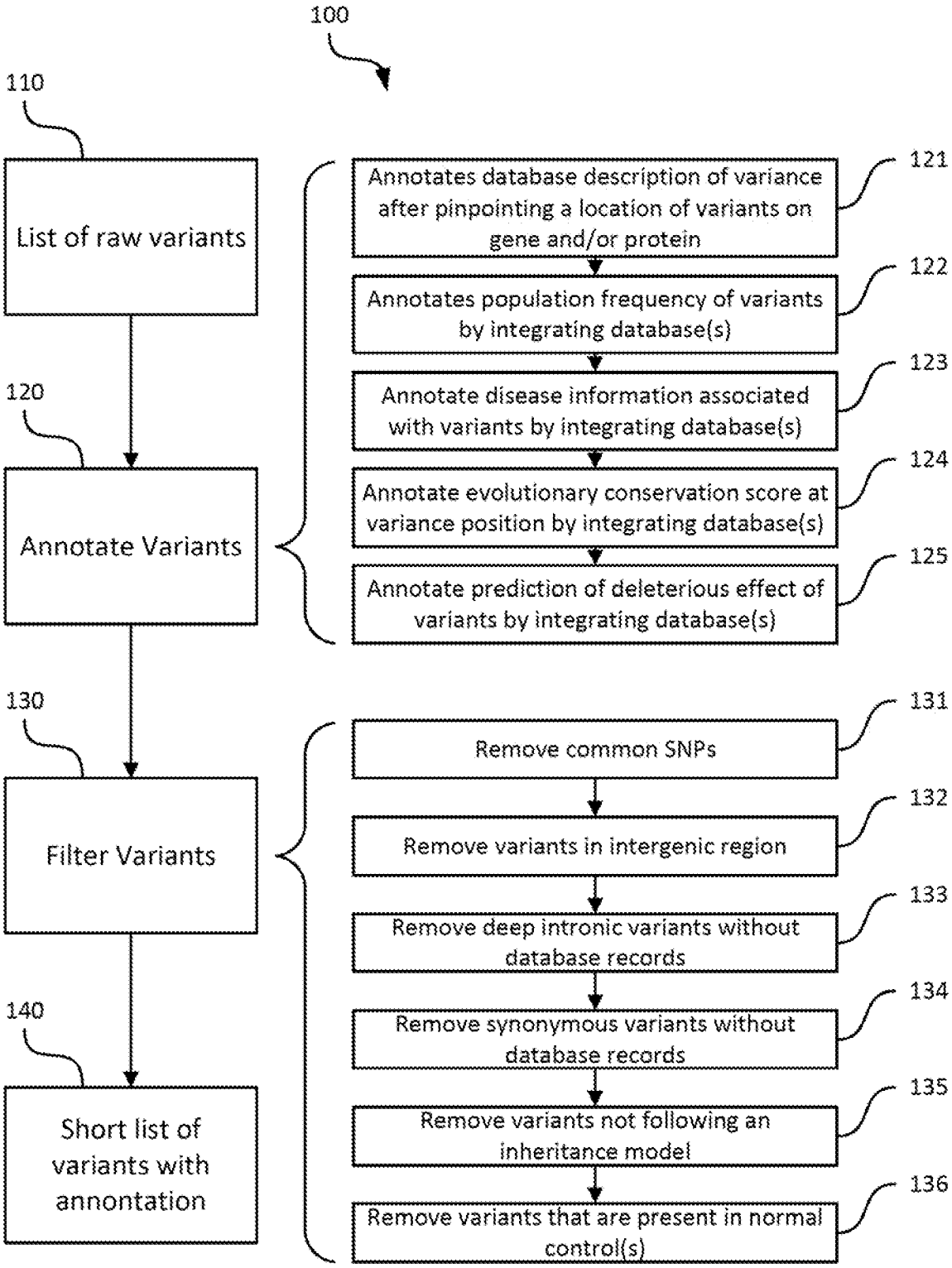
100
110
List of raw variants
120
Annotate Variants
130
Filter Variants
140
Short list of variants with annontation
Annotates database description of variance after pinpointing a location of variants on gene and/or protein
121
Annotates population frequency of variants by integrating database(s)
122
Annotate disease information associated with variants by integrating database(s)
123
Annotate evolutionary conservation score at variance position by integrating database(s)
124
Annotate prediction of deleterious effect of variants by integrating database(s)
125
Remove common SNPs
131
Remove variants in intergenic region
132
Remove deep intronic variants without database records
133
Remove synonymous variants without database records
134
Remove variants not following an inheritance model
135
Remove variants that are present in normal control(s)
136

FIG. 1

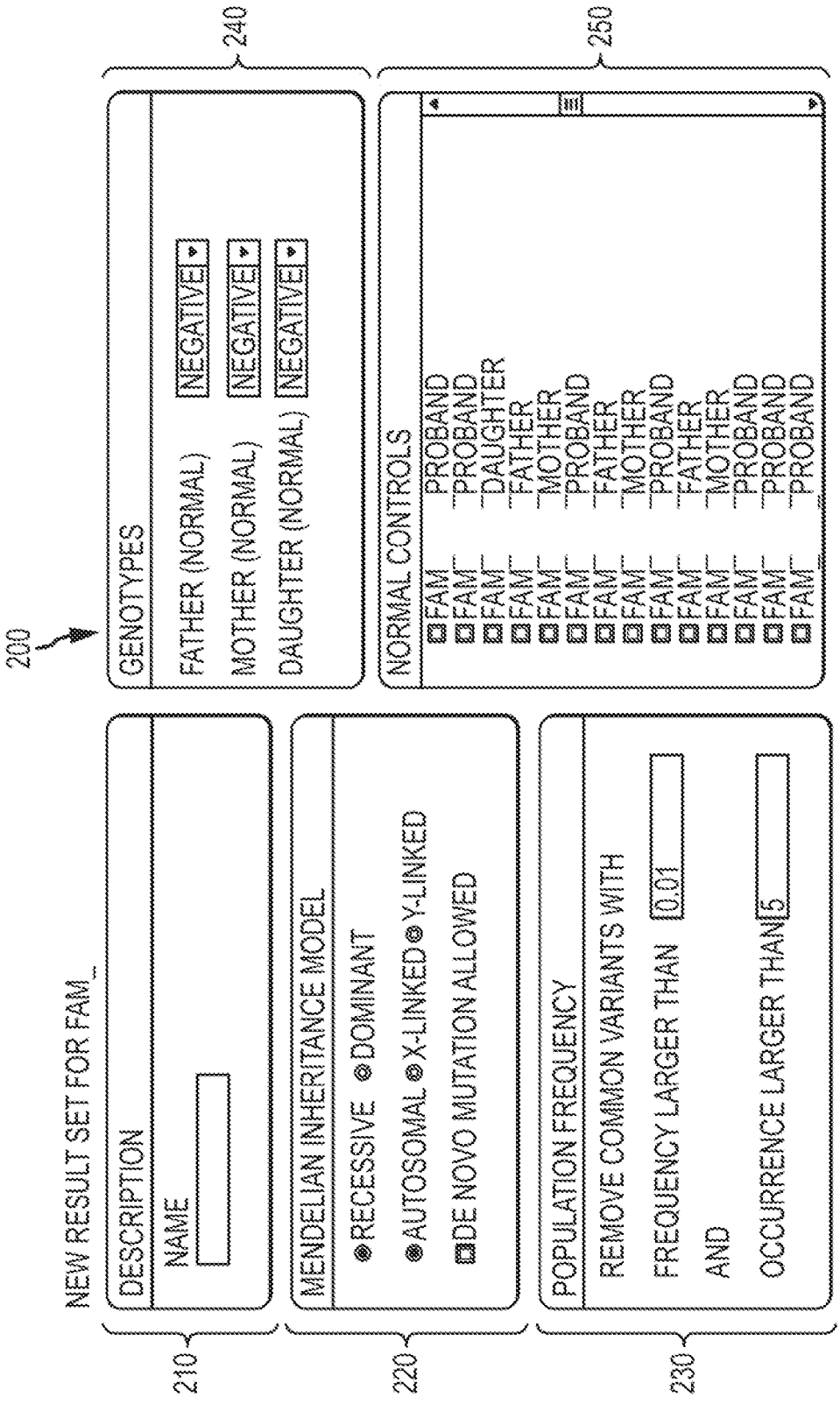
200
NEW RESULT SET FOR FAM_
DESCRIPTION
NAME
210
MENDELIAN INHERITANCE MODEL
RECESSIVE
DOMINANT
AUTOSOMAL
X-LINKED
Y-LINKED
DE NOVO MUTATION ALLOWED
220
POPULATION FREQUENCY
REMOVE COMMON VARIANTS WITH
FREQUENCY LARGER THAN 0.01
AND
OCCURRENCE LARGER THAN 5
230
GENOTYPES
FATHER (NORMAL) NEGATIVE
MOTHER (NORMAL) NEGATIVE
DAUGHTER (NORMAL) NEGATIVE
240
NORMAL CONTROLS
FAM PROBAND
FAM PROBAND
FAM DAUGHTER
FAM FATHER
FAM MOTHER
FAM PROBAND
FAM FATHER
FAM MOTHER
FAM PROBAND
FAM FATHER
FAM MOTHER
FAM PROBAND
FAM PROBAND
FAM PROBAND
250
RUN
RESET
GO BACK

FIG.2

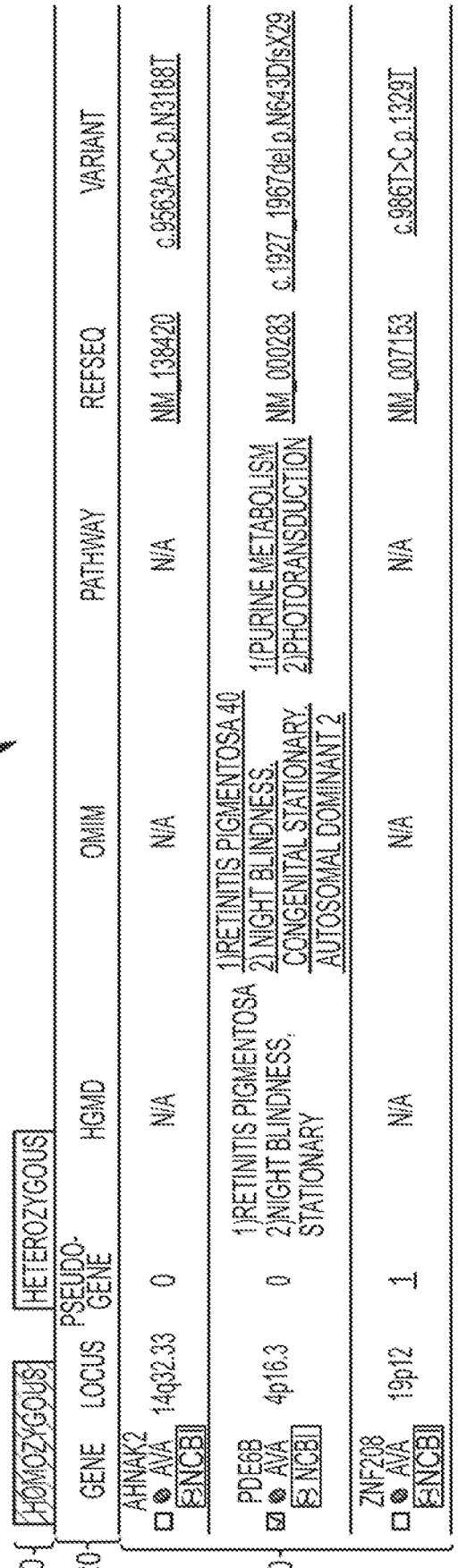
300
310
HOMOZYGOUS
HETEROZYGOUS
320
GENE
LOCUS
PSEUDO-GENE
HGMD
OMIM
PATHWAY
REFSEQ
VARIANT
330
AHNAK2
AVA
ENCBI
14q32.33
0
N/A
N/A
N/A
NM_138420
c.9563A>C p.N3188T
PDE6B
AVA
NCBI
4p16.3
0
1.RETINITIS PIGMENTOSA
2.NIGHT BLINDNESS,
STATIONARY
1.RETINITIS PIGMENTOSA 40
2.NIGHT BLINDNESS,
CONGENITAL STATIONARY,
AUTOSOMAL DOMINANT 2
1.PURINE METABOLISM
2.PHOTOTRANSDUCTION
NM_000283
c.1927_1967del p.N643DfsX29
ZNF208
AVA
ENCBI
19p12
1
N/A
N/A
N/A
NM_007153
c.9961T>C p.1329T
DOWNLOAD

FIG.3

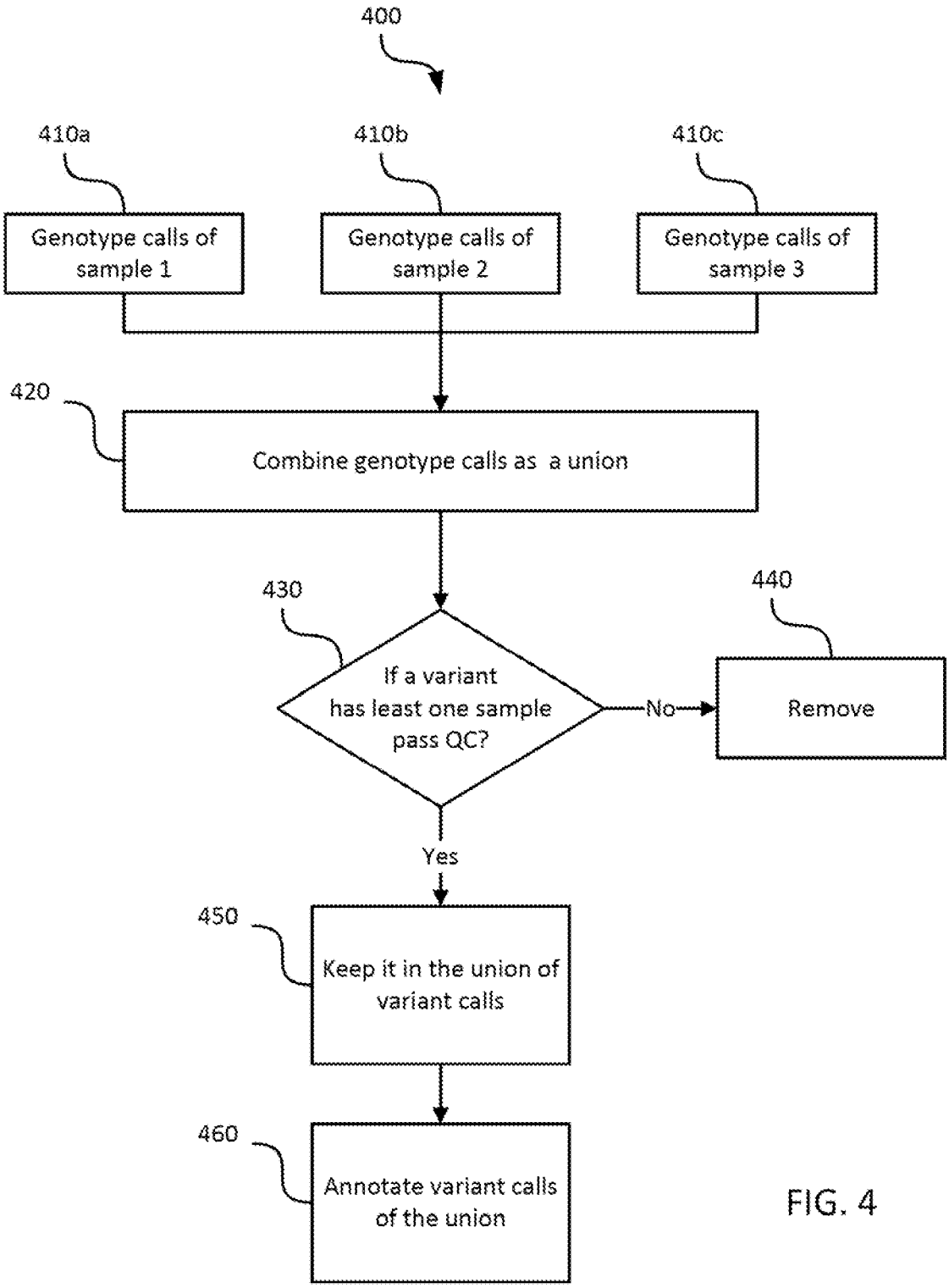
400
410a
410b
410c
Genotype calls of sample 1
Genotype calls of sample 2
Genotype calls of sample 3
420
Combine genotype calls as a union
430
If a variant has least one sample pass QC?
No
440
Remove
Yes
450
Keep it in the union of variant calls
460
Annotate variant calls of the union

FIG. 4

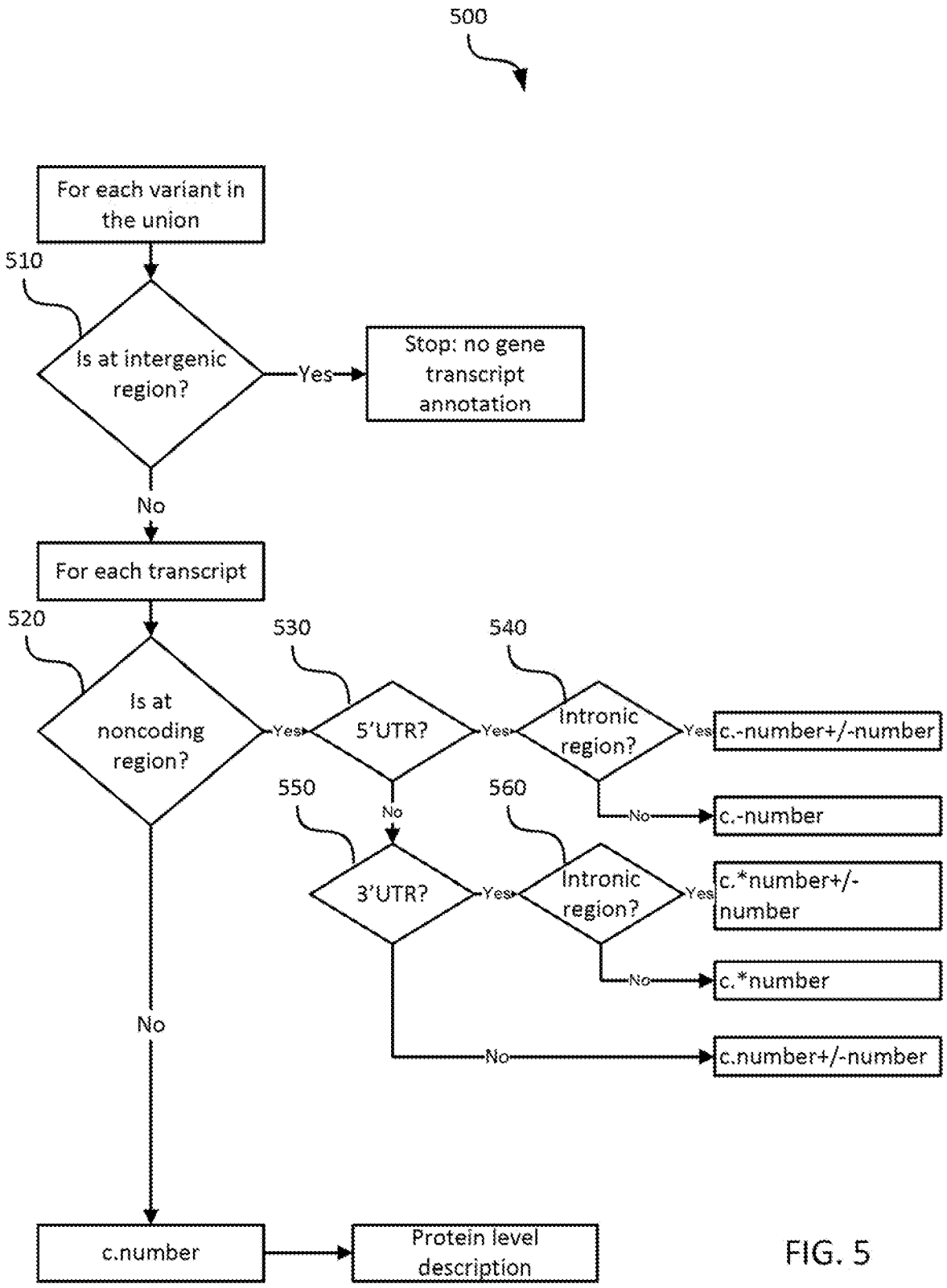
500
For each variant in the union
510
Is at intergenic region?
Yes
Stop: no gene transcript annotation
No
For each transcript
520
Is at noncoding region?
Yes
530
5'UTR?
Yes
540
Intronic region?
Yes
c.-number+/-number
No
c.-number
No
550
3'UTR?
Yes
560
Intronic region?
Yes
c.*number+/-number
No
c.*number
No
c.number+/-number
No
c.number
Protein level description

FIG. 5

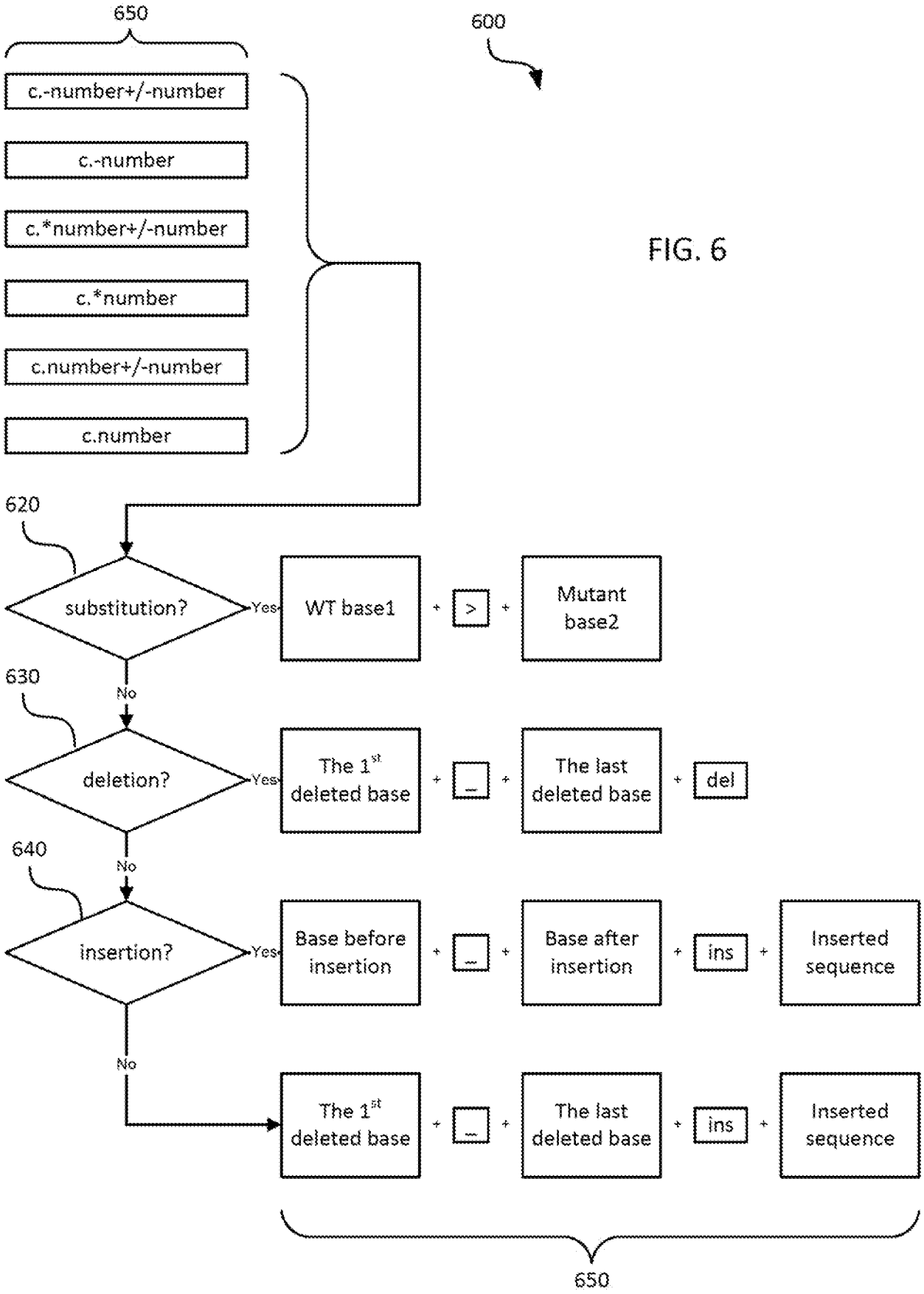
650
600
c.-number+/-number
c.-number
c.*number+/-number
c.*number
c.number+/-number
c.number
620
substitution?
Yes
WT base1
+
>
+
Mutant base2
630
No
deletion?
Yes
The 1st deleted base
+
_
+
The last deleted base
+
del
640
No
insertion?
Yes
Base before insertion
+
_
+
Base after insertion
+
ins
+
Inserted sequence
No
The 1st deleted base
+
_
+
The last deleted base
+
ins
+
Inserted sequence
650

FIG. 6

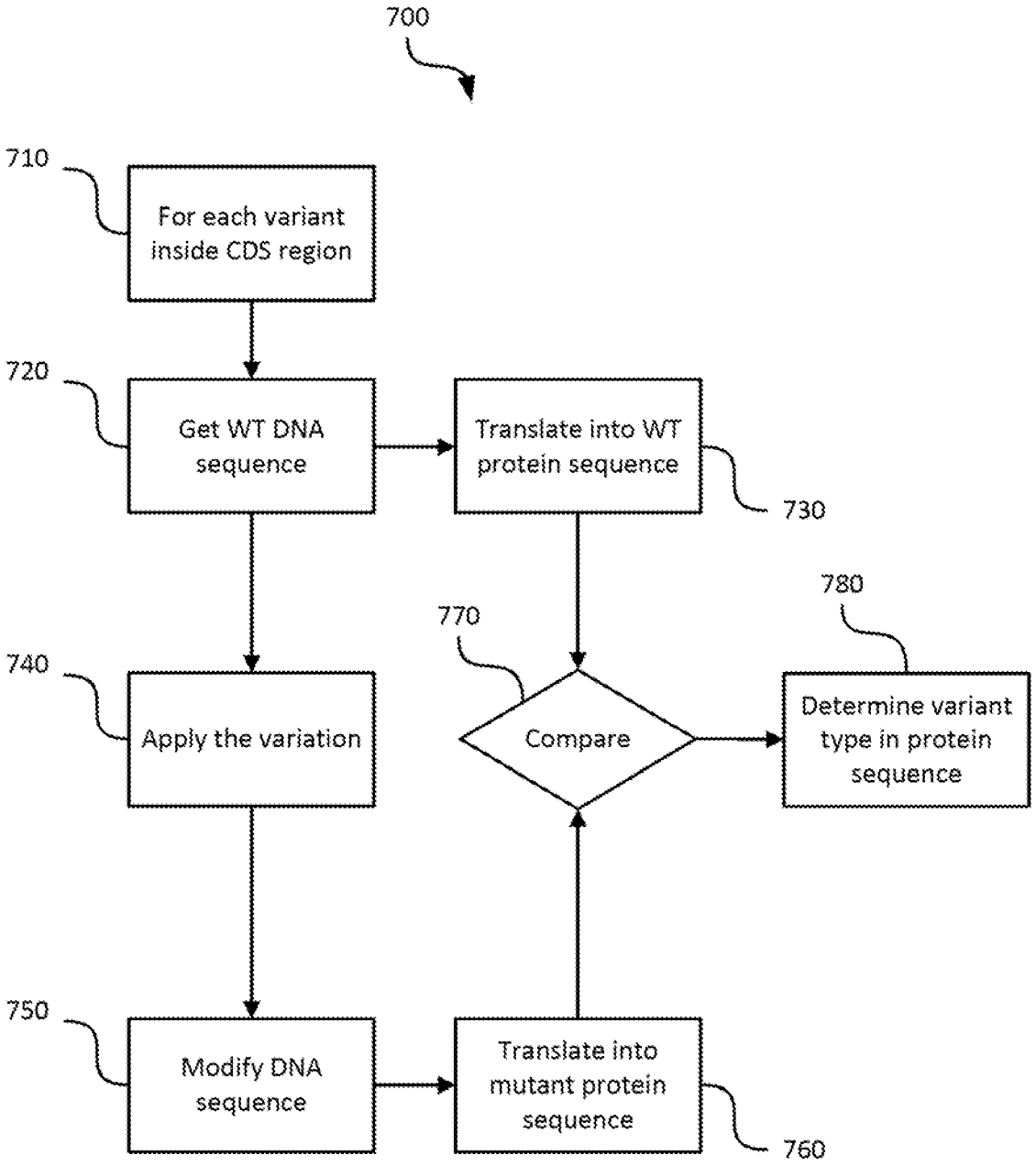
700
710
For each variant inside CDS region
720
Get WT DNA sequence
Translate into WT protein sequence
730
740
Apply the variation
770
Compare
780
Determine variant type in protein sequence
750
Modify DNA sequence
Translate into mutant protein sequence
760

FIG. 7

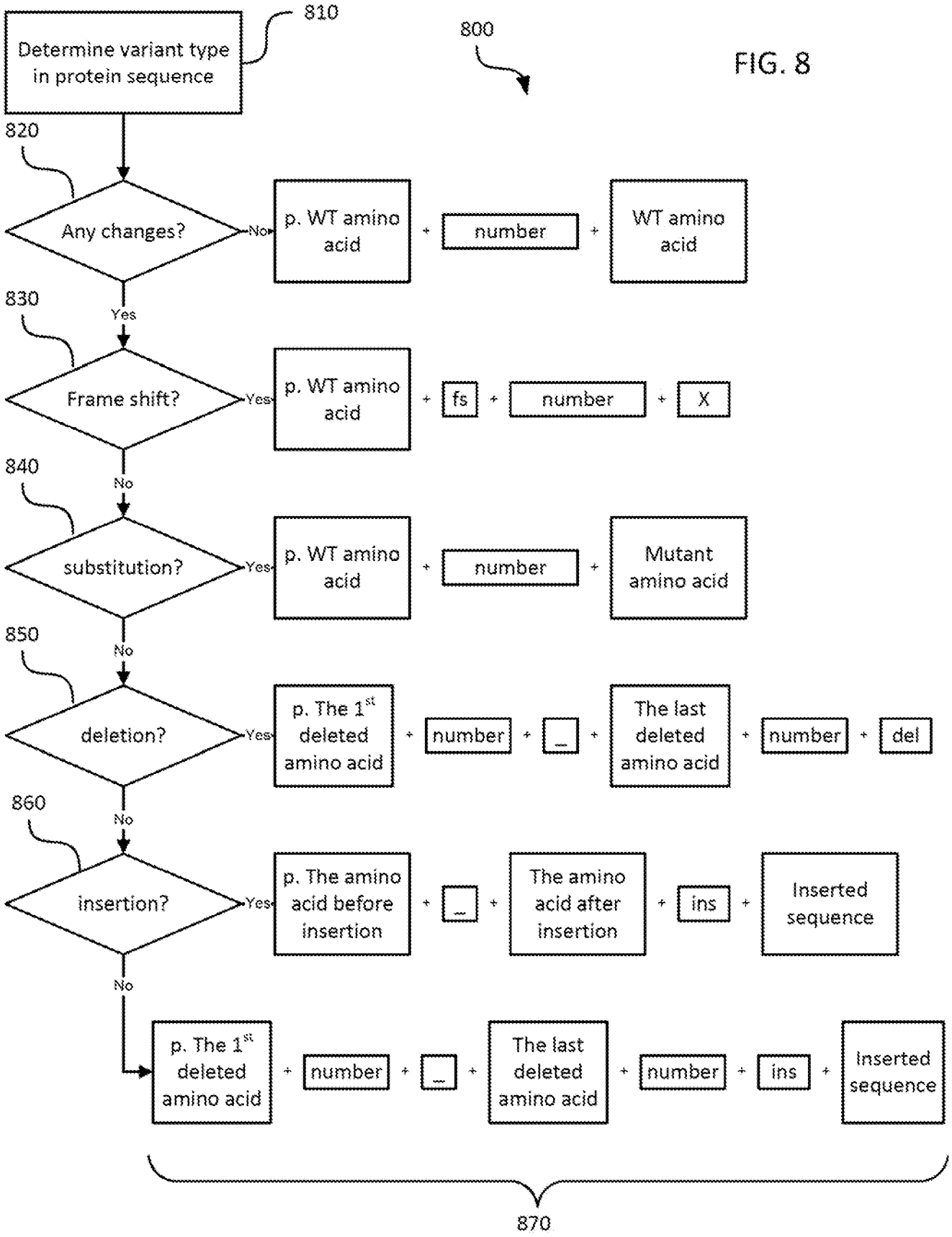
800
810
Determine variant type in protein sequence
820
Any changes?
No
p. WT amino acid
+
number
+
WT amino acid
Yes
830
Frame shift?
Yes
p. WT amino acid
+
fs
+
number
+
X
No
840
substitution?
Yes
p. WT amino acid
+
number
+
Mutant amino acid
No
850
deletion?
Yes
p. The 1st deleted amino acid
+
number
+
_
+
The last deleted amino acid
+
number
+
del
No
860
insertion?
Yes
p. The amino acid before insertion
+
_
+
The amino acid after insertion
+
ins
+
Inserted sequence
No
p. The 1st deleted amino acid
+
number
+
_
+
The last deleted amino acid
+
number
+
ins
+
Inserted sequence
870

FIG. 8

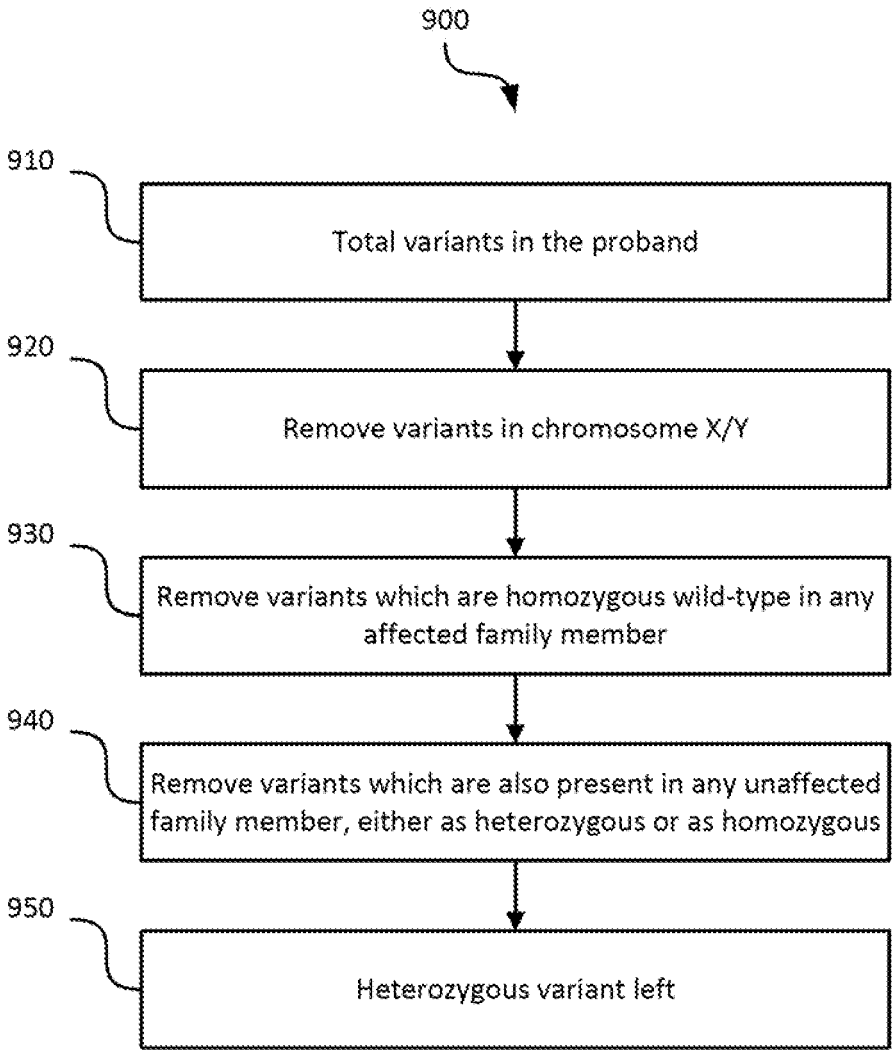
900
910
Total variants in the proband
920
Remove variants in chromosome X/Y
930
Remove variants which are homozygous wild-type in any affected family member
940
Remove variants which are also present in any unaffected family member, either as heterozygous or as homozygous
950
Heterozygous variant left

FIG. 9

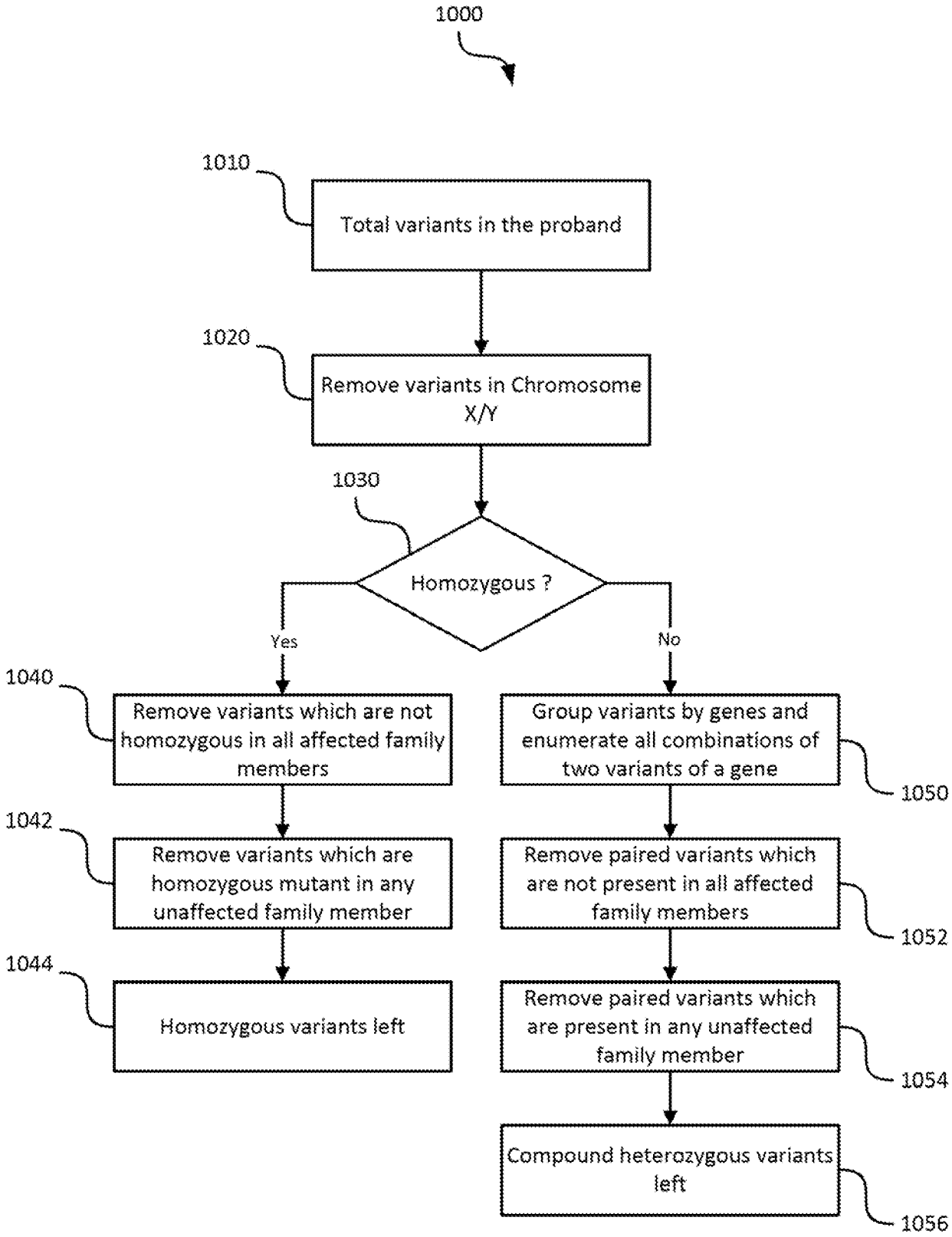
1000
1010
Total variants in the proband
1020
Remove variants in Chromosome X/Y
1030
Homozygous ?
Yes
No
1040
Remove variants which are not homozygous in all affected family members
1042
Remove variants which are homozygous mutant in any unaffected family member
1044
Homozygous variants left
1050
Group variants by genes and enumerate all combinations of two variants of a gene
1052
Remove paired variants which are not present in all affected family members
1054
Remove paired variants which are present in any unaffected family member
1056
Compound heterozygous variants left

FIG. 10

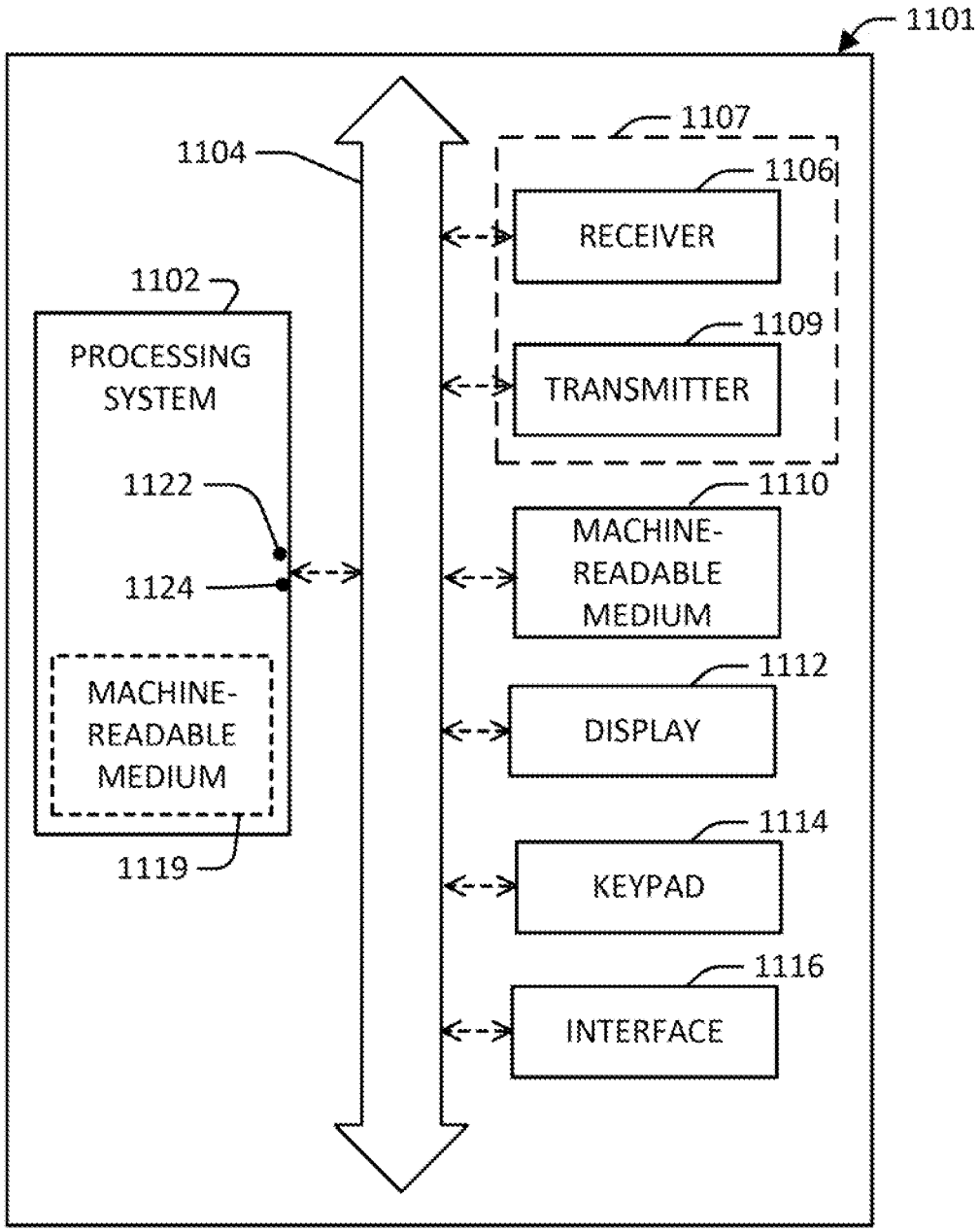
1101
1104
1107
1106
RECEIVER
1102
PROCESSING SYSTEM
1109
TRANSMITTER
1122
1110
MACHINE-READABLE MEDIUM
1124
1112
DISPLAY
MACHINE-READABLE MEDIUM
1114
KEYPAD
1119
1116
INTERFACE

FIG. 11

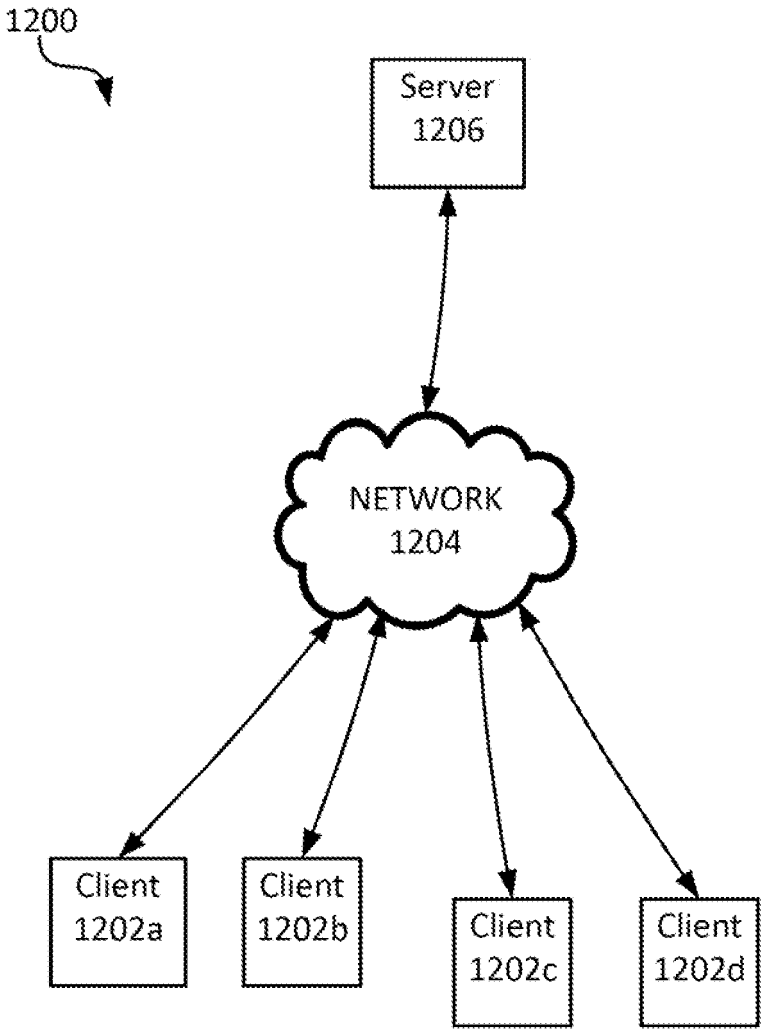
1200
Server
1206
NETWORK
1204
Client
1202a
Client
1202b
Client
1202c
Client
1202d

FIG. 12