Process Diagram and Relationship Diagram

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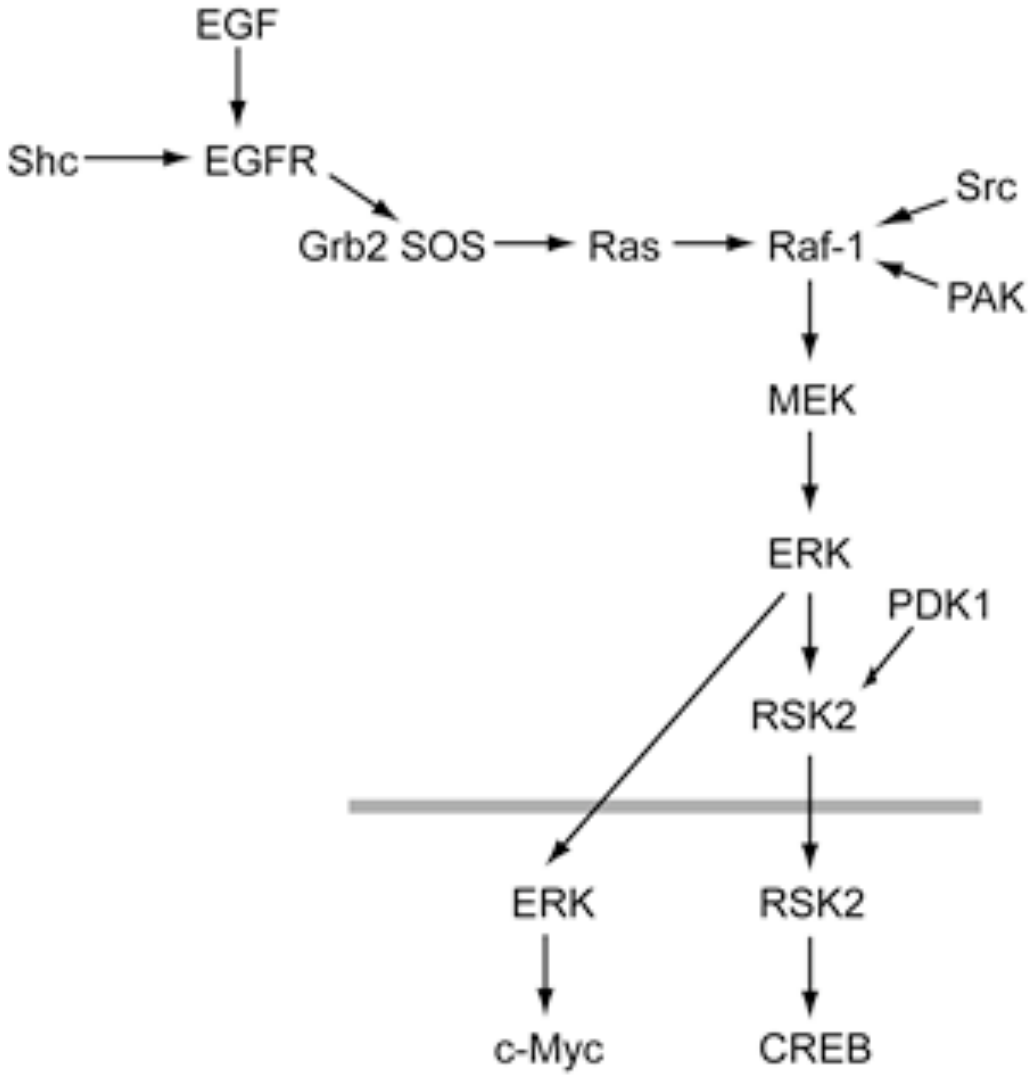
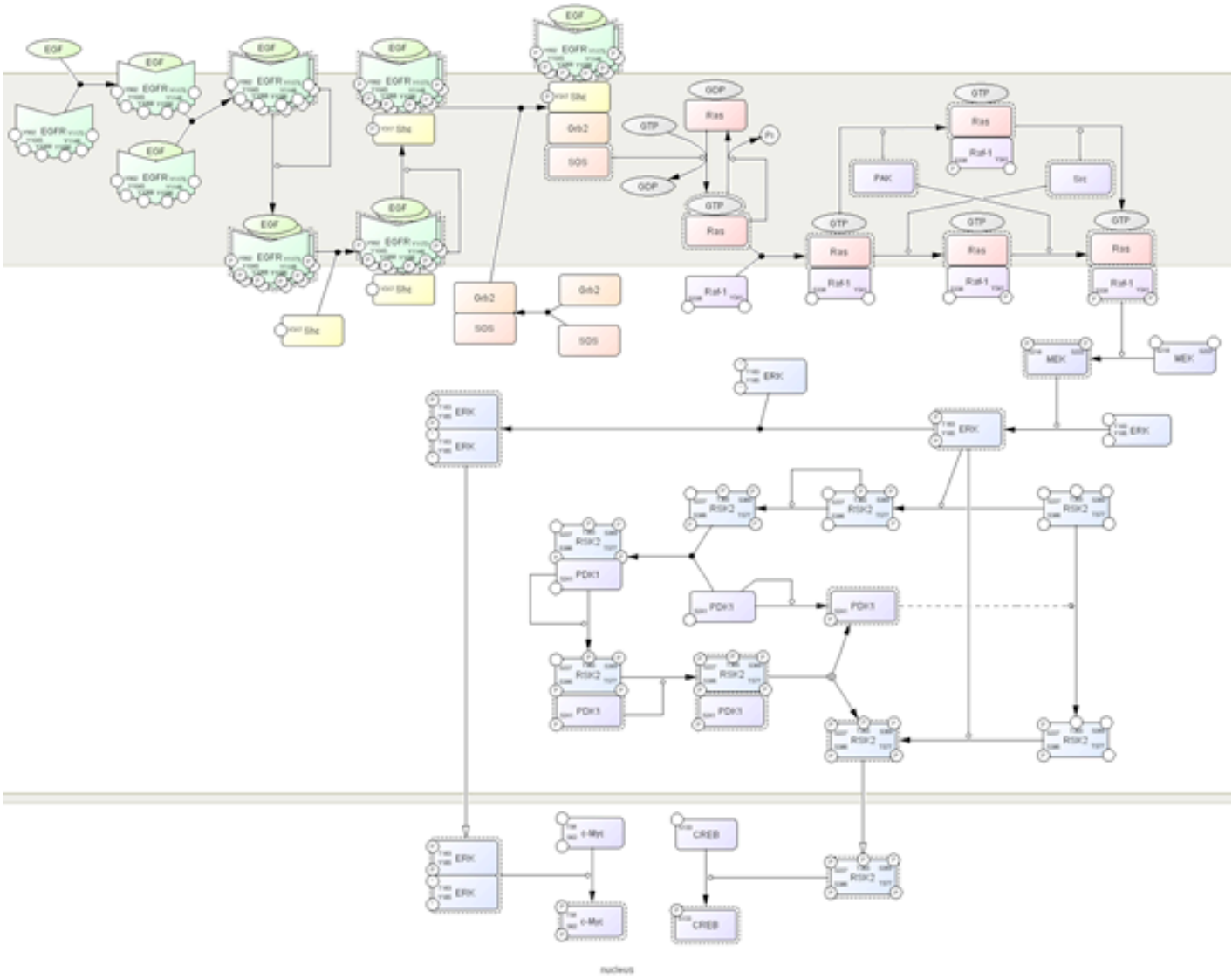
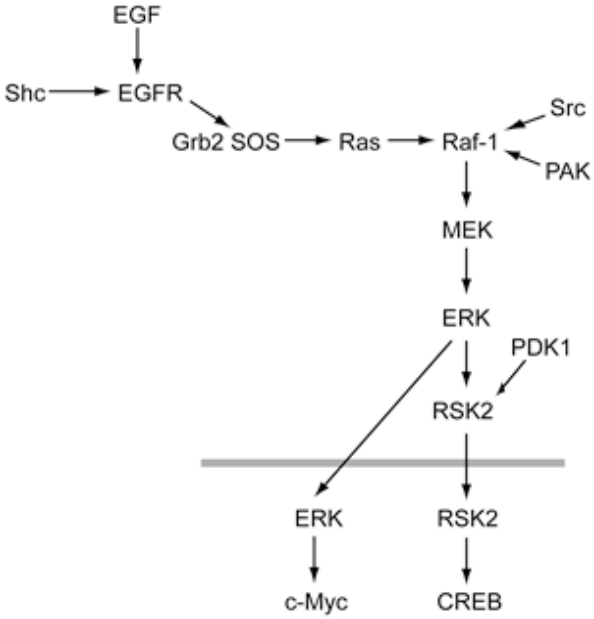
Funded by NEDO International Grant, Genome Network Project of MEXT, ERATO-SORST Program of JST.

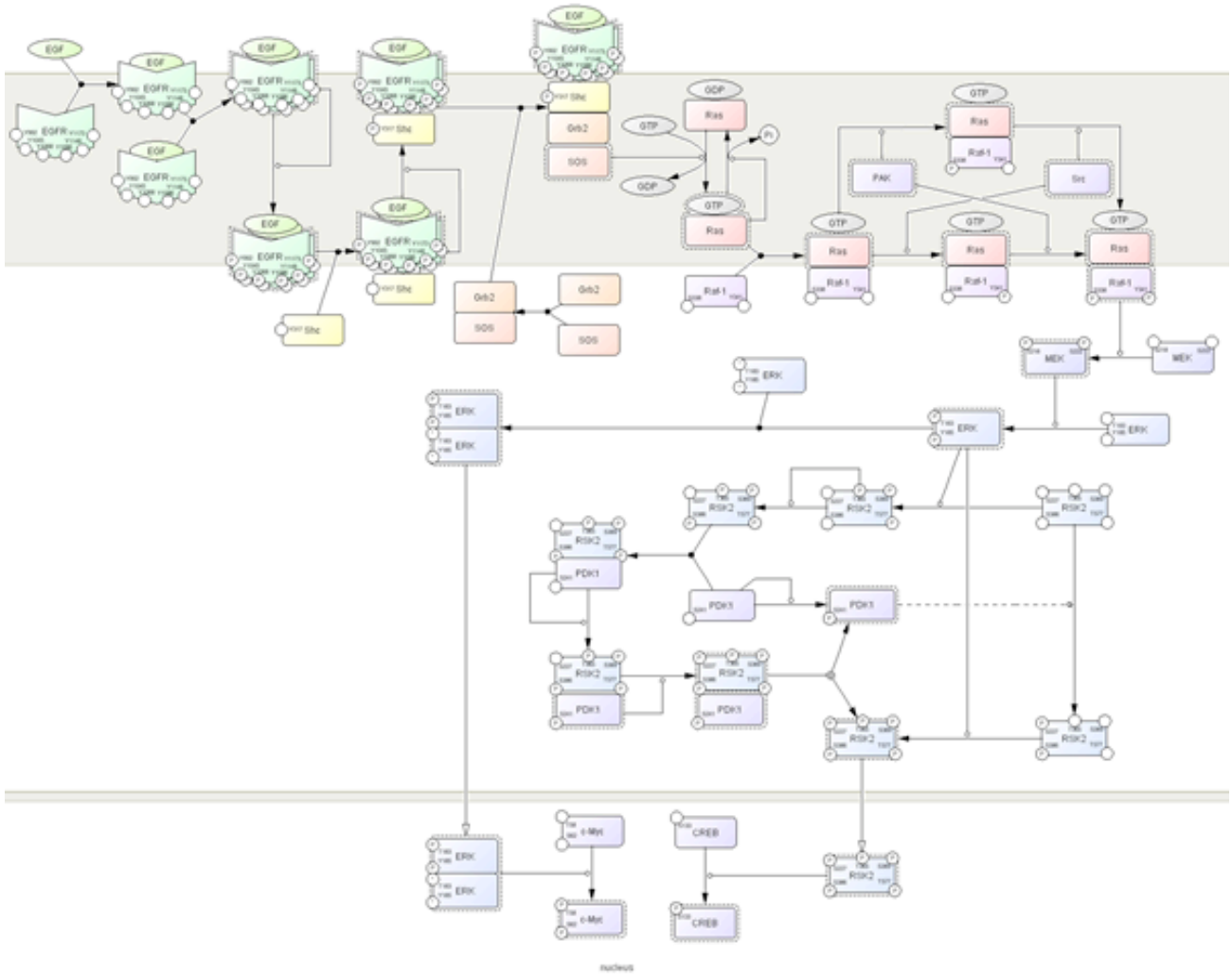
Pathway map used now

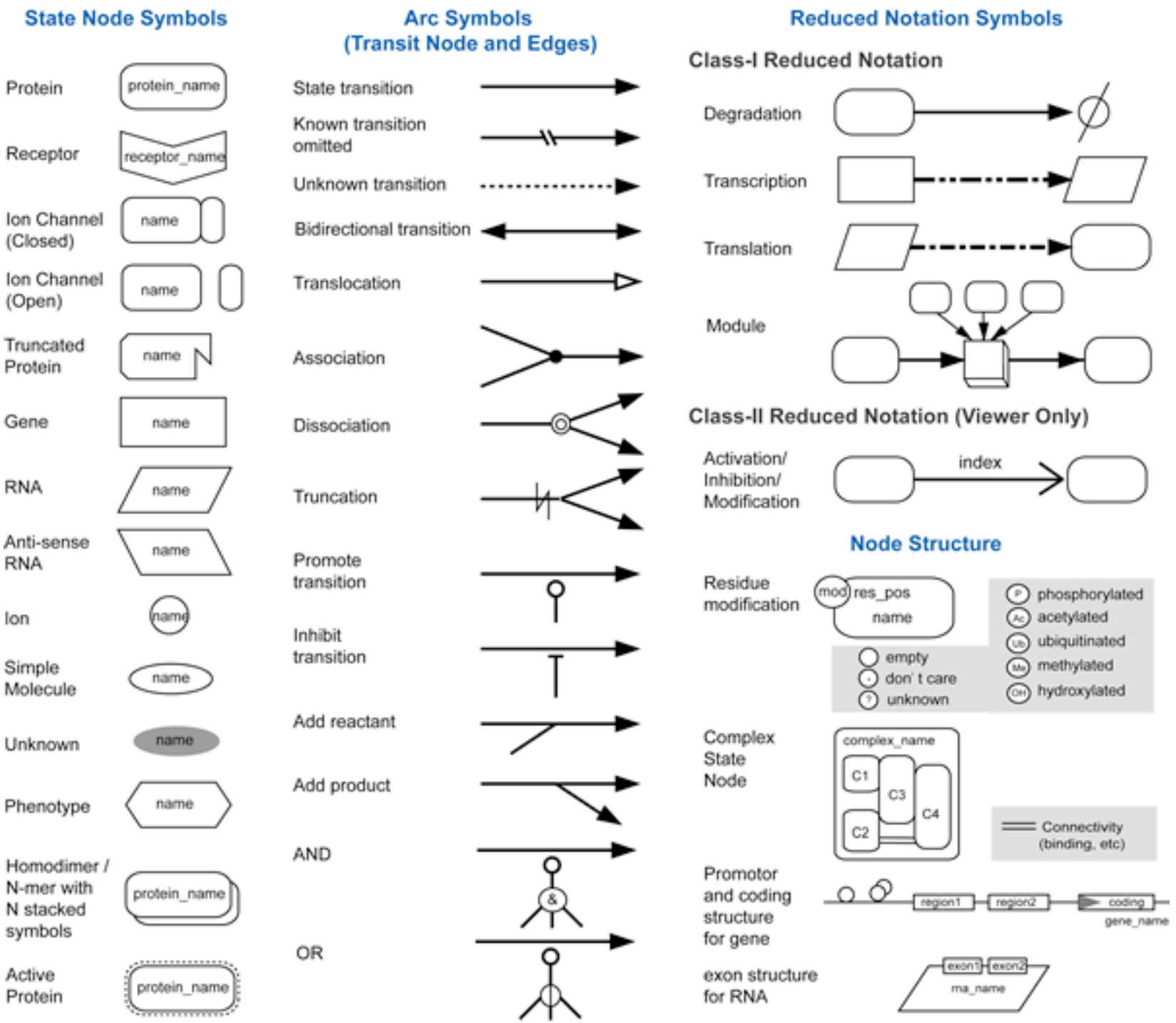


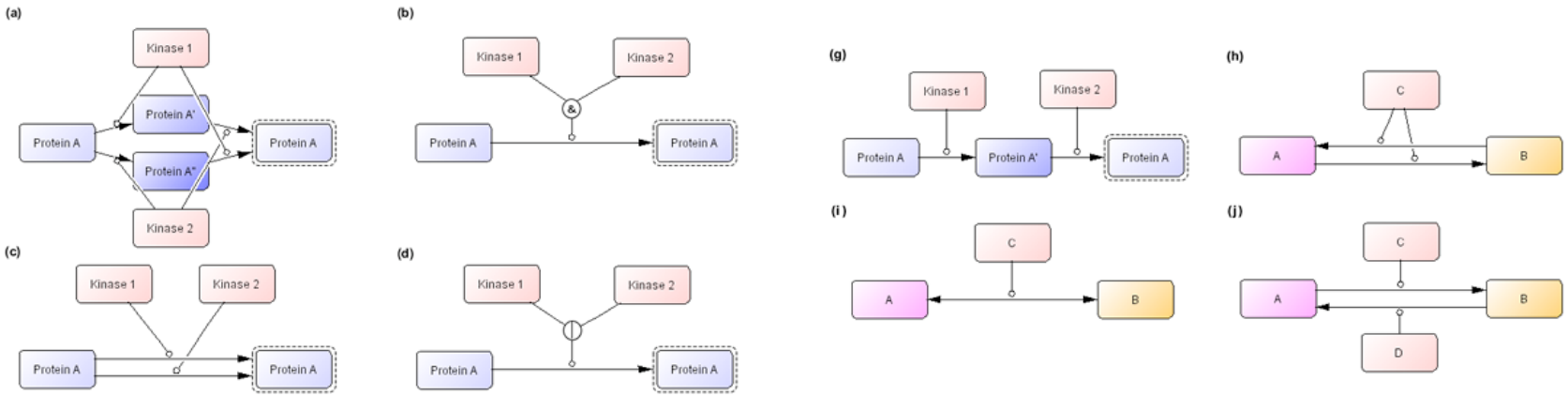
The Process Diagram



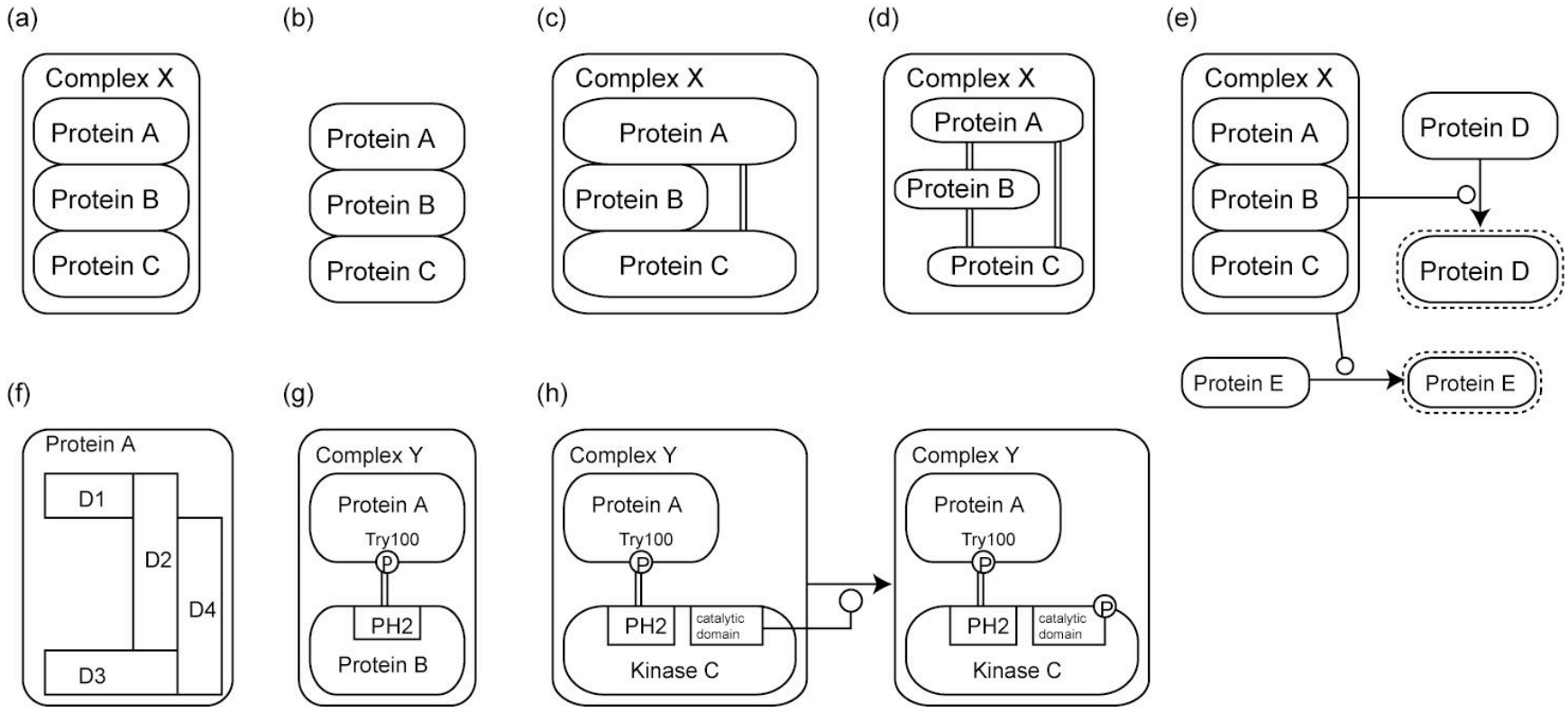

EGF
Shc
EGFR
Grb2 SOS
Ras
Raf-1
Src
PAK
MEK
ERK
PDK1
RSK2
ERK
RSK2
c-Myc
CREB




State Node Symbols
Protein
protein_name
Receptor
receptor_name
Ion Channel (Closed)
name
Ion Channel (Open)
name
Truncated Protein
name
Gene
name
RNA
name
Anti-sense RNA
name
Ion
name
Simple Molecule
name
Unknown
name
Phenotype
name
Homodimer / N-mer with N stacked symbols
protein_name
Active Protein
protein_name
Arc Symbols (Transit Node and Edges)
State transition
Known transition omitted
Unknown transition
Bidirectional transition
Translocation
Association
Dissociation
Truncation
Promote transition
Inhibit transition
Add reactant
Add product
AND
&
OR
Reduced Notation Symbols
Class-I Reduced Notation
Degradation
Transcription
Translation
Module
Class-II Reduced Notation (Viewer Only)
Activation/ Inhibition/ Modification
index
Node Structure
Residue modification
mod
res_pos
name
empty
don' t care
unknown
phosphorylated
acetylated
ubiquitinated
methylated
hydroxylated
Complex State Node
complex_name
C1
C2
C3
C4
Connectivity (binding, etc)
Promotor and coding structure for gene
region1
region2
coding
gene_name
exon structure for RNA
exon1
exon2
rna_name

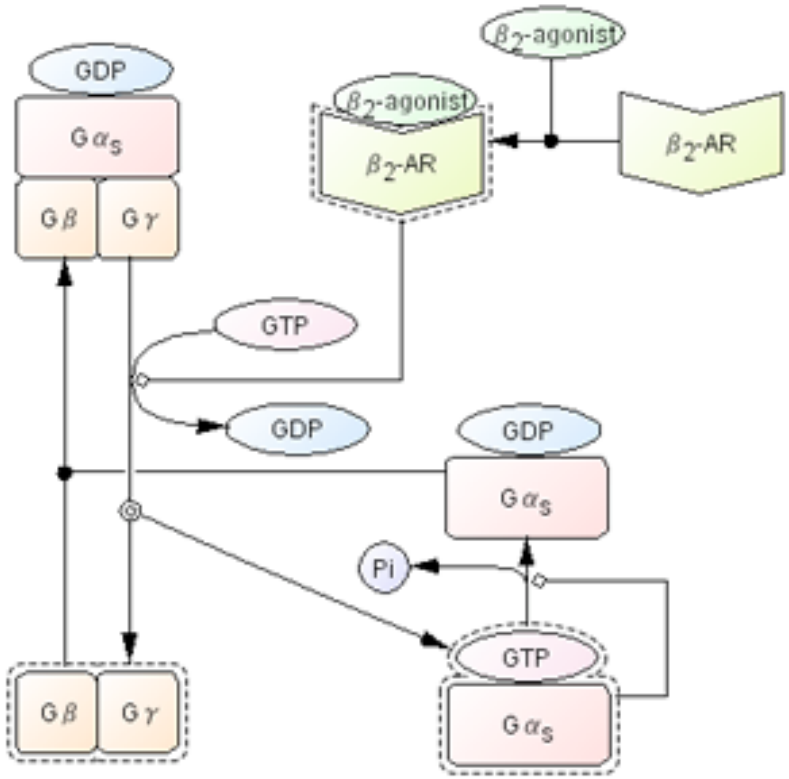

(a)
Kinase 1
Protein A'
Protein A
Protein A
Protein A"
Kinase 2
(b)
Kinase 1
Kinase 2
&
Protein A
Protein A
(c)
Kinase 1
Kinase 2
Protein A
Protein A
(d)
Kinase 1
Kinase 2
Protein A
Protein A
(g)
Kinase 1
Kinase 2
Protein A
Protein A'
Protein A
(h)
C
A
B
(i)
C
A
B
(j)
C
A
B
D

Structure of Complex

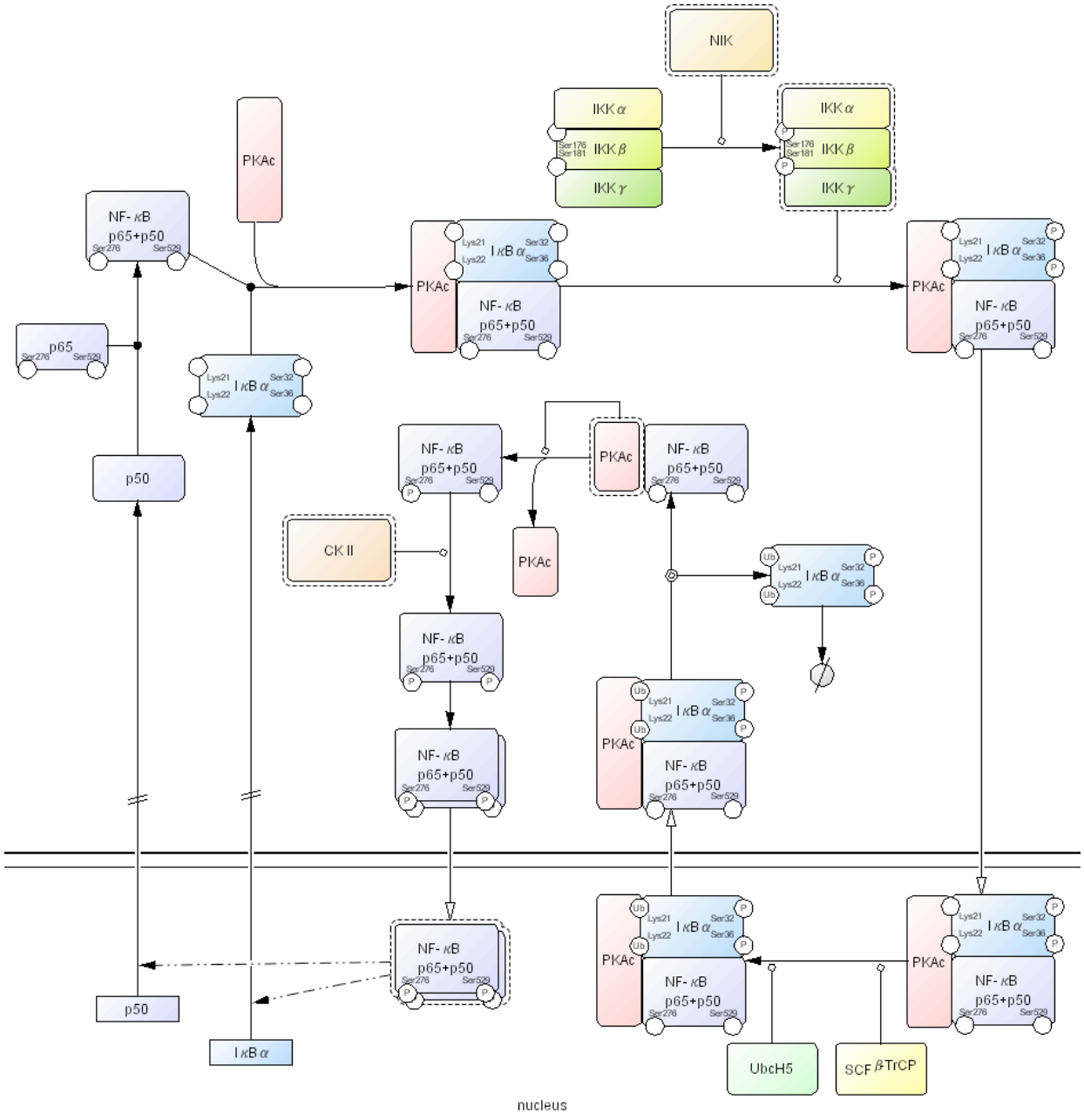


Example of
Process Diagram

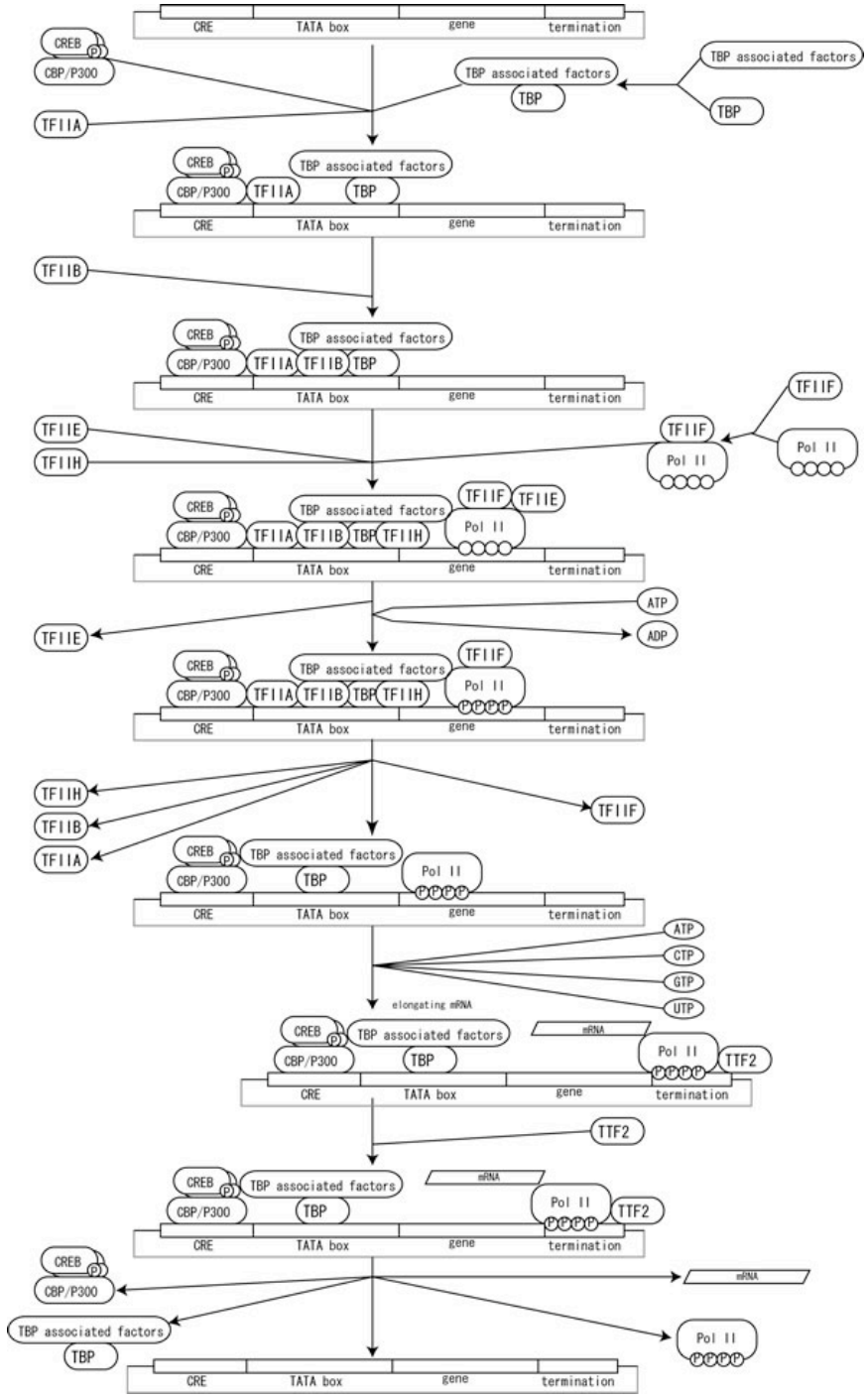
G-protein



Example of Process Diagram NFkB

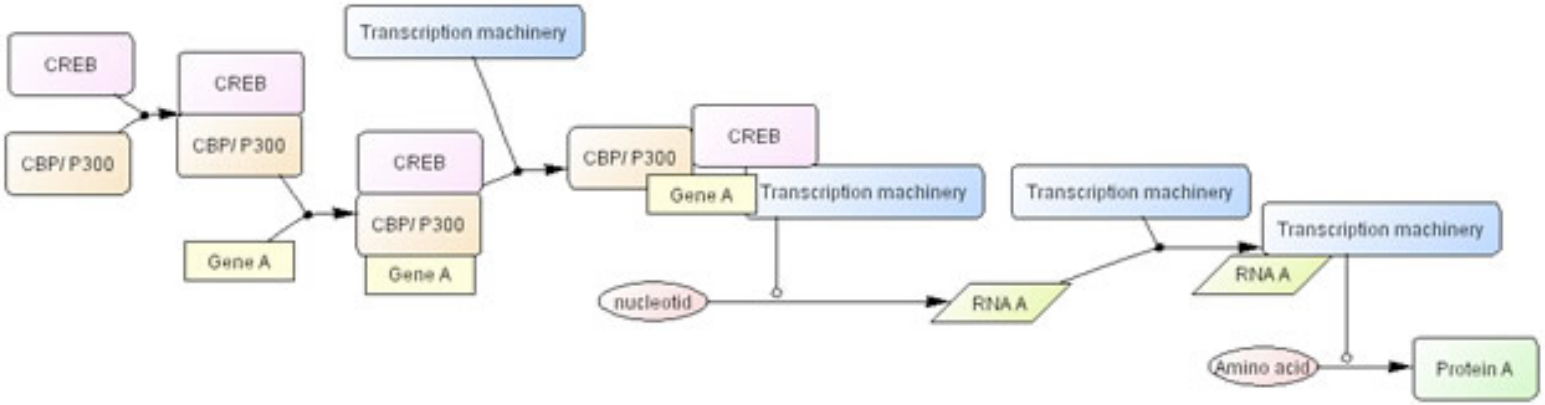


Process Diagram for Transcription

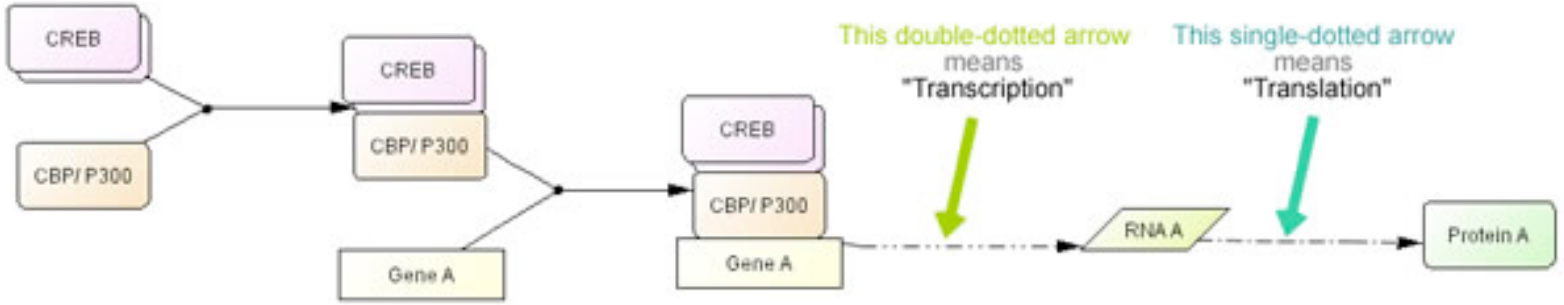


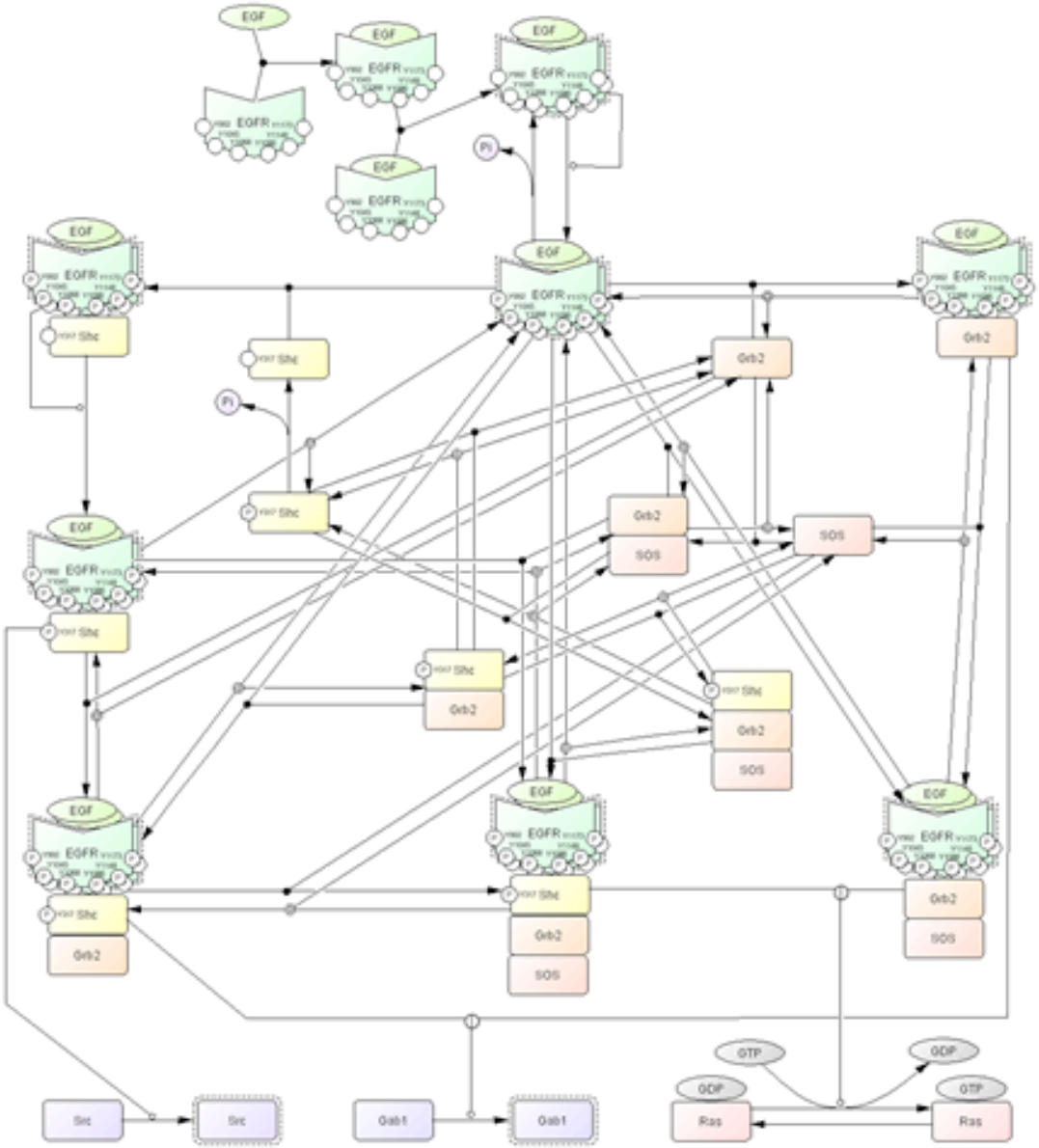
transcription and translation

Simplified notation

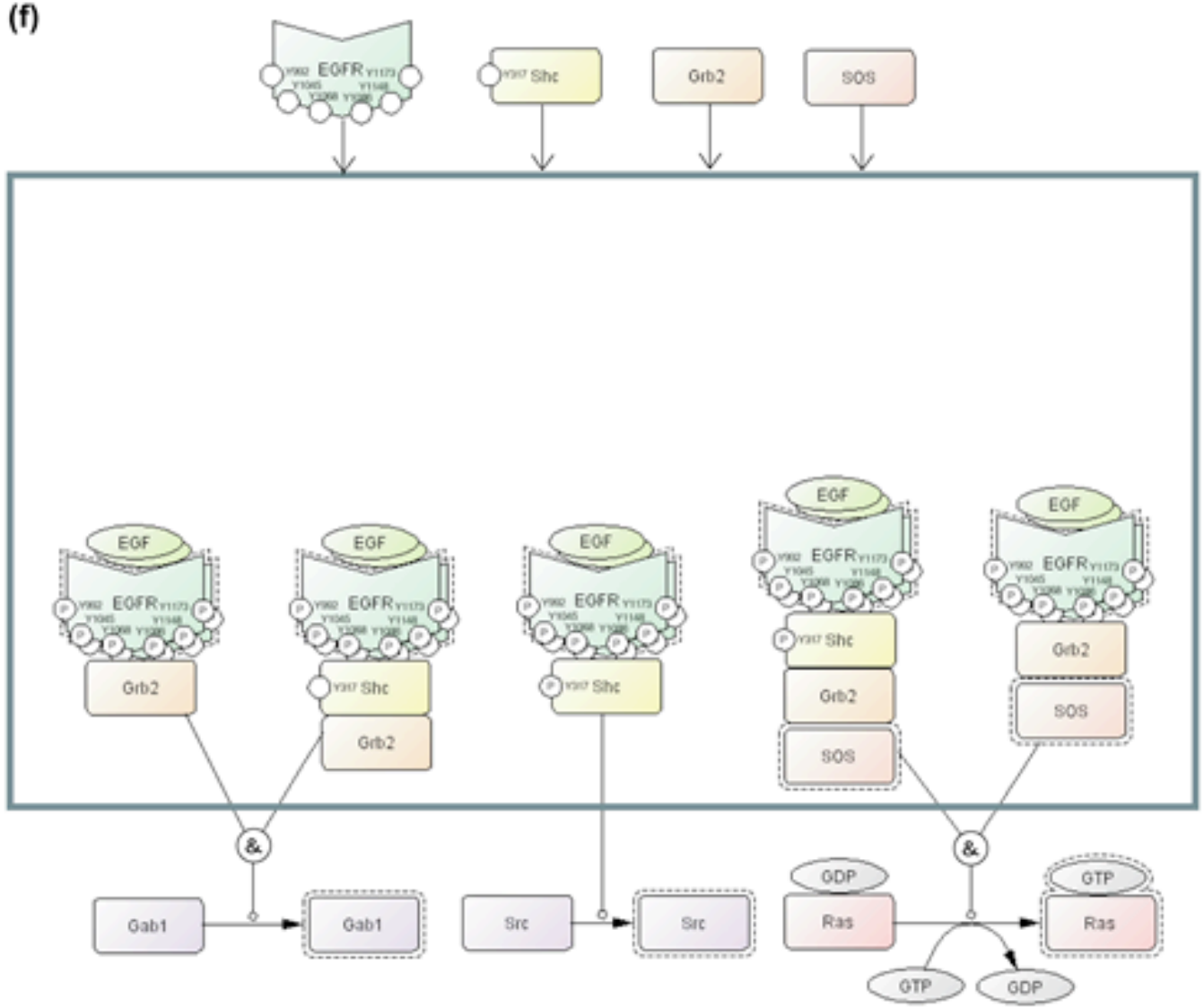


Reduced notation




EGF
EGFR
Shc
Grb2
SOS
Pi
GTP
GDP
Ras
Src
Gab1

(f)



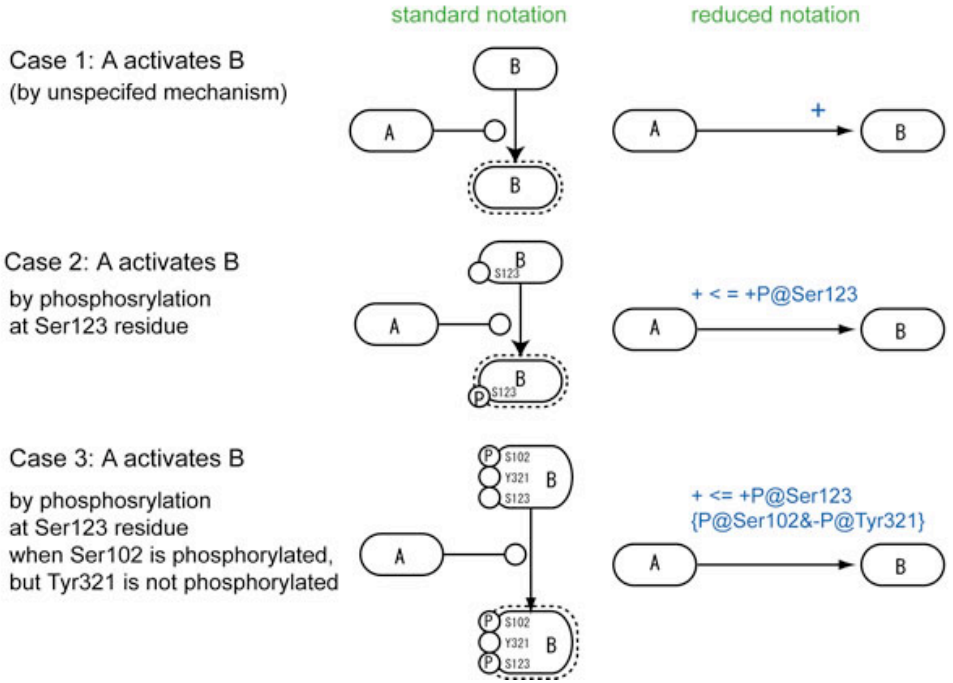
Can we simplify without losing information?

Syntax for Index on class-II reduced notation

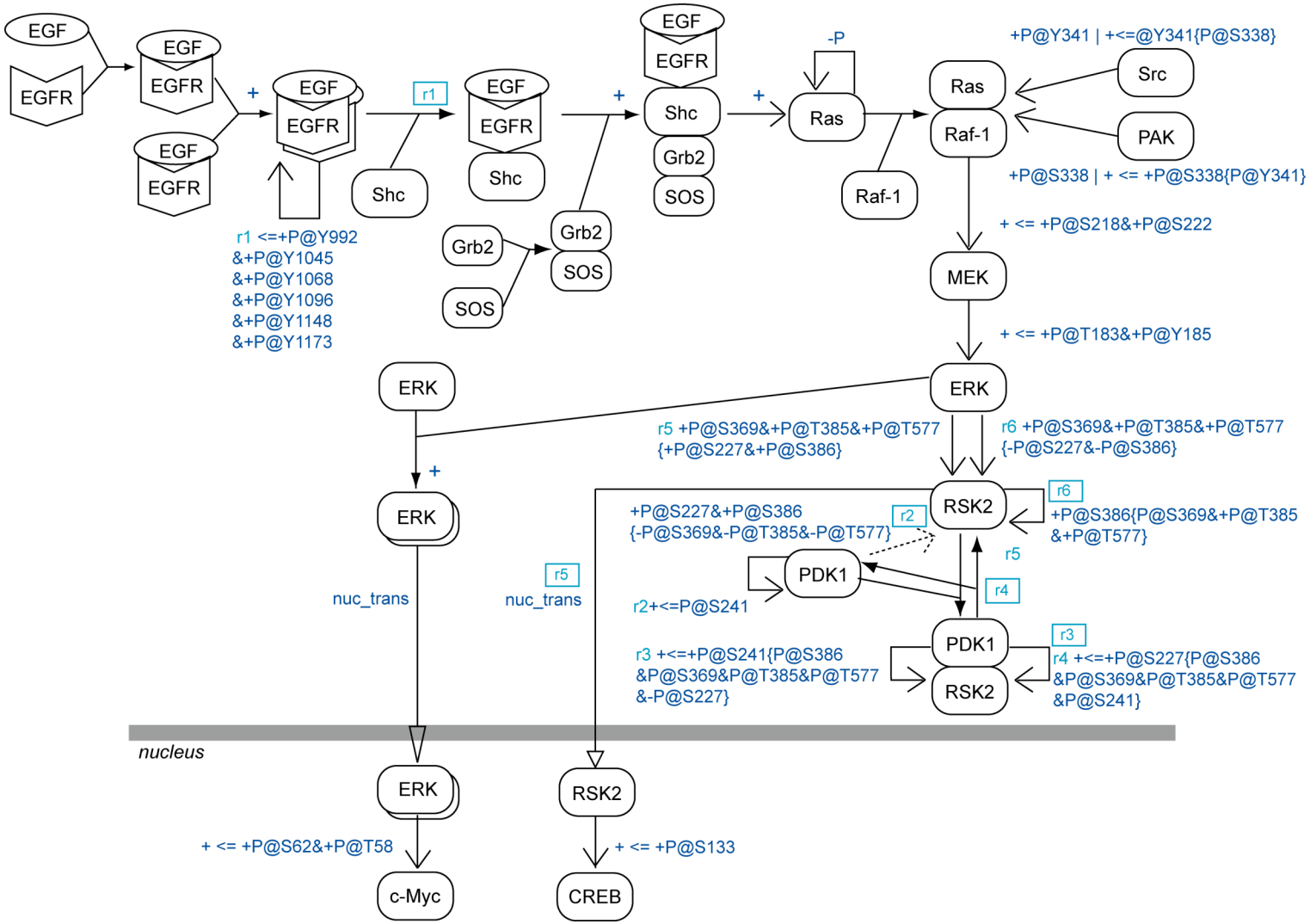
Syntax for index on class-II reduced notation

EffectDescription = Result ImmediateEffect Condition | SimpleSentence

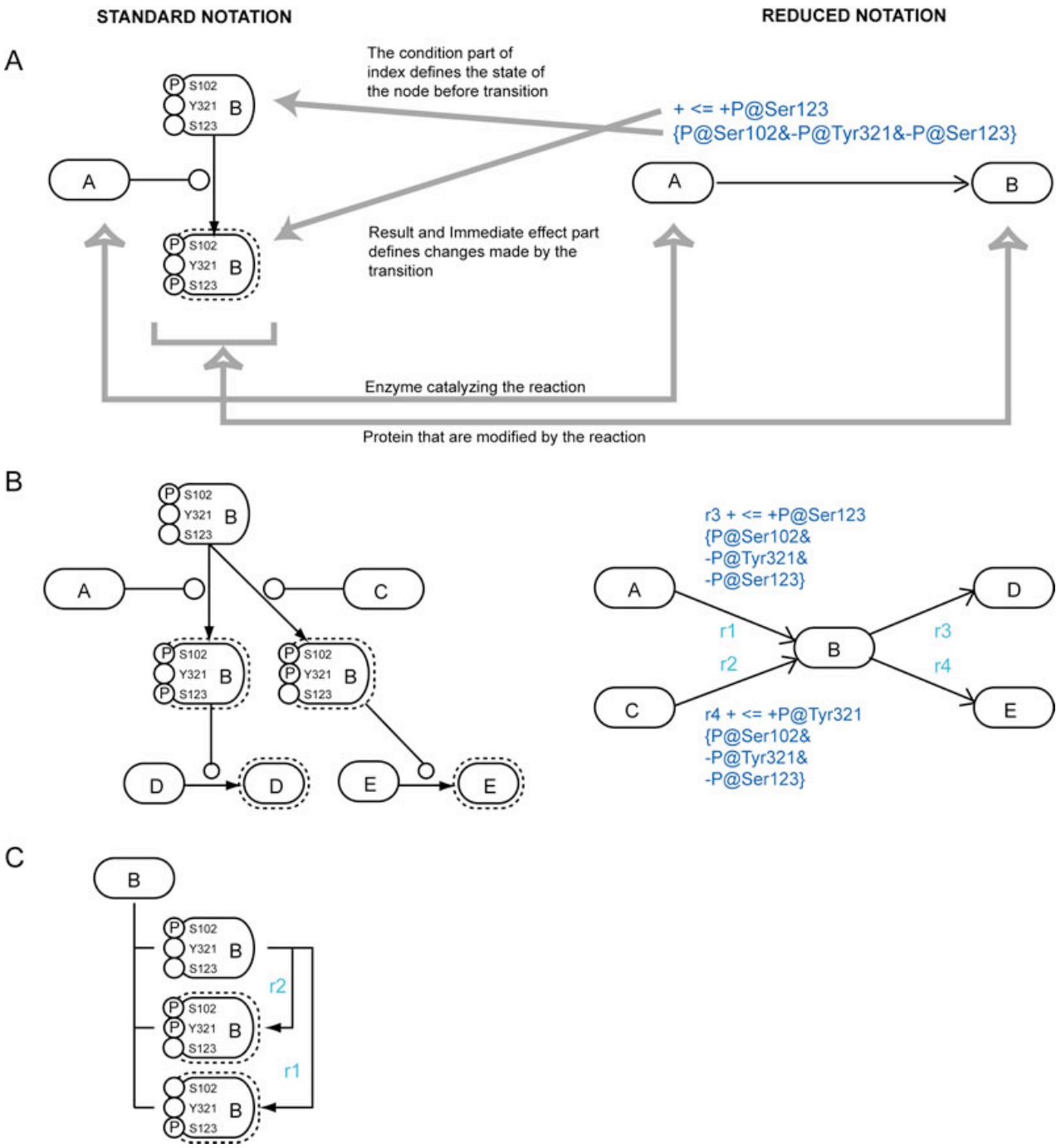
Result	= TRANSITION ('+' | '-' | empty) '<=' | empty
ImmediateEffect	= TERM_IE
Condition	= empty | '{' TERM_COND '}'
SimpleSentence	= ('+' | '-' | TRANSITION | '?')
TERM_IE	= RESIDUE_IE | TERM_IE OP TERM_IE
TERM_COND	= RESIDUE_COND | TERM_COND OP TERM_COND
RESIDUE_IE	= ('+' | '-') MODIFICATION ('@' TYPE [0-9]+ SUBUNIT | empty)
RESIDUE_COND	= ('-' | empty) MODIFICATION '@' TYPE [0-9]+
OP	= ('&' | '|')
MODIFICATION	= (P | Me | Ac | Ub | Hy) | (P | M | A | U | H)
TYPE	= (Tyr | Ser | Thr) | (Y | S | T)
SUBUNIT	= empty | '/' SUBUNIT_NAME
TRANSITION	= [a-zA-Z]+[0-9]*
SUBUNIT_NAME	= [a-zA-Z0-9]+



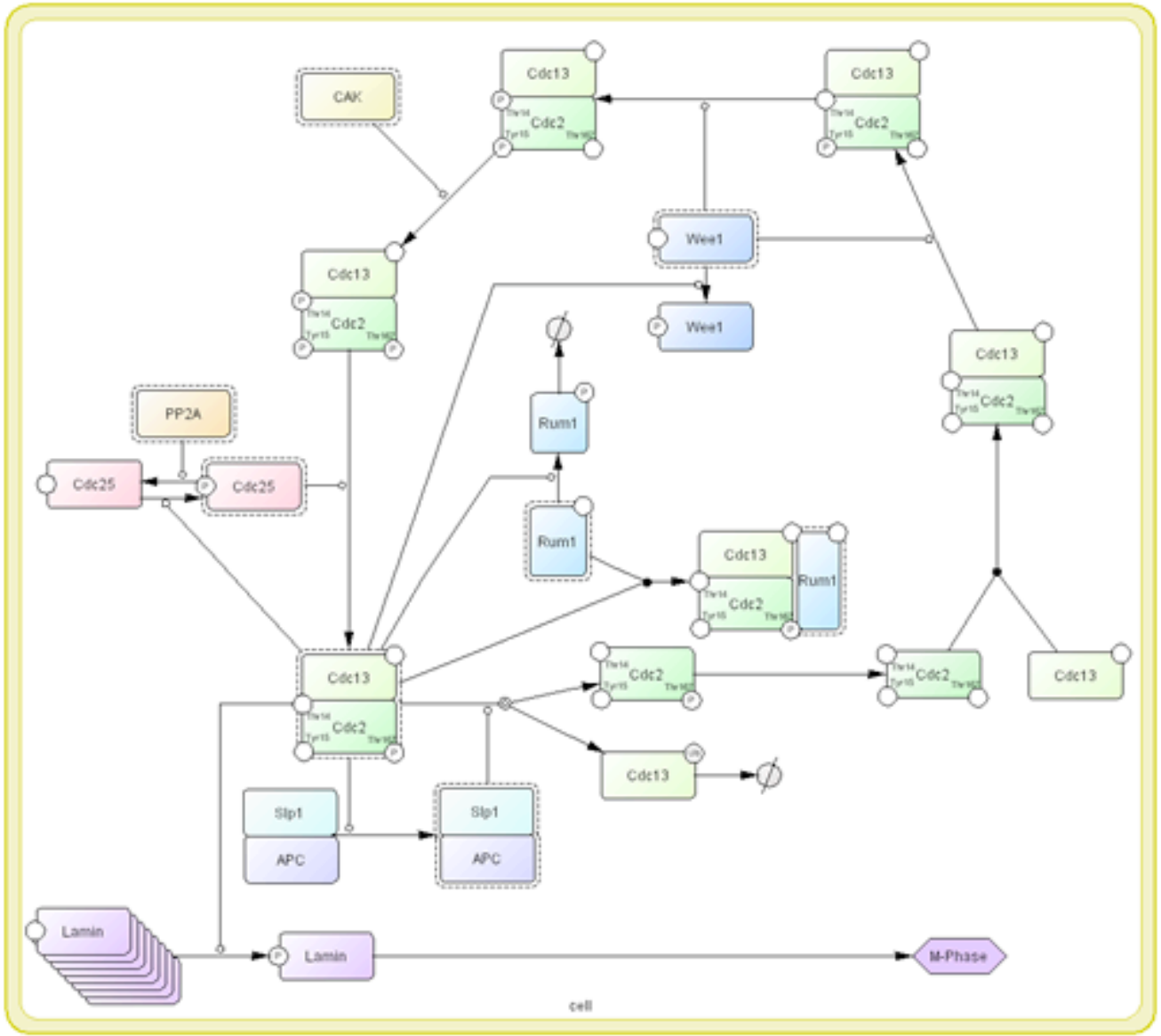
Reduced Notation

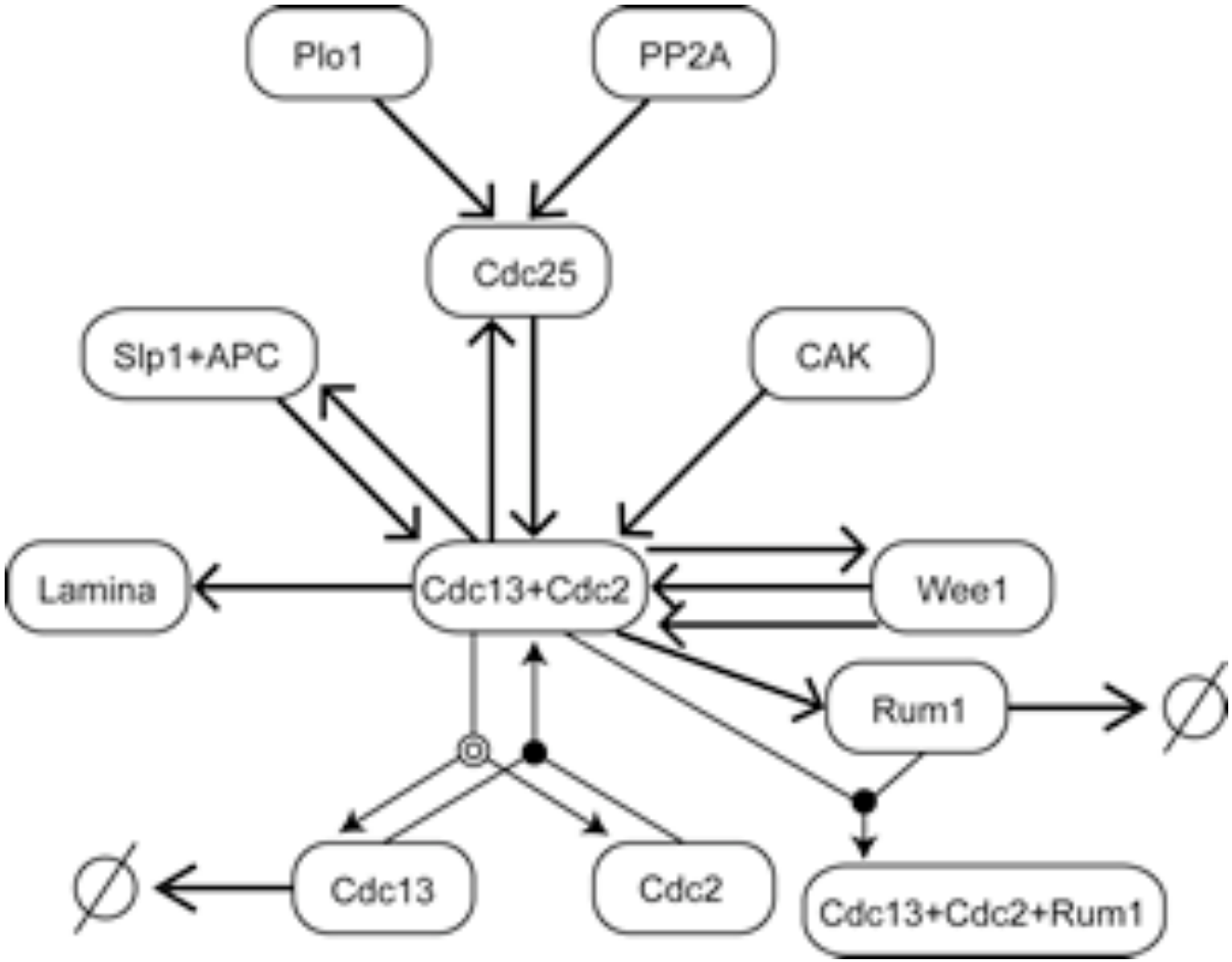


Standard Notation vs Reduced Notation

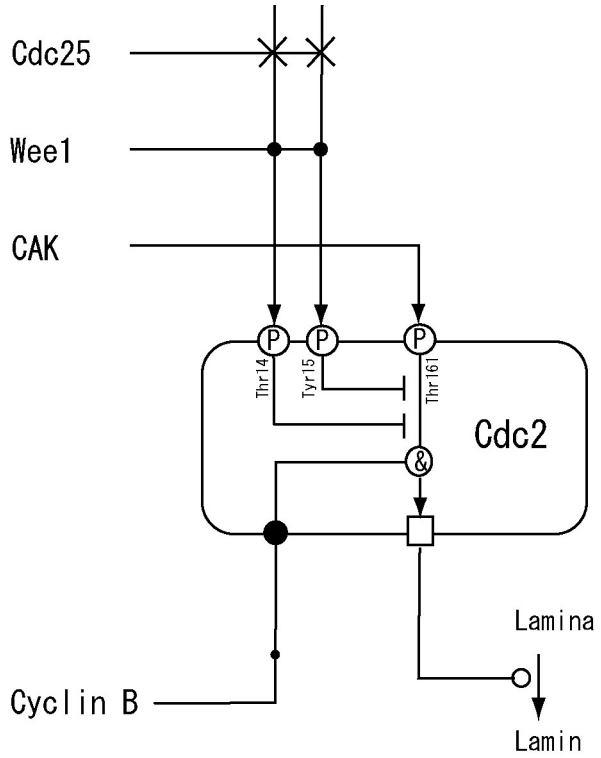


MPF cycle


CAK
Cdc13
Cdc2
Thr14
Tyr15
Thr161
Wee1
PP2A
Cdc25
Rum1
Slp1
APC
Lamin
M-Phase
cell

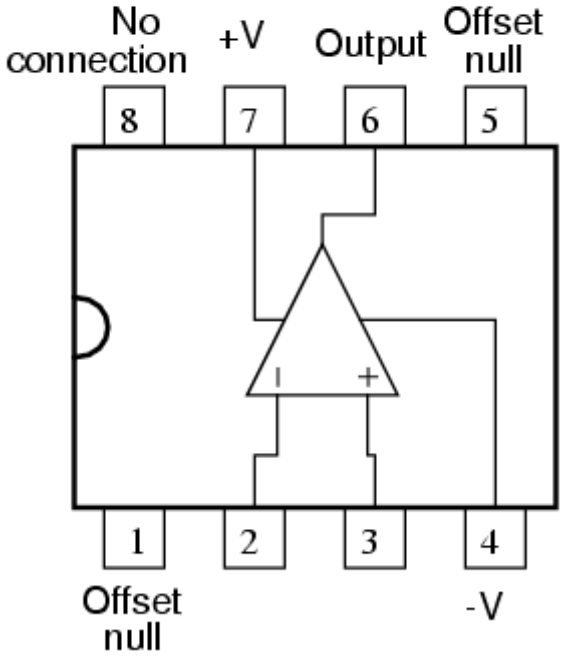

Plo1
PP2A
Cdc25
Slp1+APC
CAK
Lamina
Cdc13+Cdc2
Wee1
Rum1
∅
∅
Cdc13
Cdc2
Cdc13+Cdc2+Rum1

Relationship View

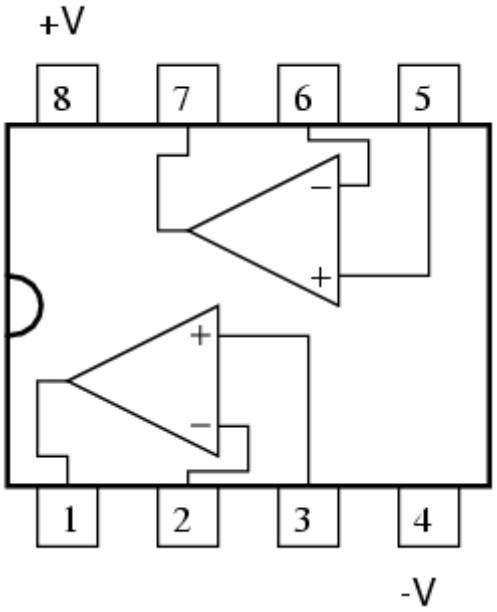


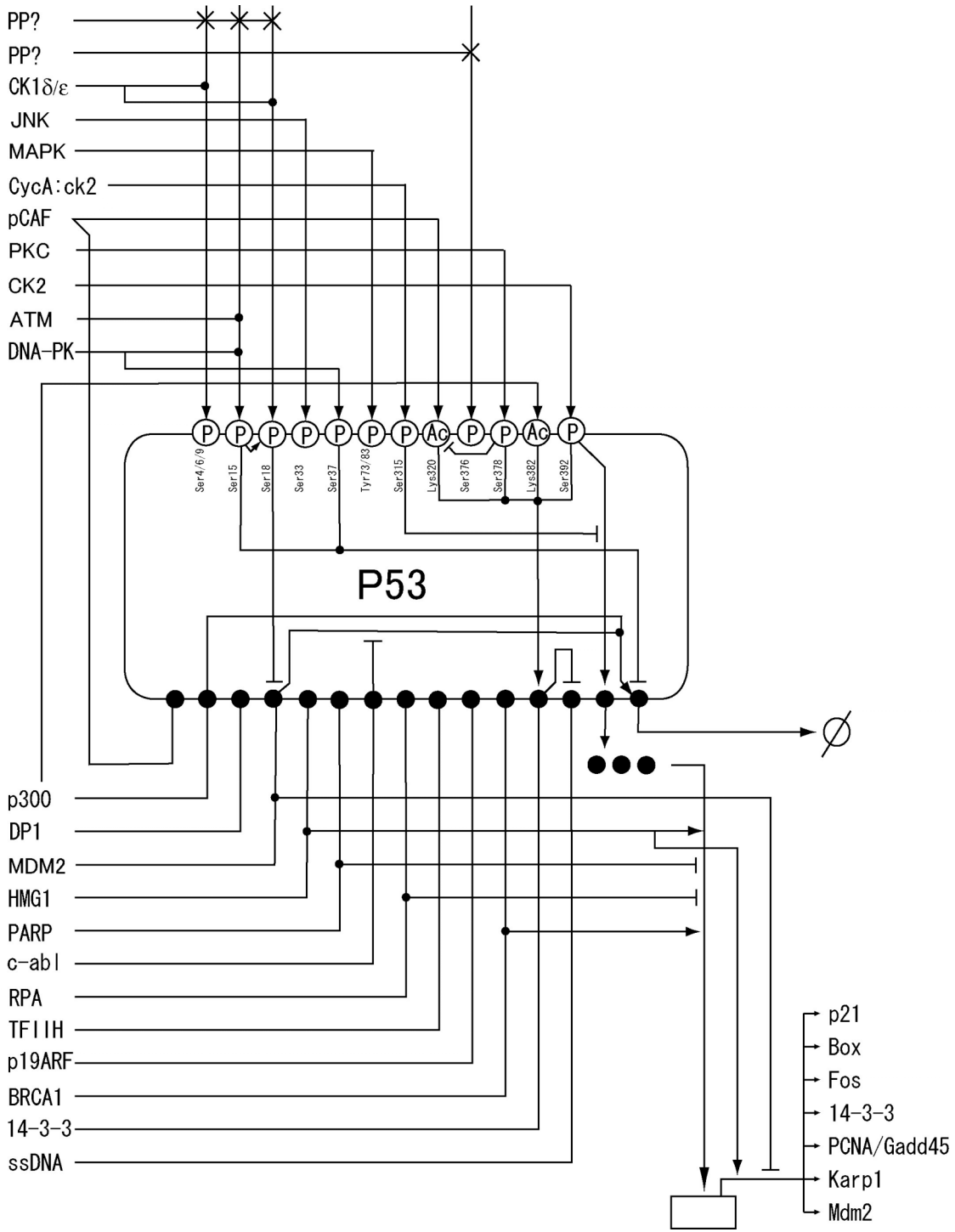
LSI diagram

Typical 8-pin "DIP" op-amp integrated circuit

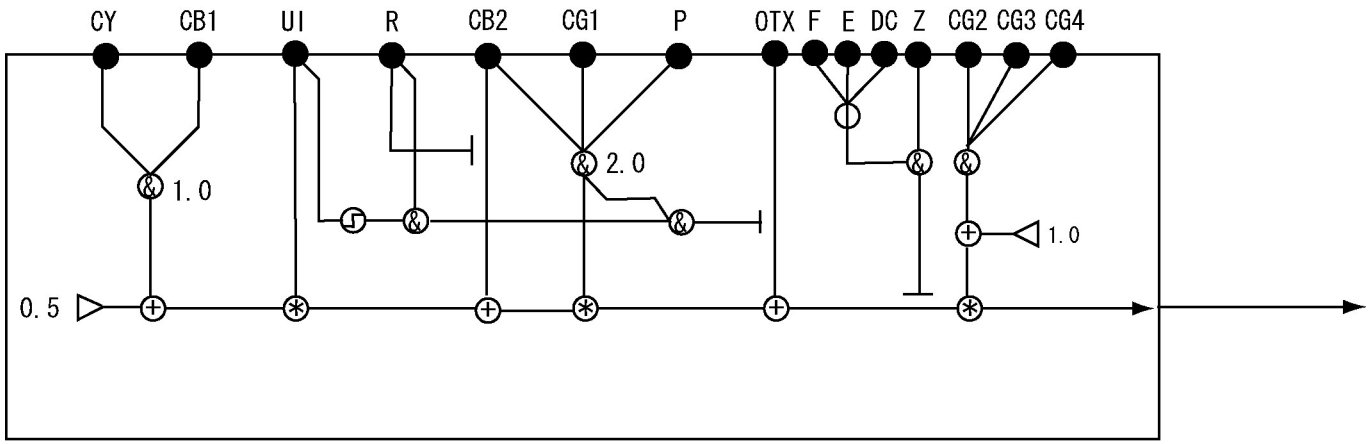


Dual op-amp in 8-pin DIP

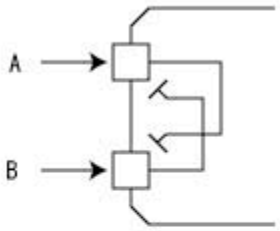



PP?
PP?
CK1δ/ε
JNK
MAPK
CycA:ck2
pCAF
PKC
CK2
ATM
DNA-PK
P
Ac
Ser4/6/9
Ser15
Ser18
Ser33
Ser37
Tyr73/83
Ser315
Lys320
Ser376
Ser378
Lys382
Ser392
P53
∅
p300
DP1
MDM2
HMG1
PARP
c-abl
RPA
TFIIH
p19ARF
BRCA1
14-3-3
ssDNA
p21
Box
Fos
14-3-3
PCNA/Gadd45
Karp1
Mdm2

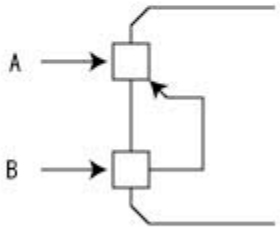
endo16



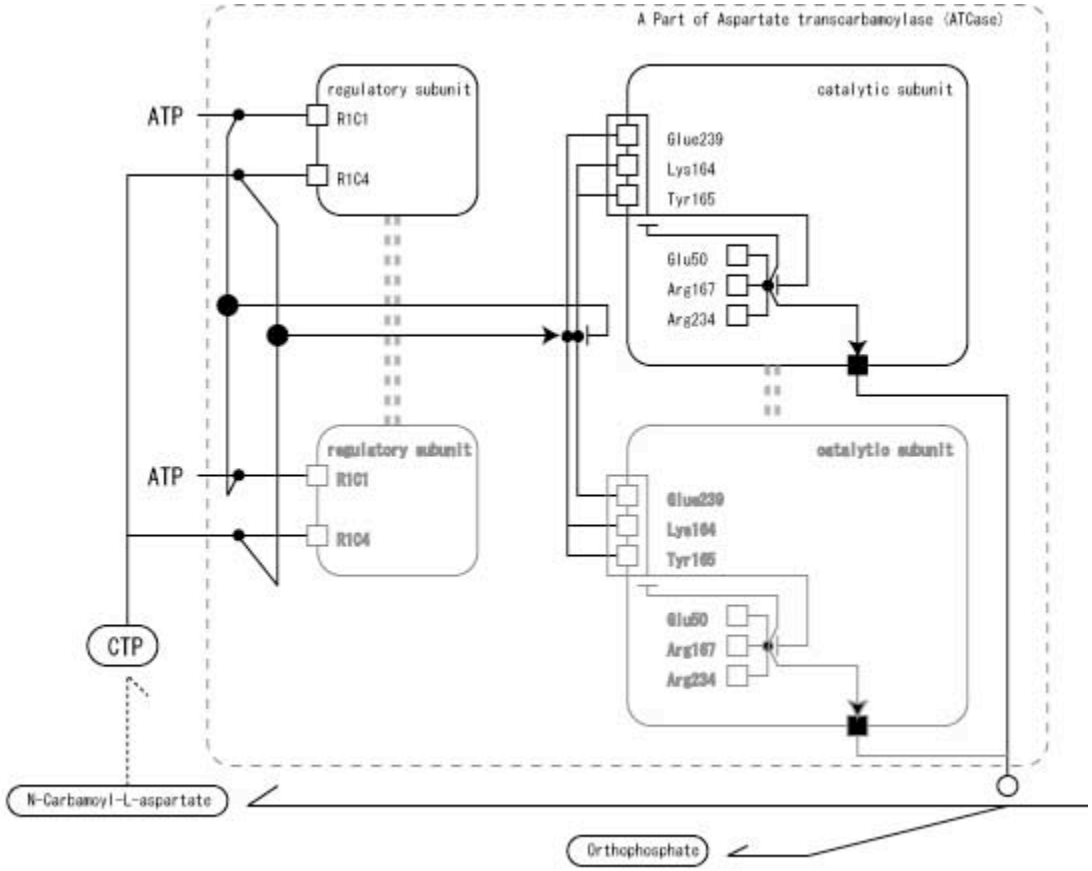
Allosteric Reaction



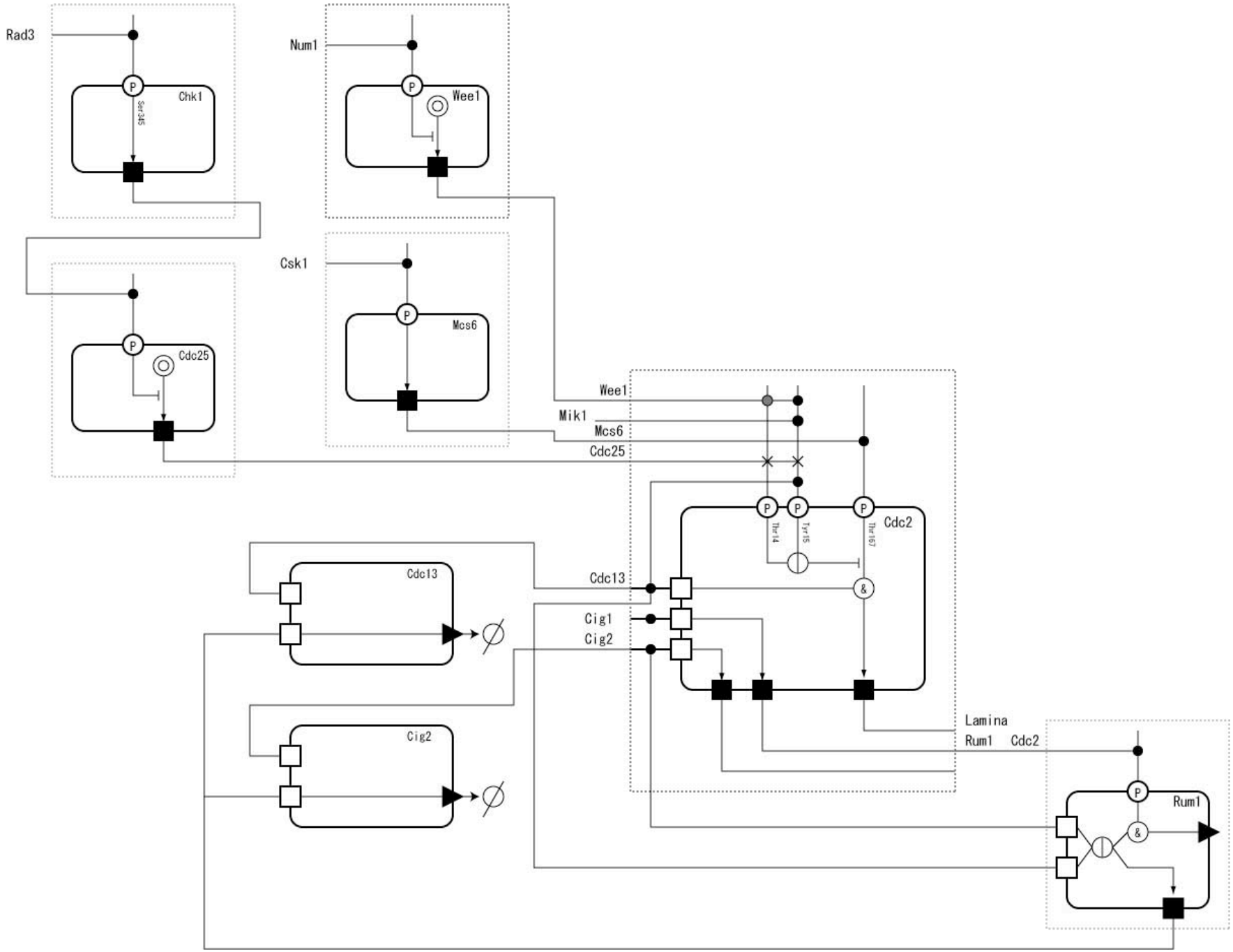
(A) Inhibitory Allosteric Reaction



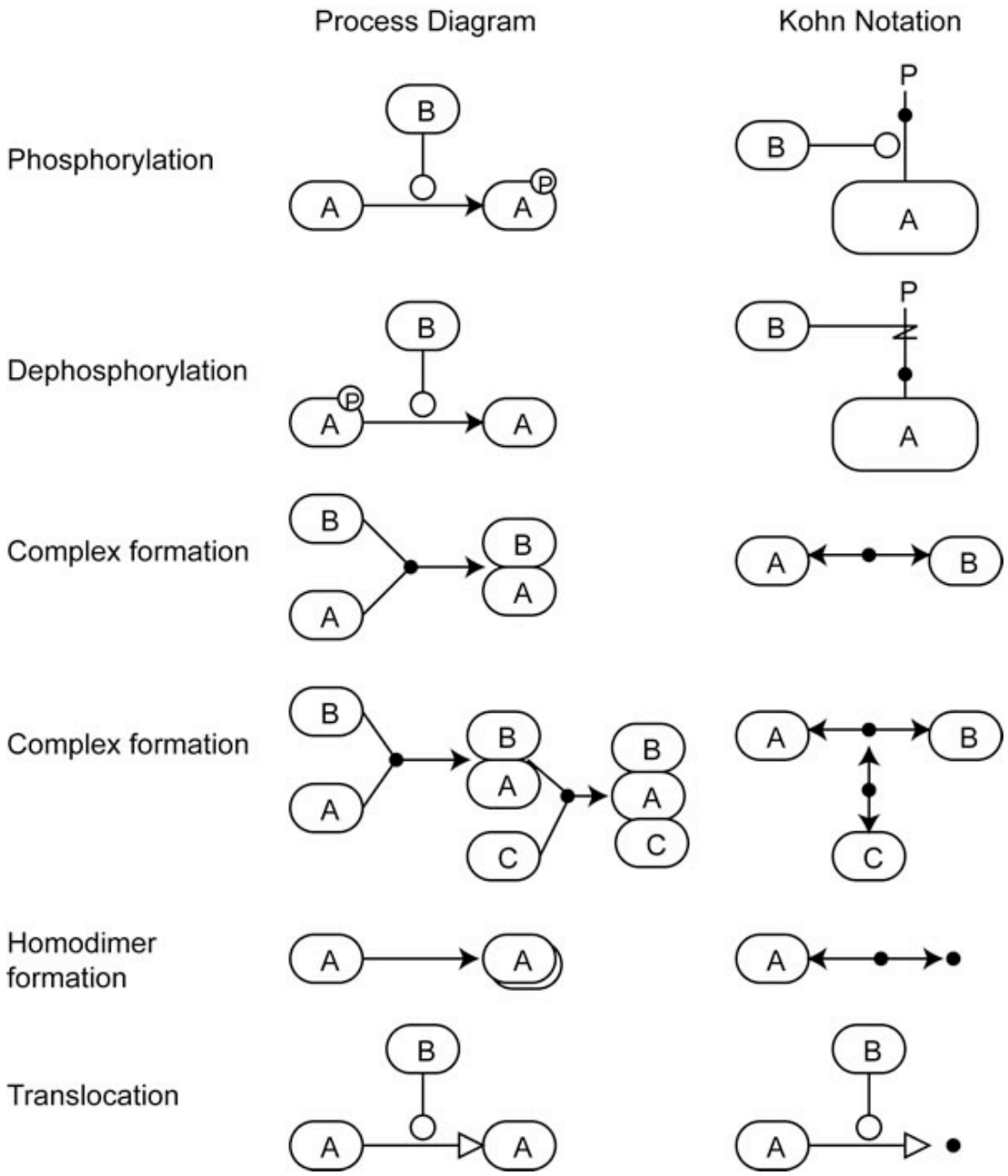
(B) Cooperative Allosteric Reaction



(C) A Part of Allosteric Reactions in aspartate transcarbamoylase


Rad3
P
Chk1
Ser345
Num1
P
Wee1
Csk1
P
Mcs6
P
Cdc25
Wee1
Mik1
Mcs6
Cdc25
P
P
P
Cdc2
Thr14
Tyr15
Thr167
&
Cdc13
Cig1
Cig2
Cdc13
Cig2
Lamina
Rum1
Cdc2
P
Rum1
&

Process Diagram vs Kohn Notation



Summary

- Process diagram (state-transition) + entity-relationship diagram
- Reduced notation can be “information/activation flow diagram”
- Not on PPI, etc.
- Compatibility need to be ensured.

Motivation

- Graphical diagram is an essential aspects of systems science
  - Electronics industry could not have prospered without solid circuit diagram notation
- Graphical diagram in biology is very informal
  - Lack information contents
  - Ambiguous or even misleading
  - Not grounded on mathematical basis
  - Hampers large-scale efforts
- Systems Biology Graphical Notation (SBGN: http://www.sbgn.org/) as the standard graphical notation

SBGN features

- Well defined graphical notation
- Consistent with SBML and other standards
- Model-View Approach
  - Process Diagram View
    - One state = One Node
    - State Transition Diagram
  - Relationship Diagram View (similar to Kohn Map)
    - One Species = One Node
    - Entity-Relationship Diagram