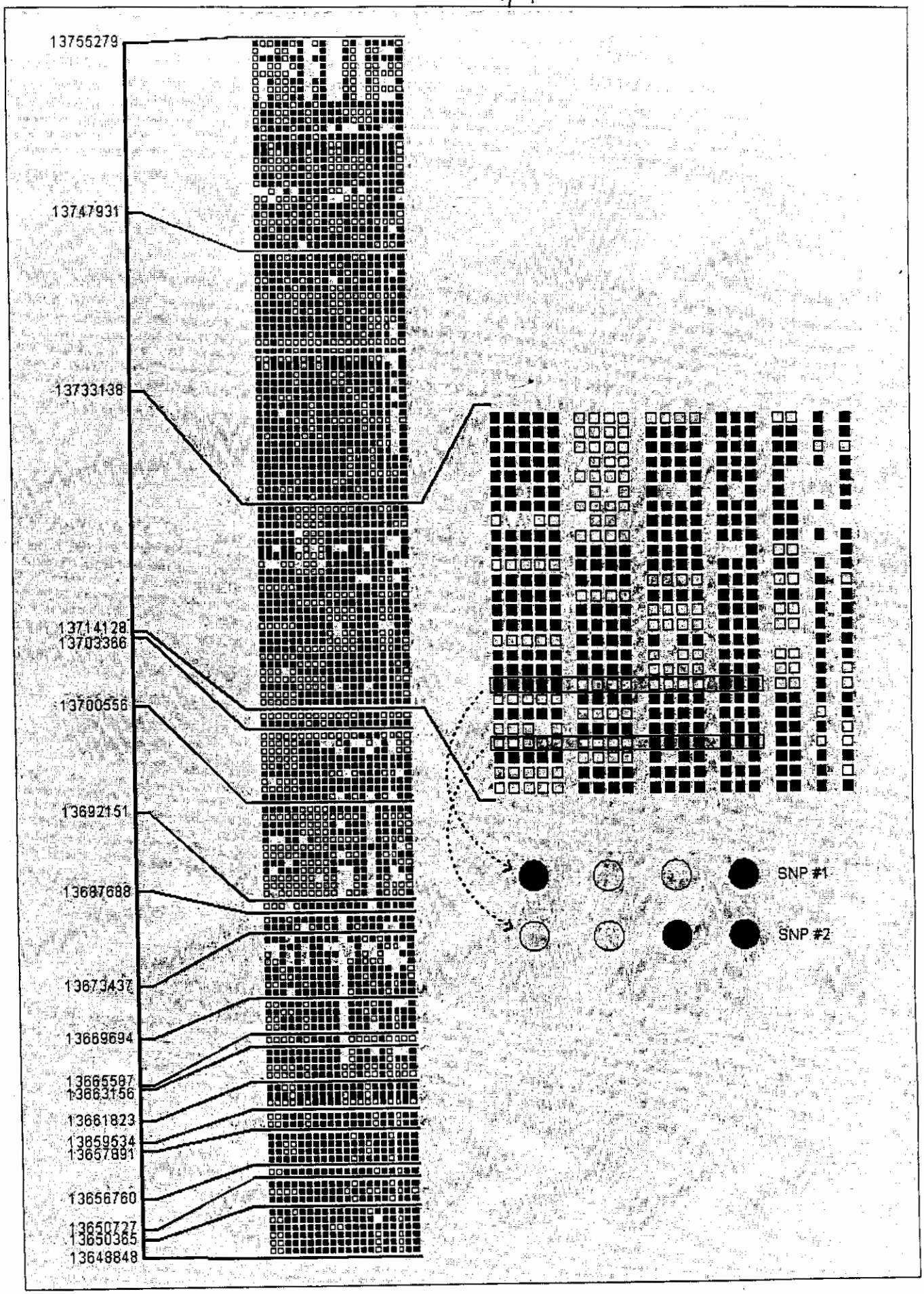

13755279
13747931
13733138
13714128
13703366
13700556
13692151
13687688
13673437
13669694
13665587
13663156
13661823
13659634
13657891
13656760
13650727
13650365
13648848
SNP #1
SNP #2

Figure 14

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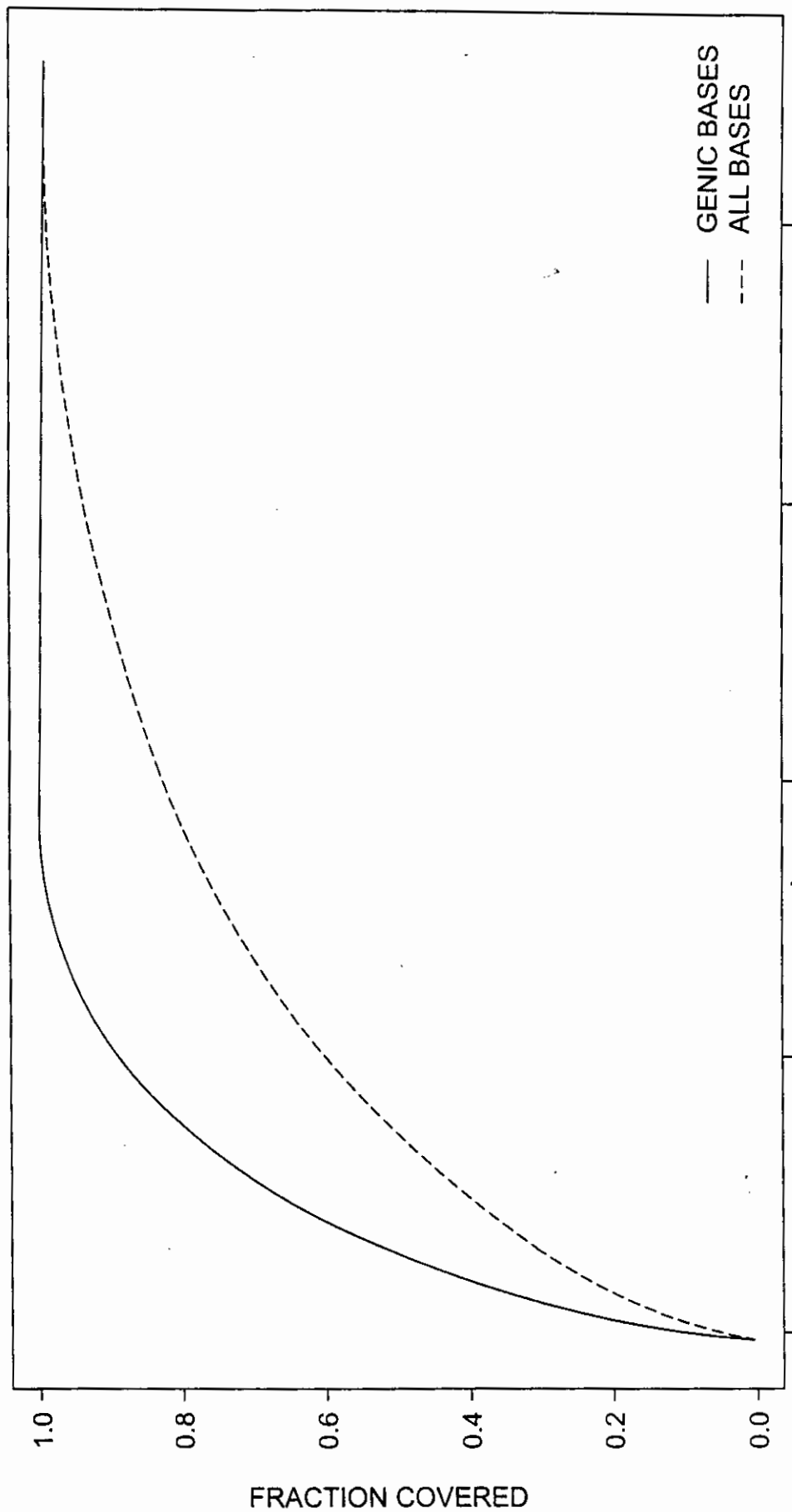


Fig. 15