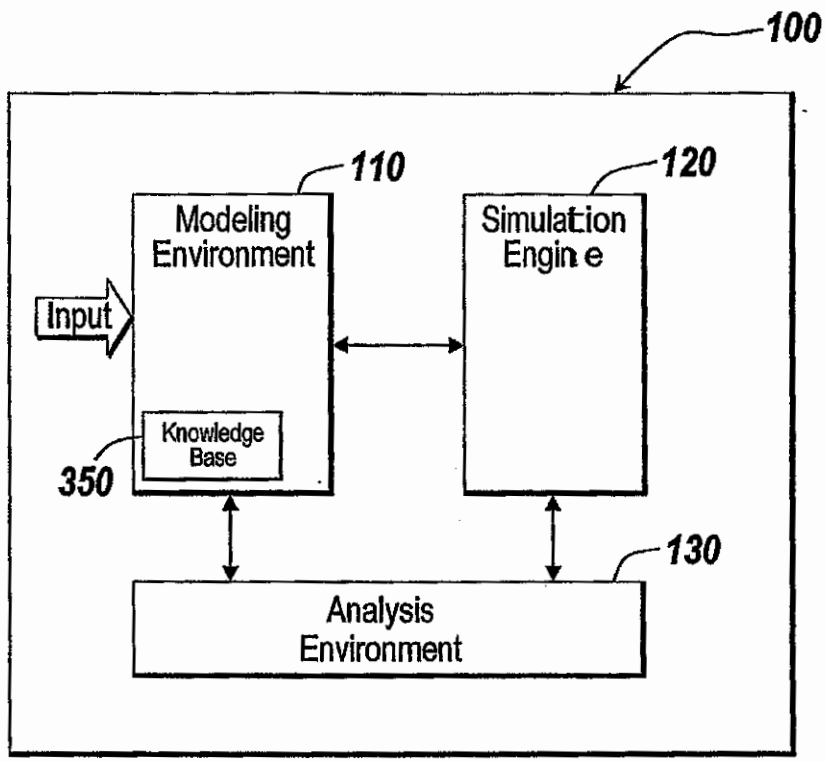

100
110
120
Modeling Environment
Simulation Engine
Input
Knowledge Base
350
130
Analysis Environment

Fig. 1

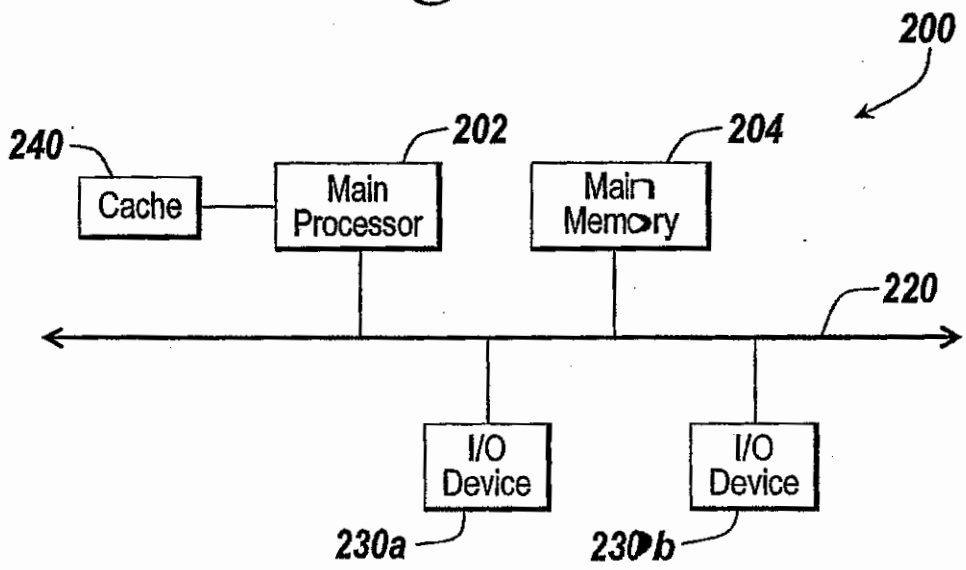

200
240
202
204
Cache
Main Processor
Main Memory
220
I/O Device
I/O Device
230a
230b

Fig. 2A

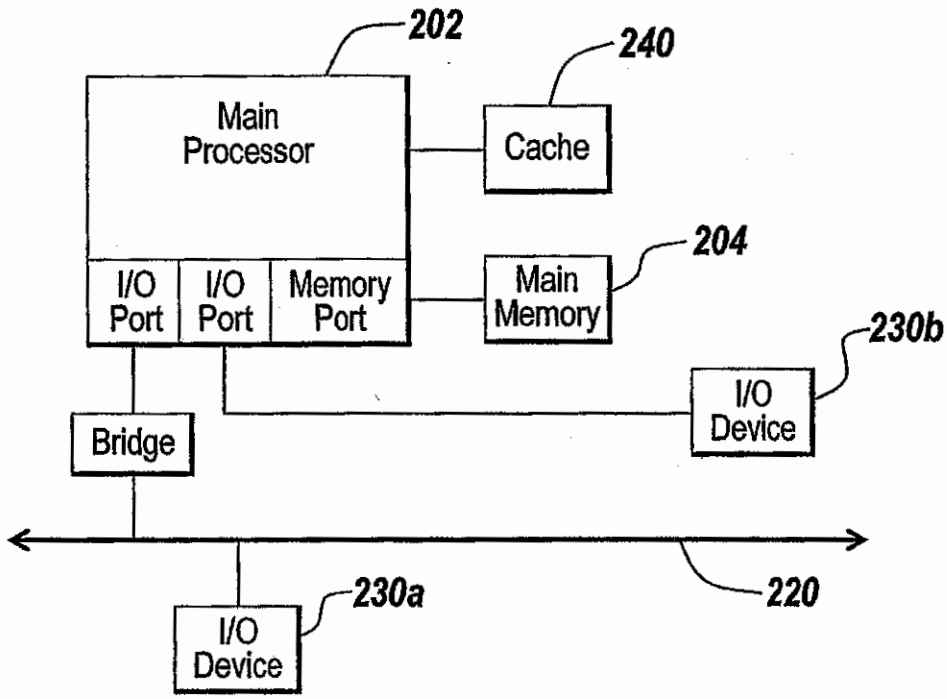

202
240
Main Processor
Cache
I/O Port
I/O Port
Memory Port
Main Memory
204
230b
I/O Device
Bridge
220
230a
I/O Device

Fig. 2B

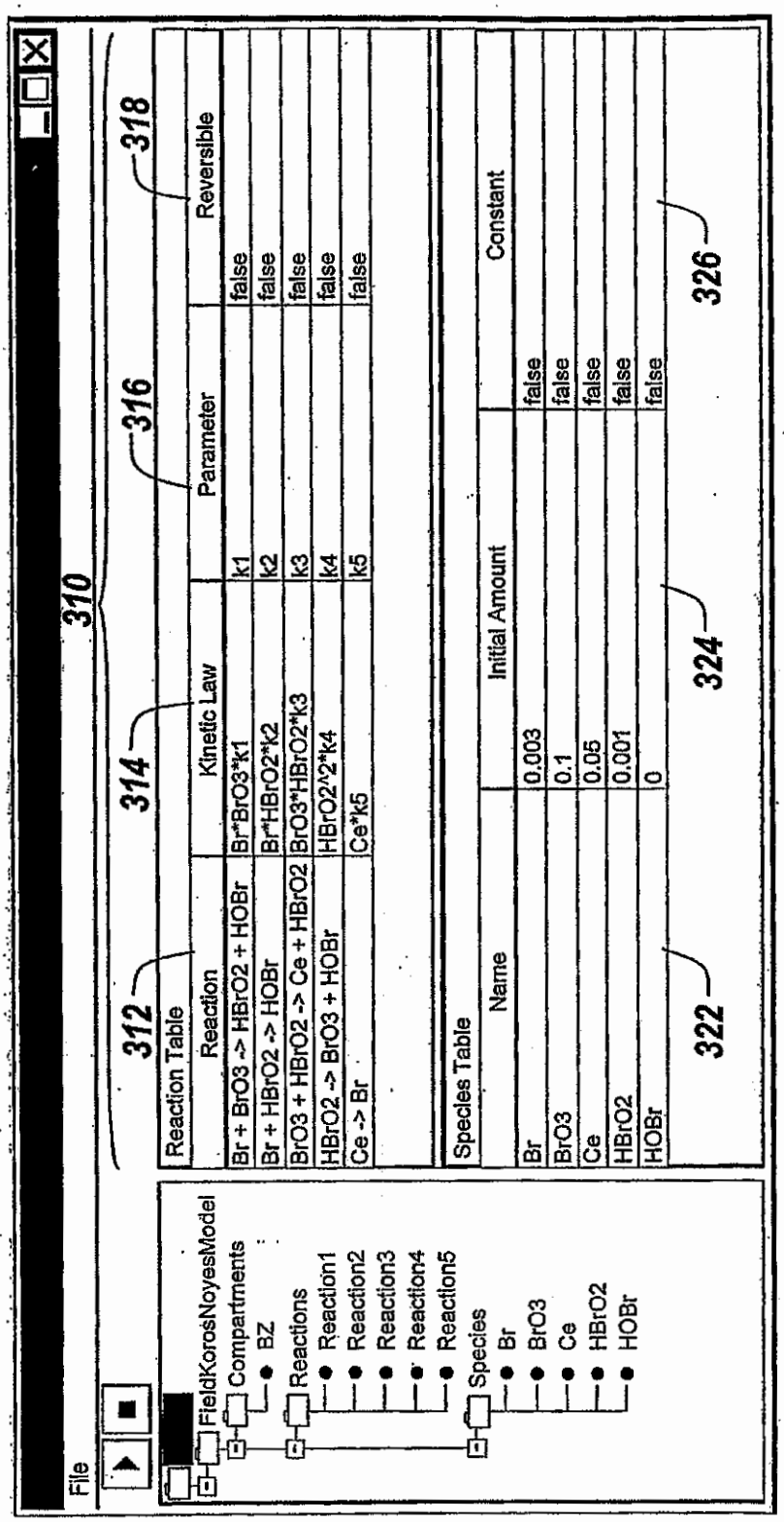

300
310
File
FieldKorosNoyesModel
Compartments
BZ
Reactions
Reaction1
Reaction2
Reaction3
Reaction4
Reaction5
Species
Br
BrO3
Ce
HBrO2
HOBr
302
312
314
316
318
320
322
324
326
Reaction Table
Reaction
Kinetic Law
Parameter
Reversible
Br + BrO3 -> HBrO2 + HOBr
Br*BrO3*k1
k1
false
Br + HBrO2 -> HOBr
Br*HBrO2*k2
k2
false
BrO3 + HBrO2 -> Ce + HBrO2
BrO3*HBrO2*k3
k3
false
HBrO2 -> BrO3 + HOBr
HBrO2^2*k4
k4
false
Ce -> Br
Ce*k5
k5
false
Species Table
Name
Initial Amount
Constant
Br
0.003
false
BrO3
0.1
false
Ce
0.05
false
HBrO2
0.001
false
HOBr
0
false

Fig. 3A

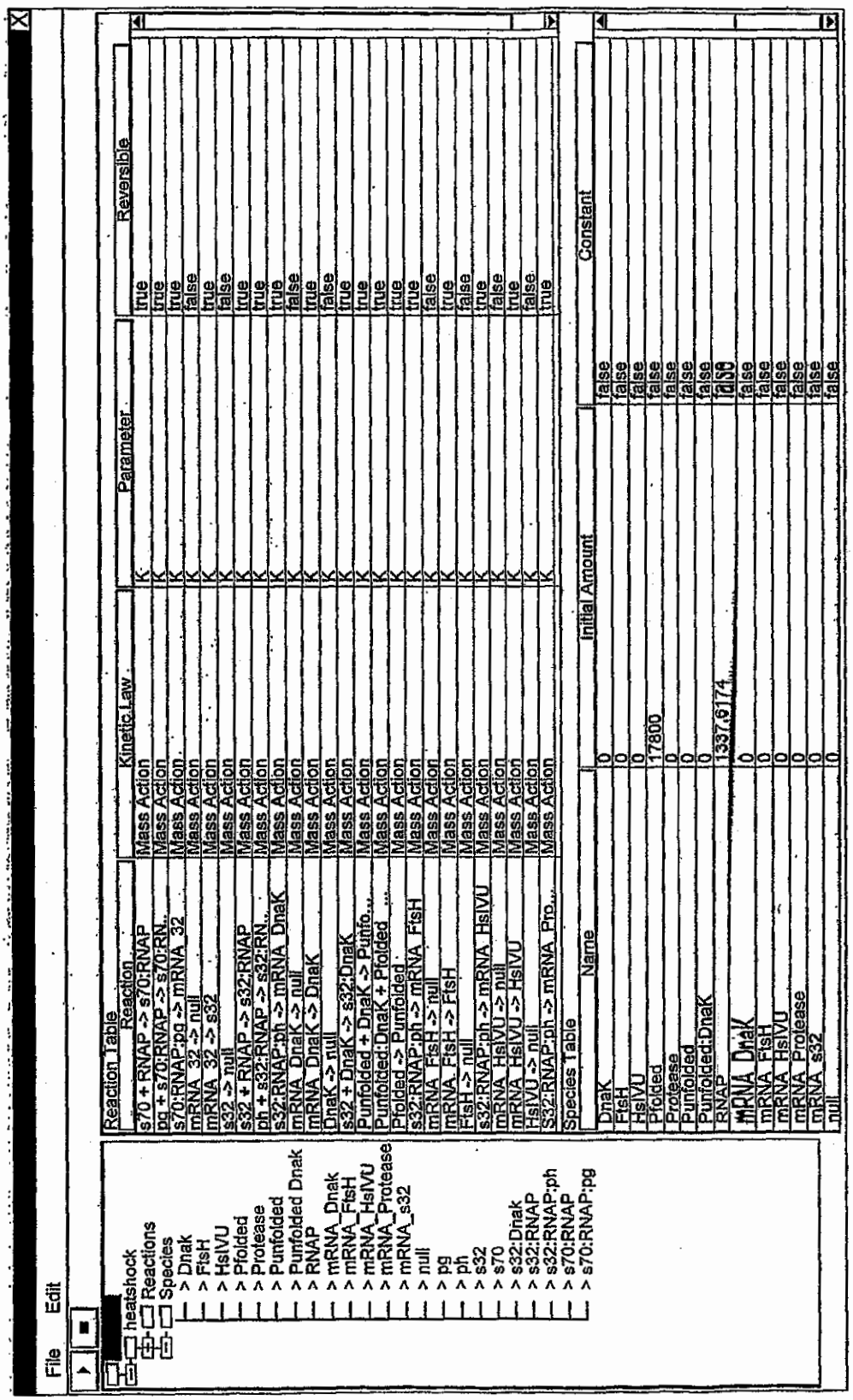

File
Edit
heatshock
Reactions
Species
Dnak
FtsH
HslVU
Pfolded
Protease
Punfolded
Punfolded Dnak
RNAP
mRNA_Dnak
mRNA_FtsH
mRNA_HslVU
mRNA_Protease
mRNA_s32
null
pg
ph
s32
s70
s32:Dnak
s32:RNAP
s32:RNAP:ph
s70:RNAP
s70:RNAP:pg
Reaction Table
Reaction
Kinetic Law
Parameter
Reversible
s70 + RNAP -> s70:RNAP
Mass Action
K
true
pg + s70:RNAP -> s70:RN...
s70:RNAP:pg -> mRNA_32
mRNA_32 -> null
mRNA_32 -> s32
s32 -> null
s32 + RNAP -> s32:RNAP
ph + s32:RNAP -> s32:RN...
s32:RNAP:ph -> mRNA_DnaK
mRNA_DnaK -> null
mRNA_DnaK -> DnaK
DnaK -> null
s32 + DnaK -> s32:DnaK
Punfolded + DnaK -> Punfo...
Punfolded:DnaK + Pfolded ...
Pfolded -> Punfolded
s32:RNAP:ph -> mRNA_FtsH
mRNA_FtsH -> null
mRNA_FtsH -> FtsH
FtsH -> null
s32:RNAP:ph -> mRNA_HslVU
mRNA_HslVU -> null
mRNA_HslVU -> HslVU
HslVU -> null
s32:RNAP:ph -> mRNA_Pro...
Species Table
Name
Initial Amount
Constant
DnaK
FtsH
HslVU
Pfolded
Protease
Punfolded
Punfolded:DnaK
RNAP
mRNA_DnaK
mRNA_FtsH
mRNA_HslVU
mRNA_Protease
mRNA_s32
null

Fig. 3B

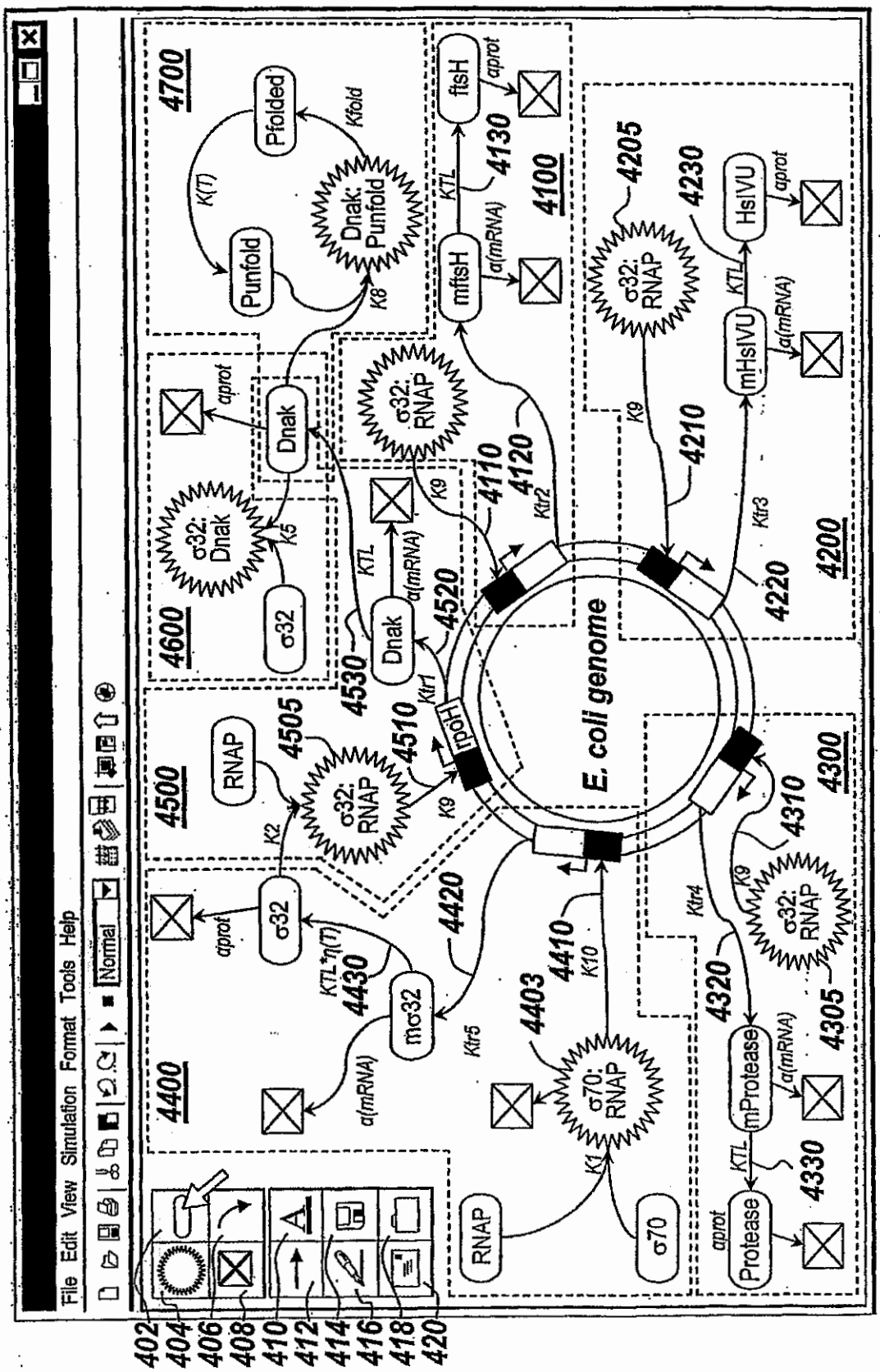

File Edit View Simulation Format Tools Help
Normal
402
404
406
408
410
412
414
416
418
420
4400
4500
4600
4700
4100
4200
4300
E. coli genome
RNAP
σ70
σ70: RNAP
σ32
σ32: Dnak
σ32: RNAP
Dnak
Pfolded
Punfold
Dnak: Punfold
mftsH
ftsH
HslVU
mHslVU
Protease
mProtease
mσ32
rpoH
aprot
α(mRNA)
K(T)
Kfold
K1
K2
K5
K8
K9
K10
KTL
KTL*η(T)
Ktr1
Ktr2
Ktr3
Ktr4
Ktr5
4110
4120
4130
4205
4210
4220
4230
4305
4310
4320
4330
4403
4410
4420
4505
4510
4520
4530
4605
4610
4620
4630
4705
4710
4720
4730
4740
4750
4760
4770
4780
4790
4795
4797
4799
4430

Fig. 4

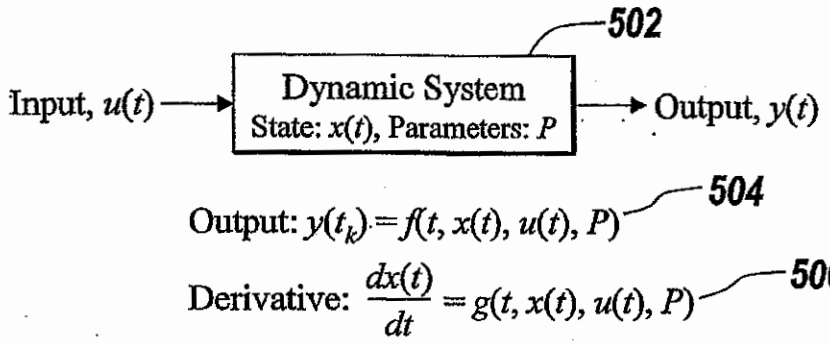


Fig. 5A

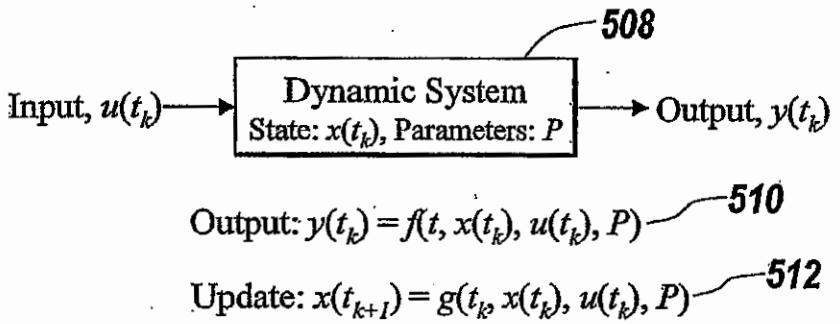


Fig. 5B

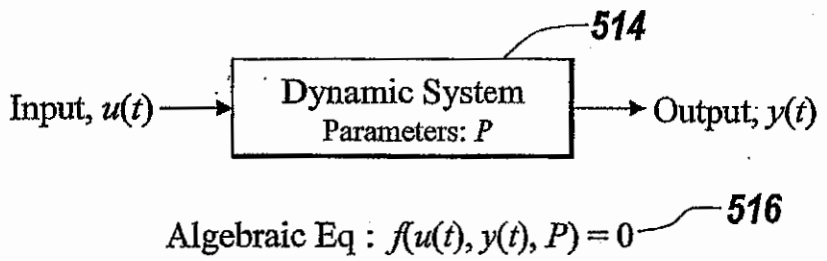


Fig. 5C

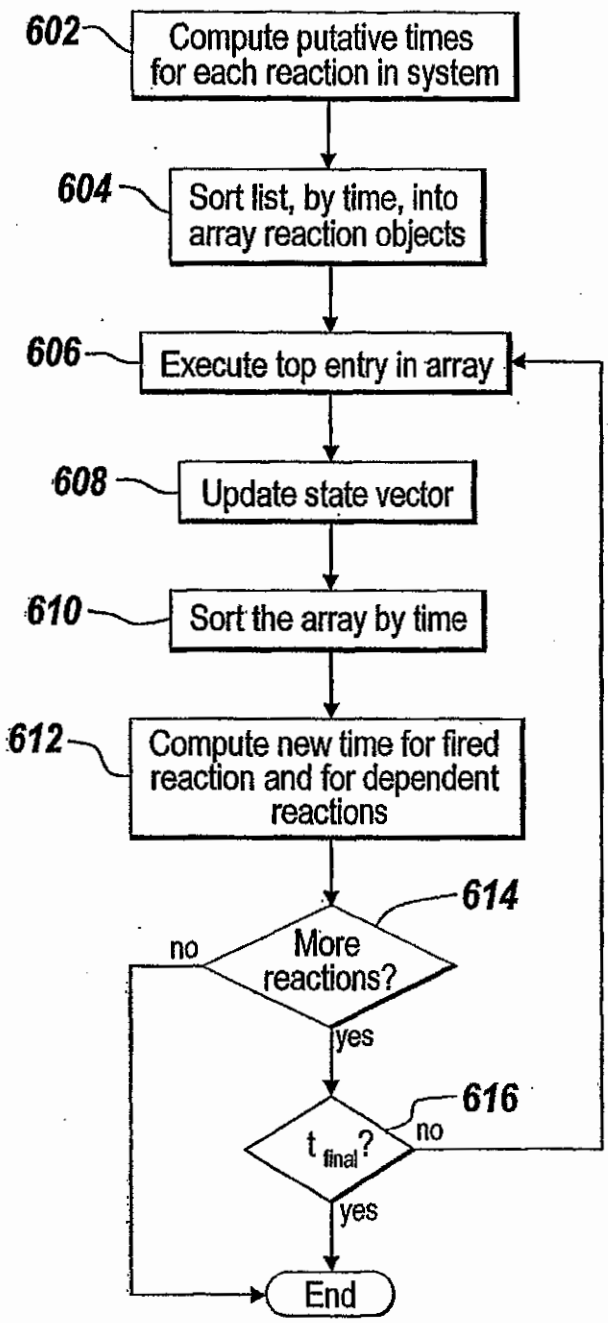

602
Compute putative times for each reaction in system
604
Sort list, by time, into array reaction objects
606
Execute top entry in array
608
Update state vector
610
Sort the array by time
612
Compute new time for fired reaction and for dependent reactions
614
More reactions?
no
yes
616
t_{final}?
no
yes
End

Fig. 6

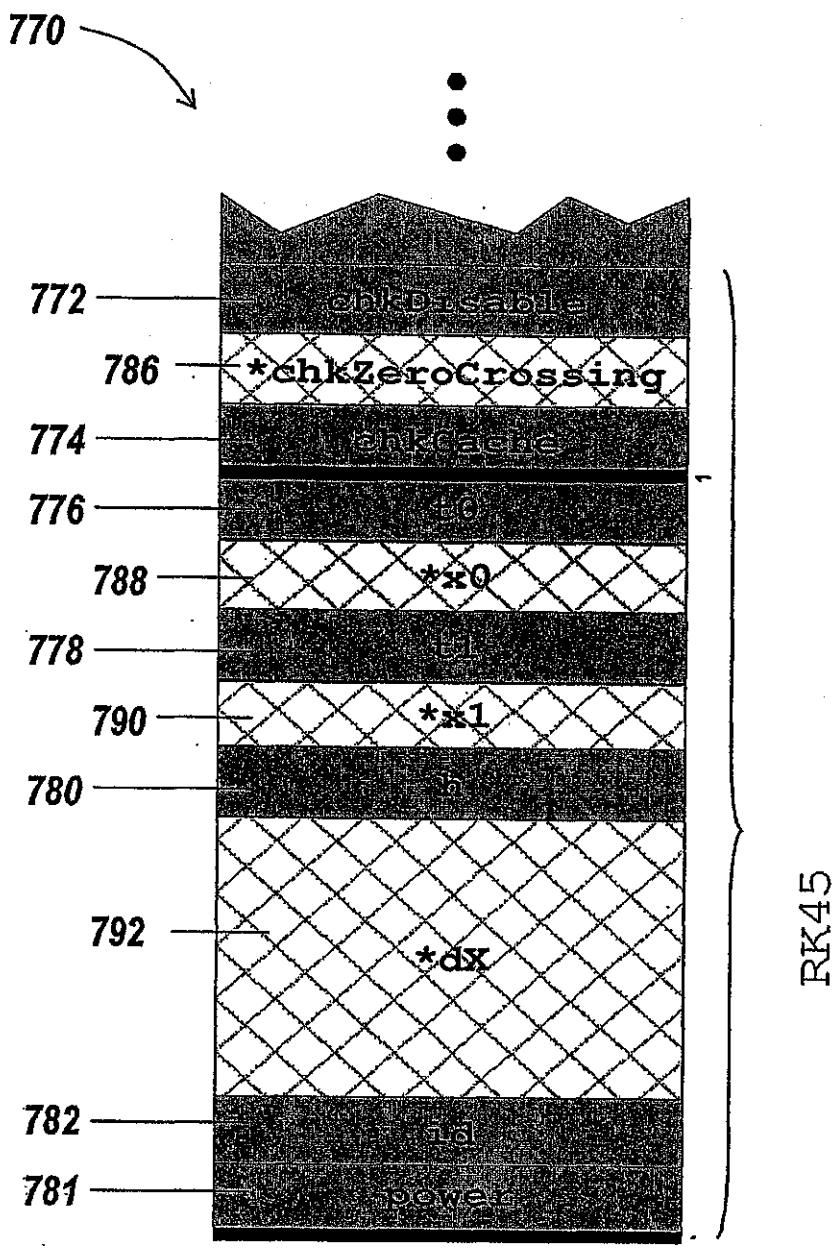

770
772
chkDisable
786
*chkZeroCrossing
774
chkCache
776
t0
788
*x0
778
t1
790
*x1
780
h
792
*dx
782
td
781
power
1
RK45

Fig. 7

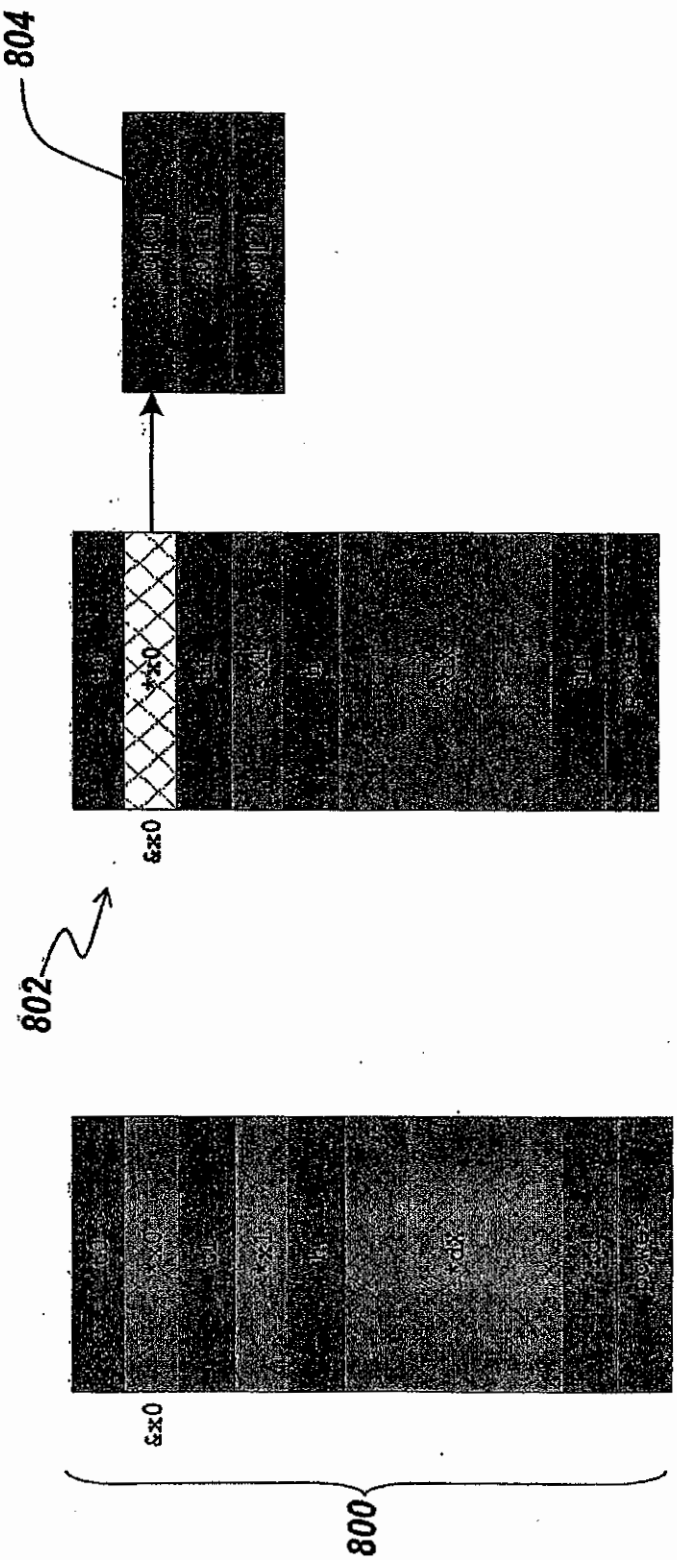


Fig. 8B

Fig. 8A

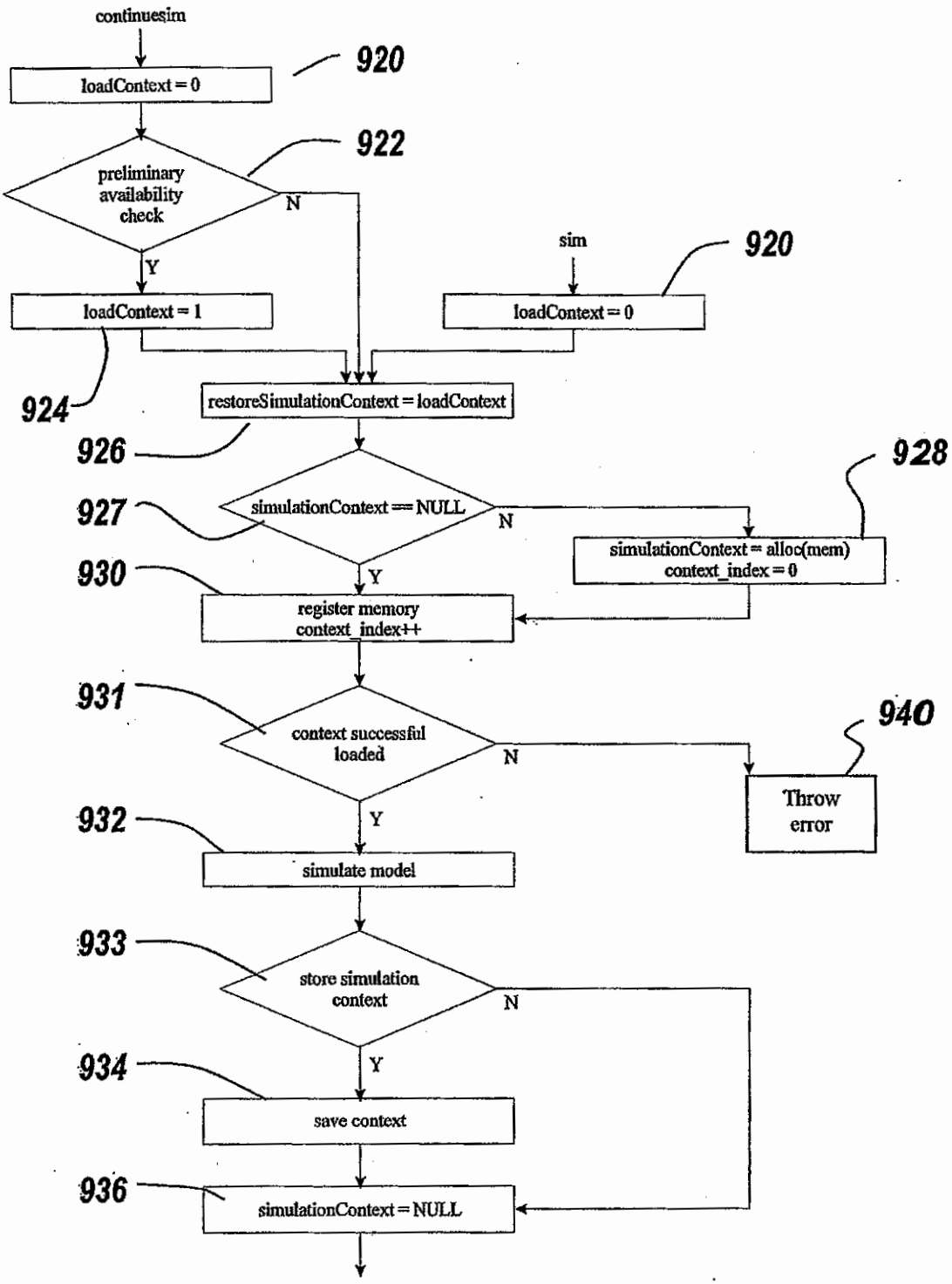

continuesim
loadContext = 0
920
preliminary availability check
922
N
Y
loadContext = 1
sim
loadContext = 0
920
924
restoreSimulationContext = loadContext
926
simulationContext == NULL
927
N
928
simulationContext = alloc(mem)
context_index = 0
Y
930
register memory
context_index++
931
context successful loaded
N
940
Throw error
Y
932
simulate model
933
store simulation context
N
Y
934
save context
936
simulationContext = NULL

Fig. 9