

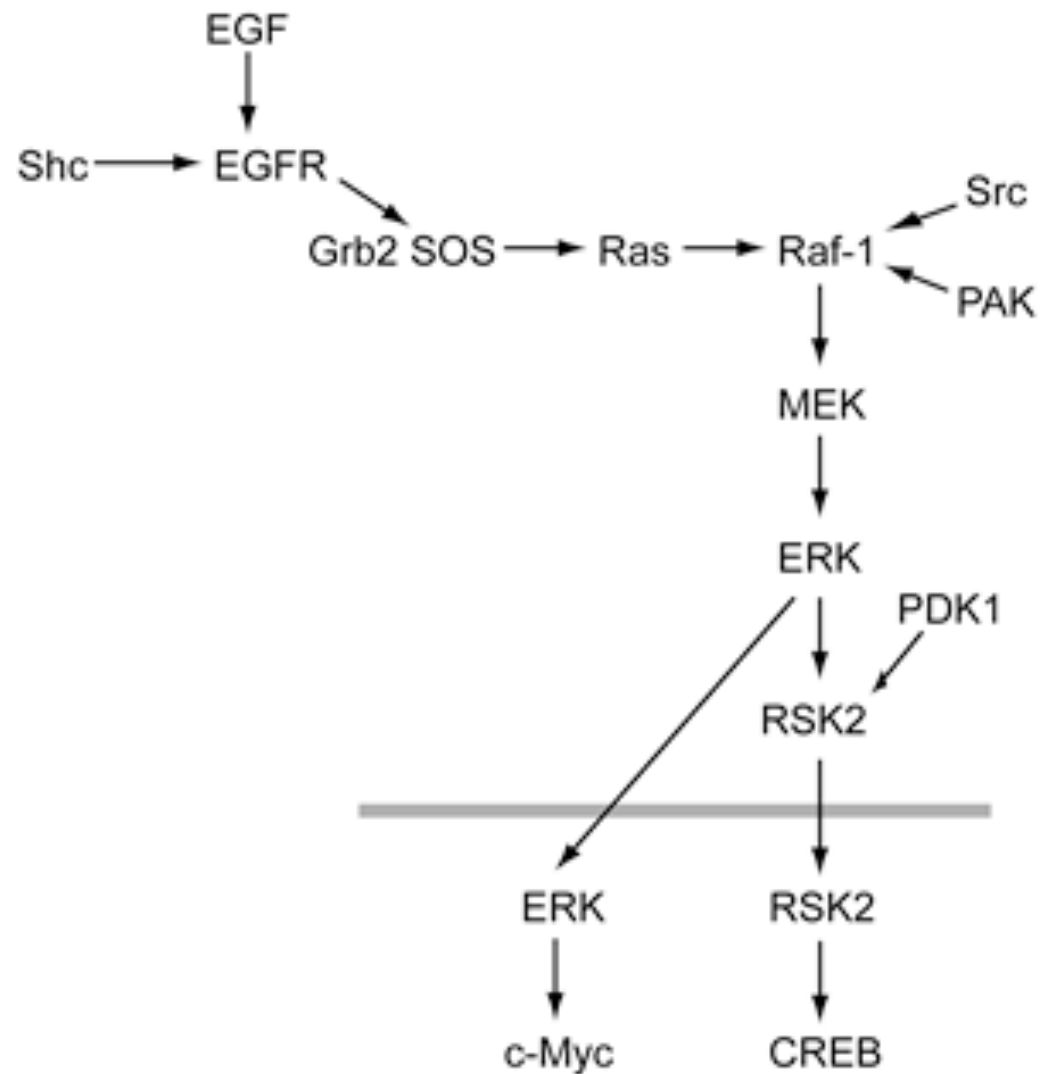


Process Diagram and Relationship Diagram

Hiroaki Kitano
The Systems Biology Institute

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ERATO-SORST Program of JST.

Pathway map used now

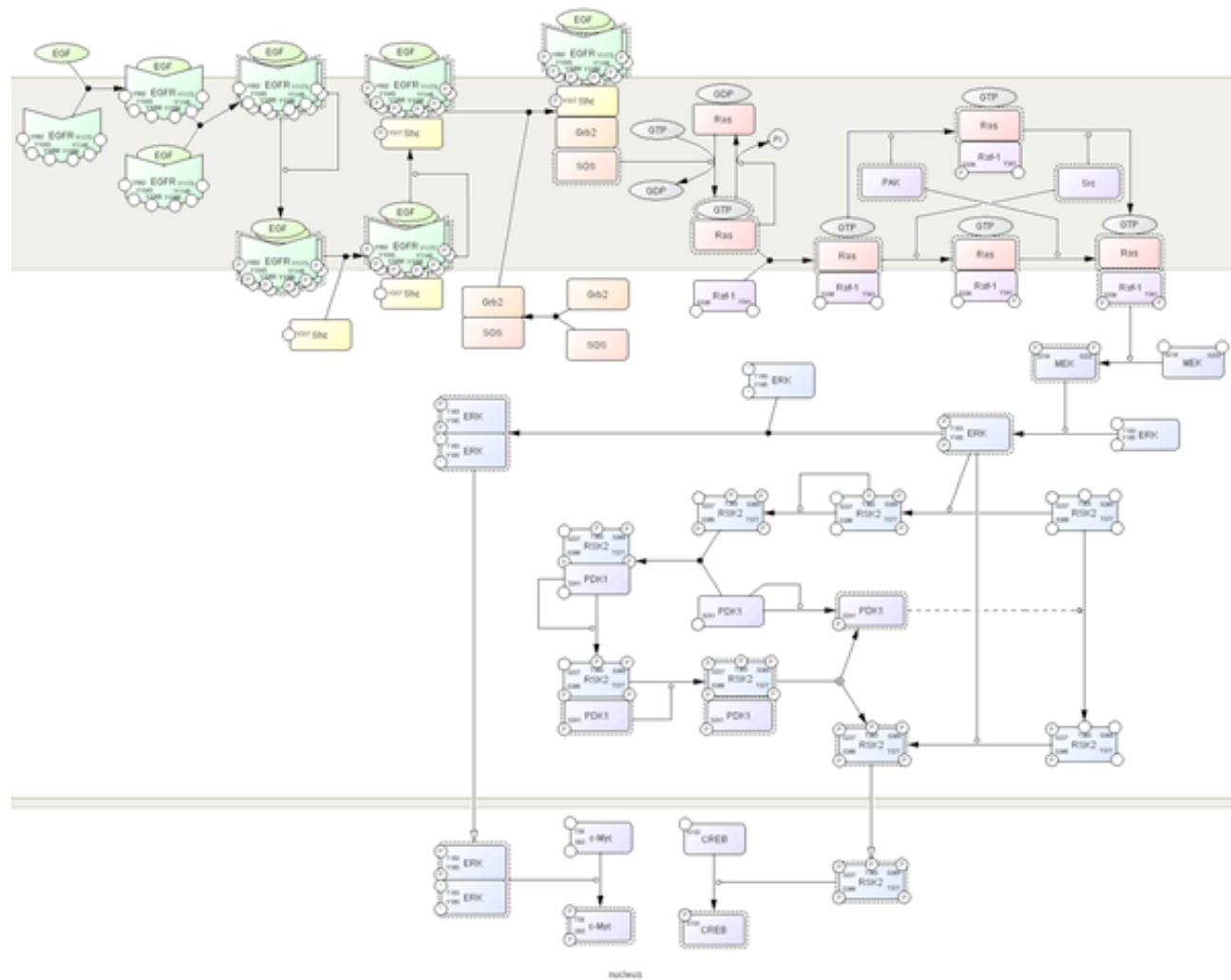
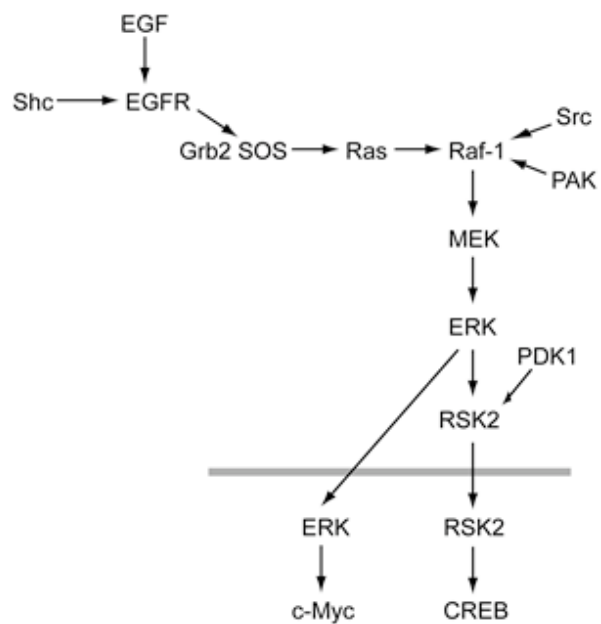


The diagram illustrates the EGF signaling pathway across the cell membrane and into the nucleus.

Cell Membrane: EGF ligands bind to EGFR, causing dimerization and autophosphorylation. This recruits Shc, which binds to Grb2. Grb2's SOS domain facilitates the exchange of GDP for GTP on Ras, activating it. Activated Ras then recruits Raf-1.

Cytoplasm: Activated Raf-1 phosphorylates MEK, which in turn phosphorylates ERK. There are multiple instances of these proteins shown, indicating a complex network of interactions.

Nucleus: Activated ERK translocates into the nucleus where it phosphorylates transcription factors such as c-Myc and CREB, leading to changes in gene expression.



State Node Symbols

Protein	
Receptor	
Ion Channel (Closed)	
Ion Channel (Open)	
Truncated Protein	
Gene	
RNA	
Anti-sense RNA	
Ion	
Simple Molecule	
Unknown	
Phenotype	
Homodimer / N-mer with N stacked symbols	
Active Protein	

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	

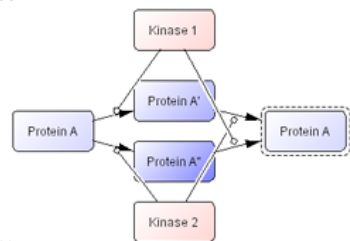
Class-II Reduced Notation (Viewer Only)

Activation/ Inhibition/ Modification	
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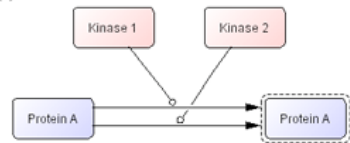
Node Structure

Residue modification	<ul style="list-style-type: none"> phosphorylated acetylated ubiquitinated methylated hydroxylated empty don't care unknown
Complex State Node	<ul style="list-style-type: none"> Connectivity (binding, etc)
Promotor and coding structure for gene	
exon structure for RNA	

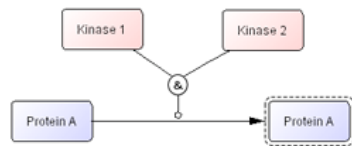
(a)



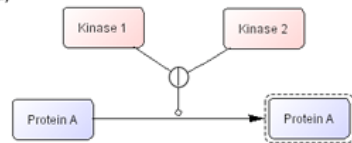
(c)



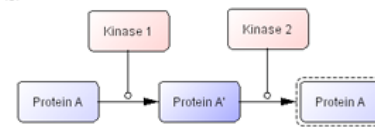
(b)



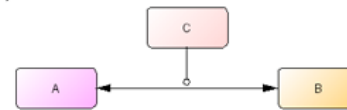
(d)



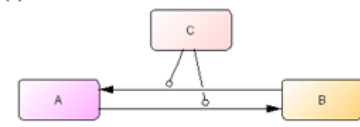
(g)



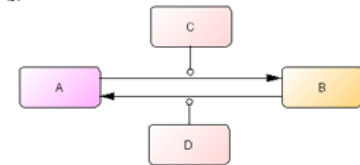
(i)



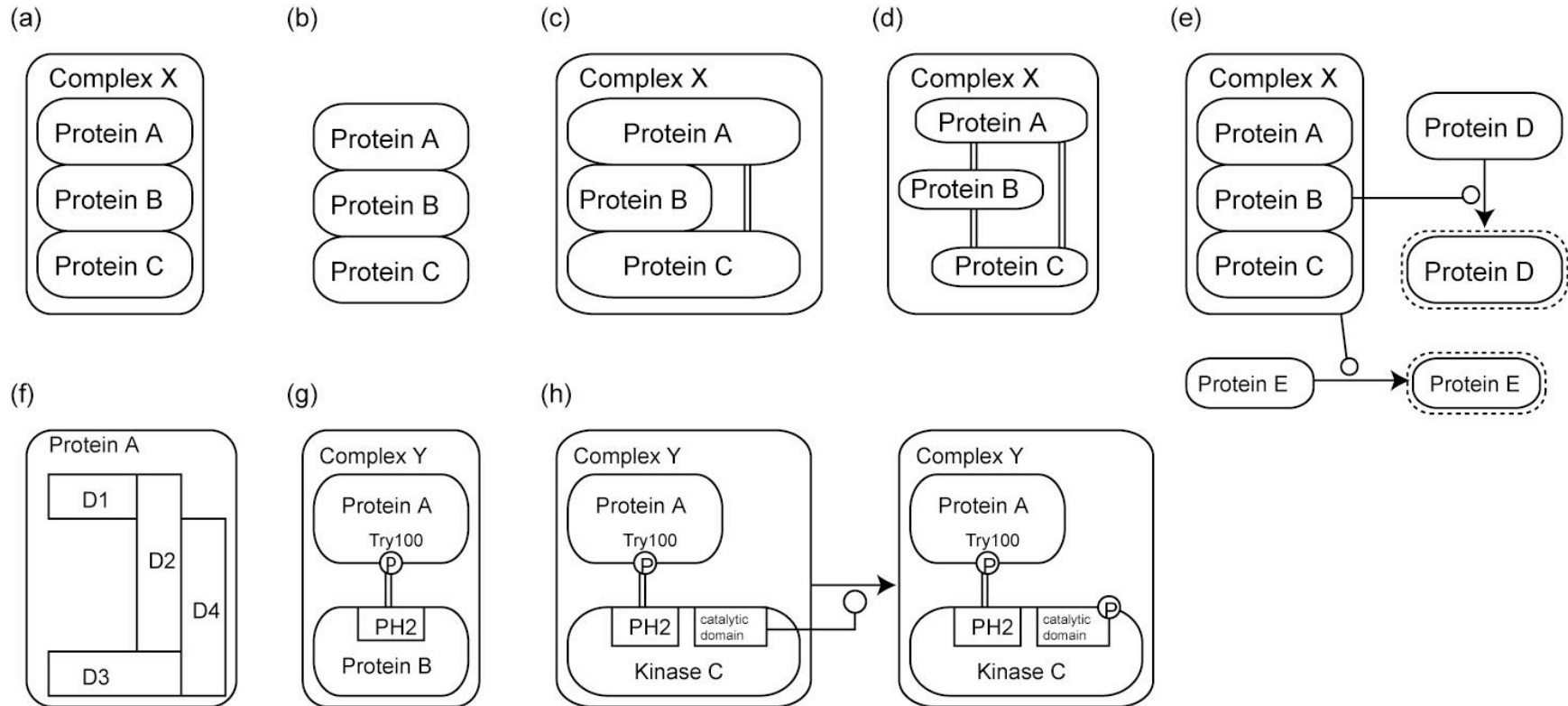
(h)



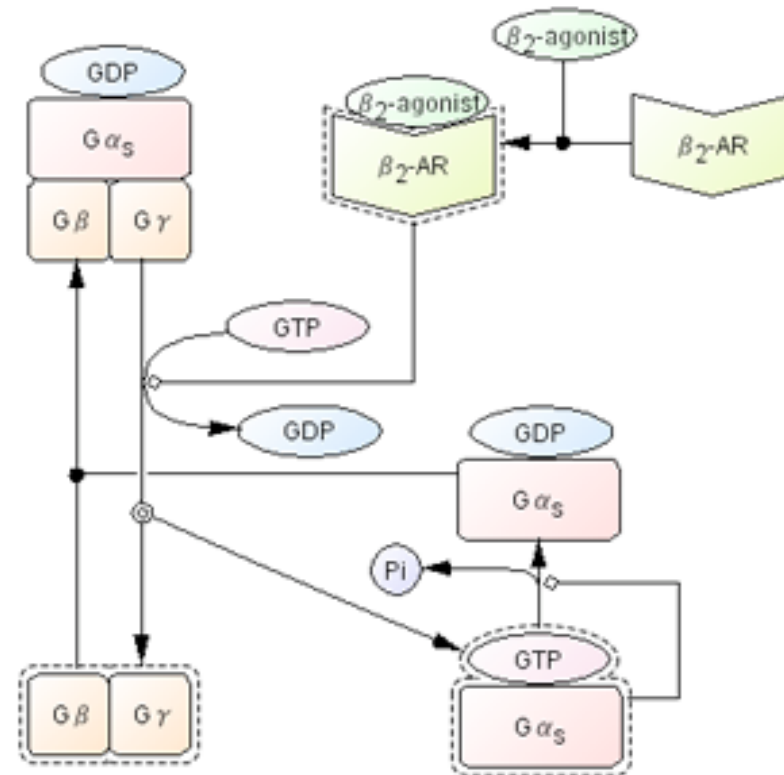
(j)



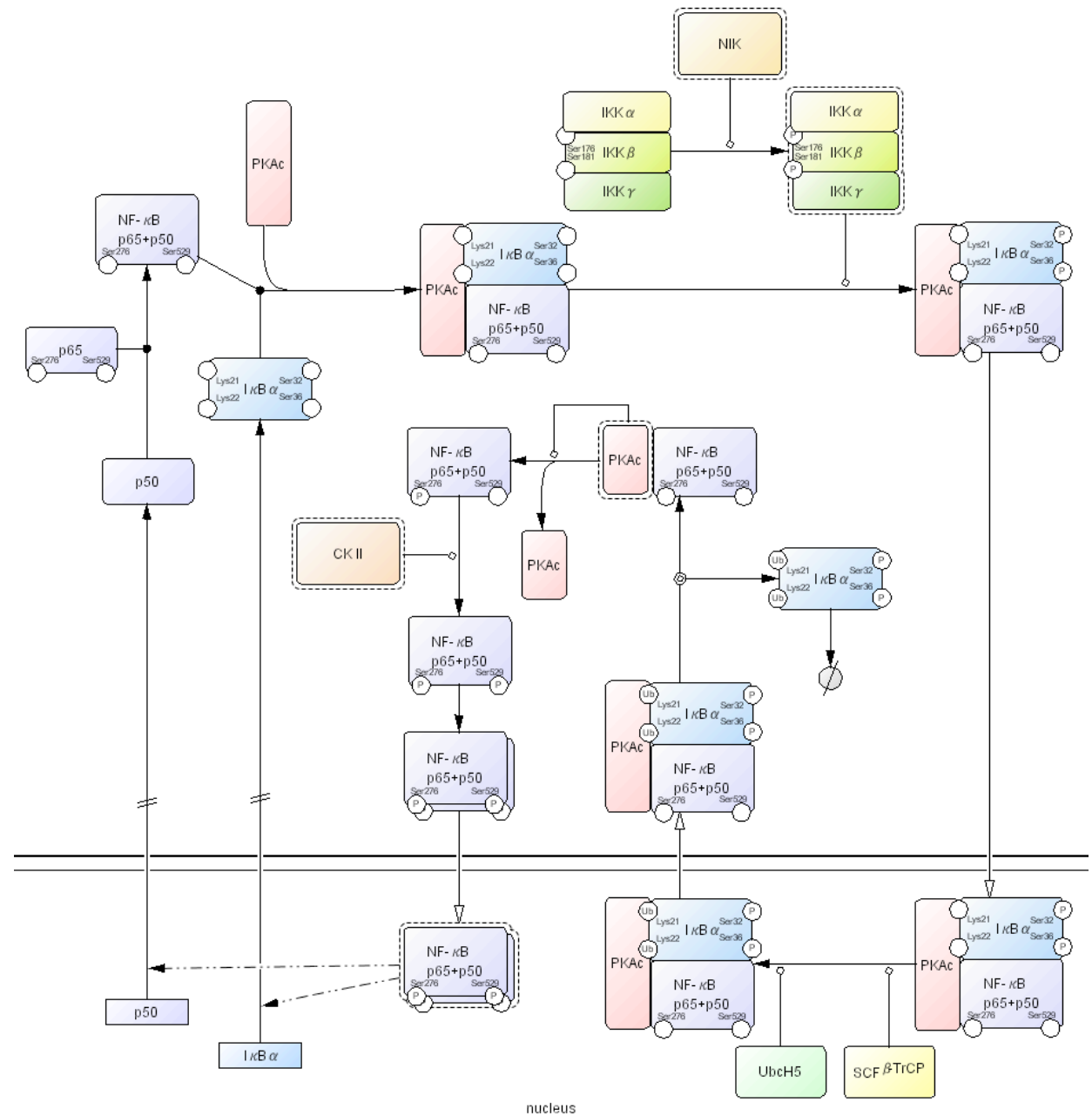
Structure of Complex



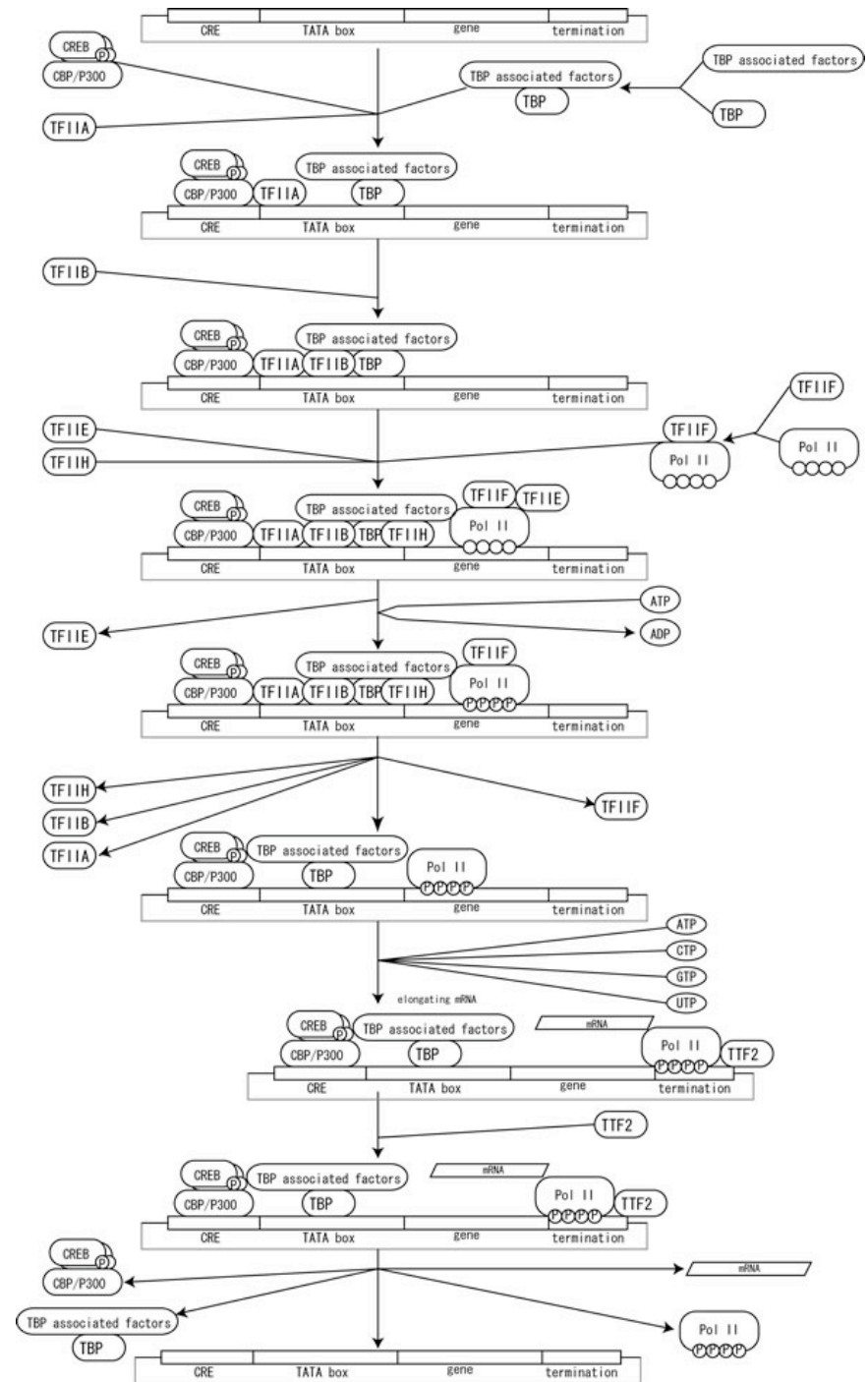
Example of Process Diagram G-protein



Example of Process Diagram NFkB

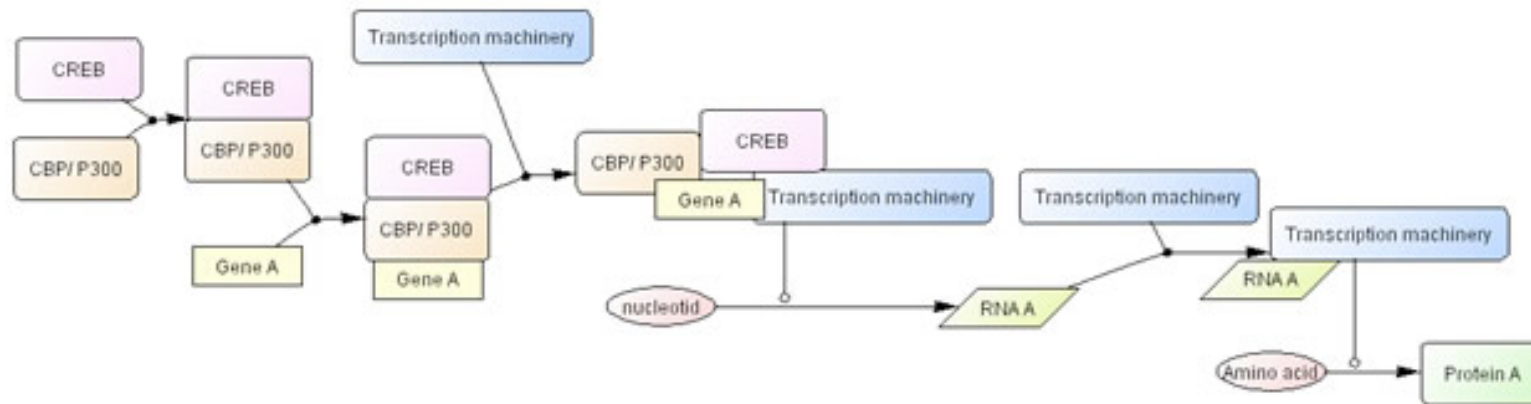


Process Diagram for Transcription

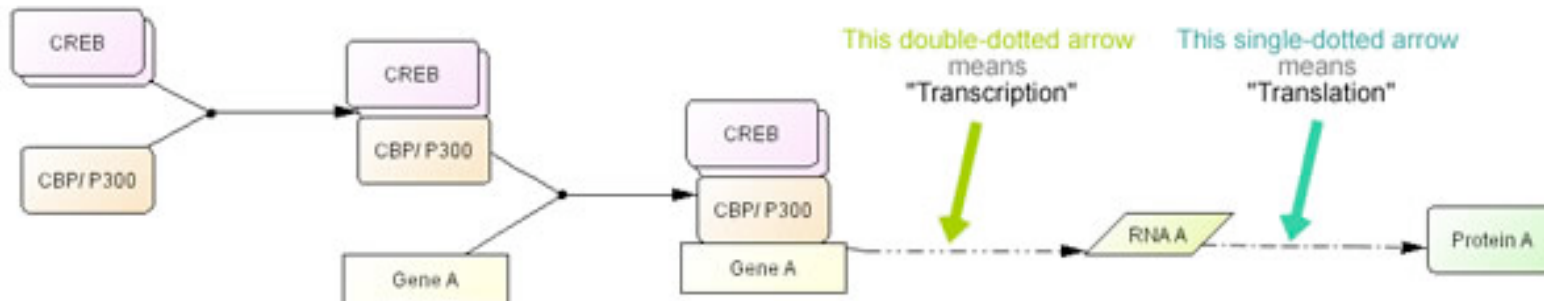


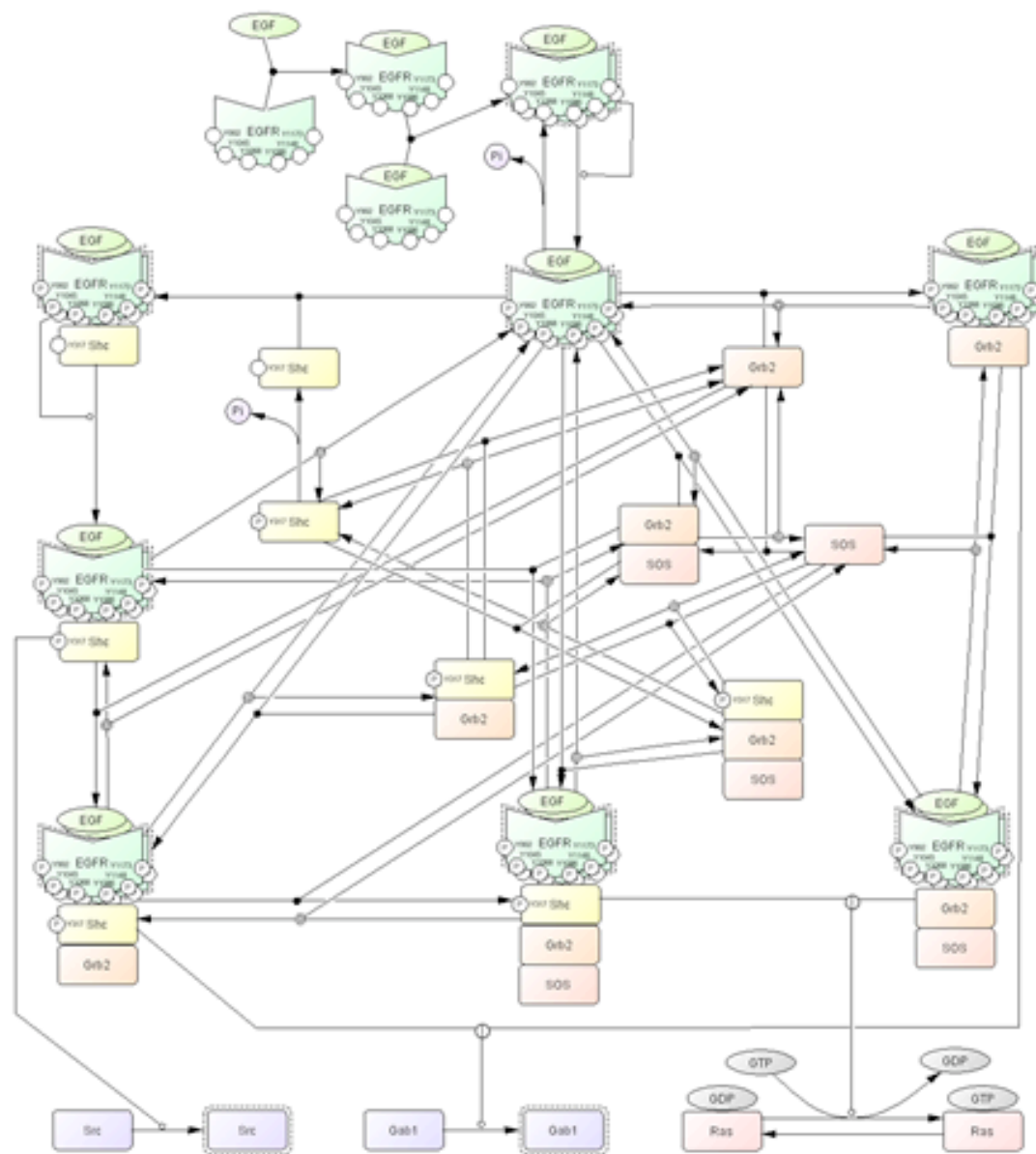
transcription and translation

Simplified notation

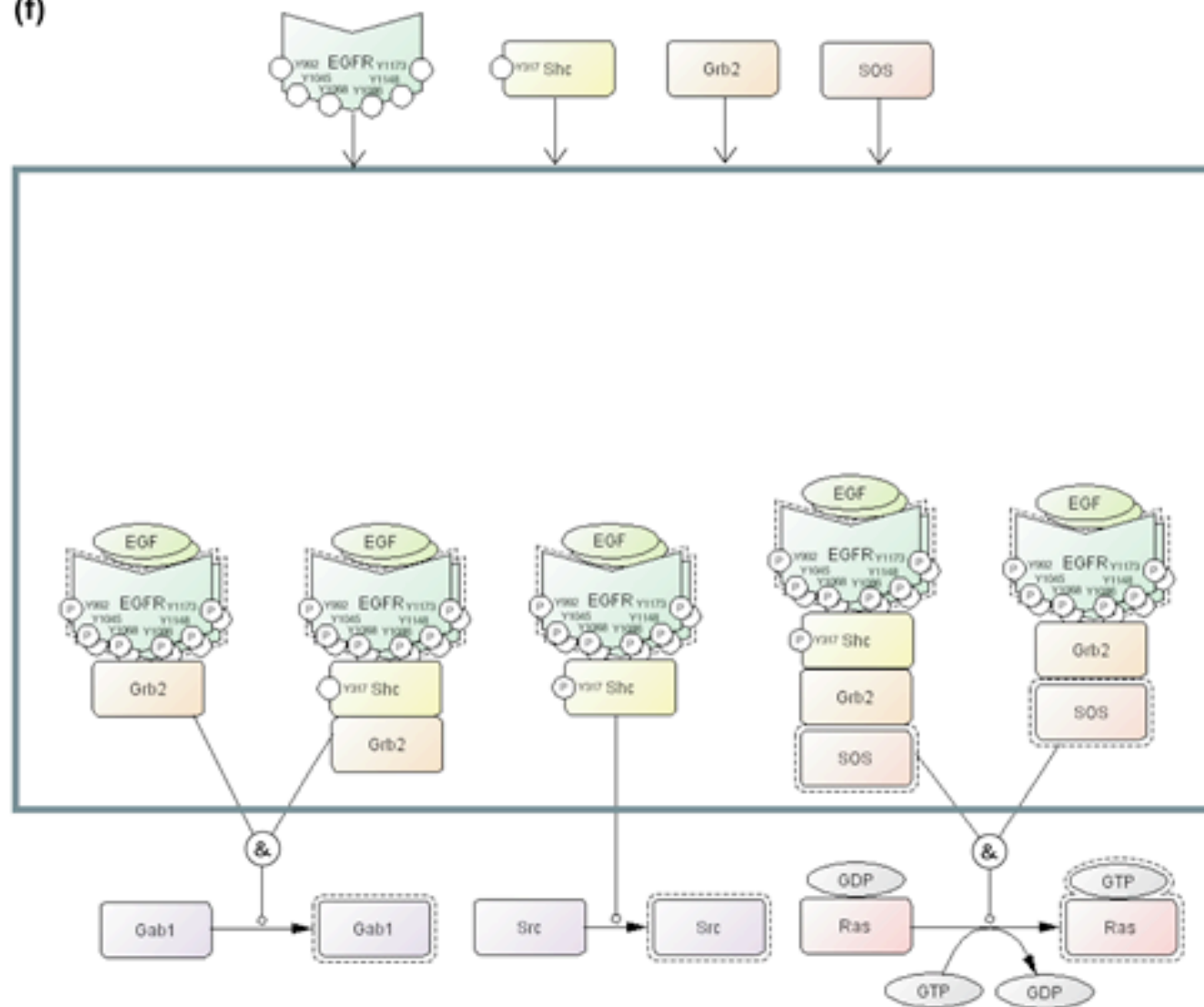


Reduced notation





(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

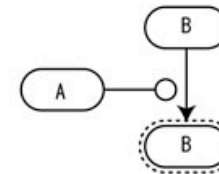
Result = TRANSITION ('+' | '-' | empty) '<=' | empty
 ImmediateEffect = TERM_IE
 Condition = empty | '{ TERM_COND }'
 SimpleSentence = ('+' | '-' | TRANSITION | '?')

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]+

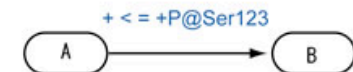
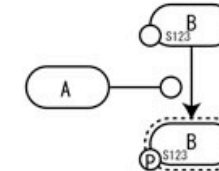
standard notation

reduced notation

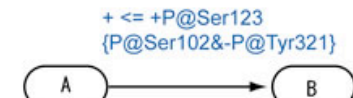
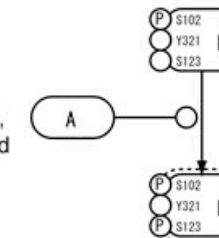
Case 1: A activates B
(by unspecified mechanism)



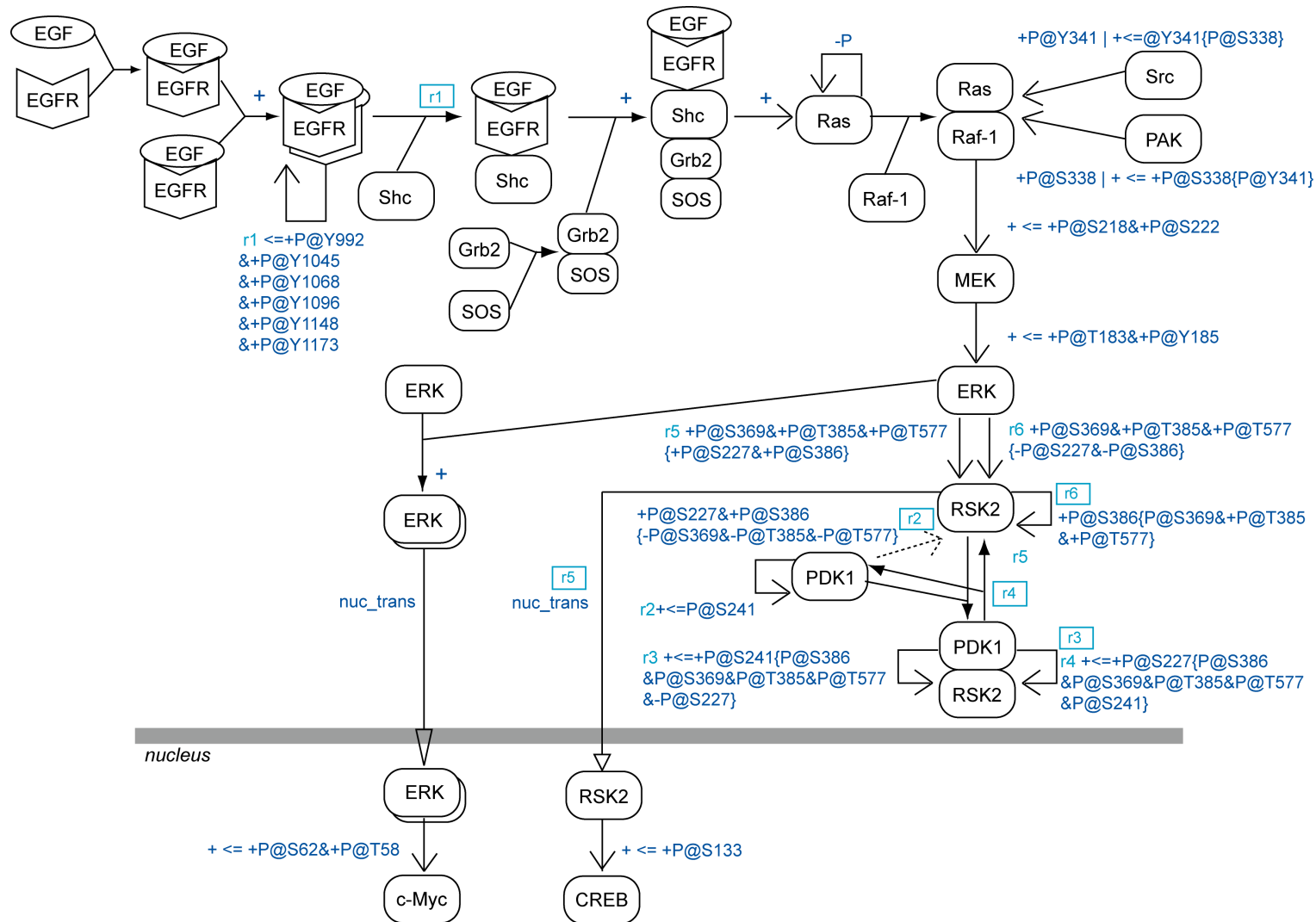
Case 2: A activates B
by phosphorylation
at Ser123 residue



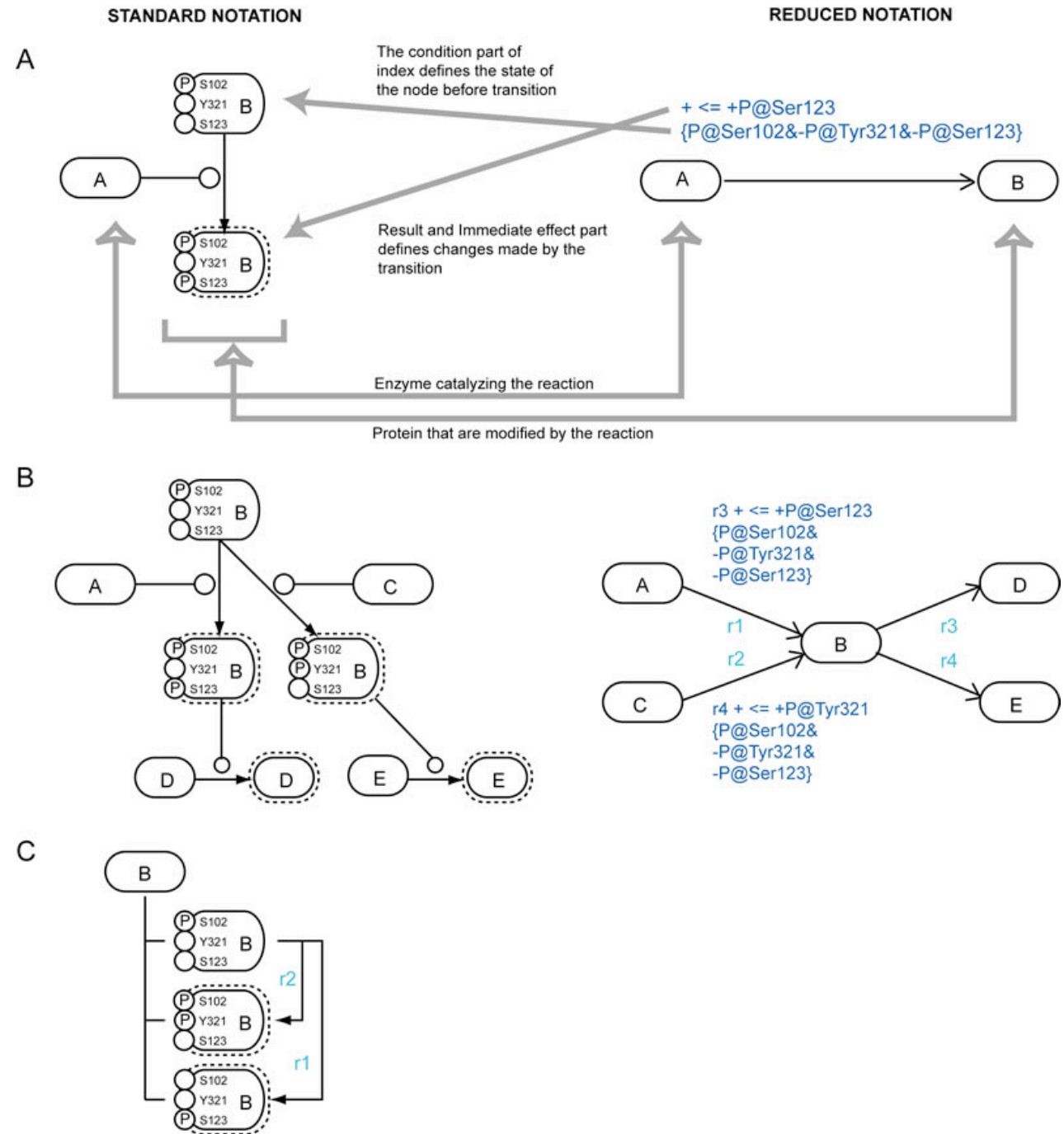
Case 3: A activates B
by phosphorylation
at Ser123 residue
when Ser102 is phosphorylated,
but Tyr321 is not phosphorylated



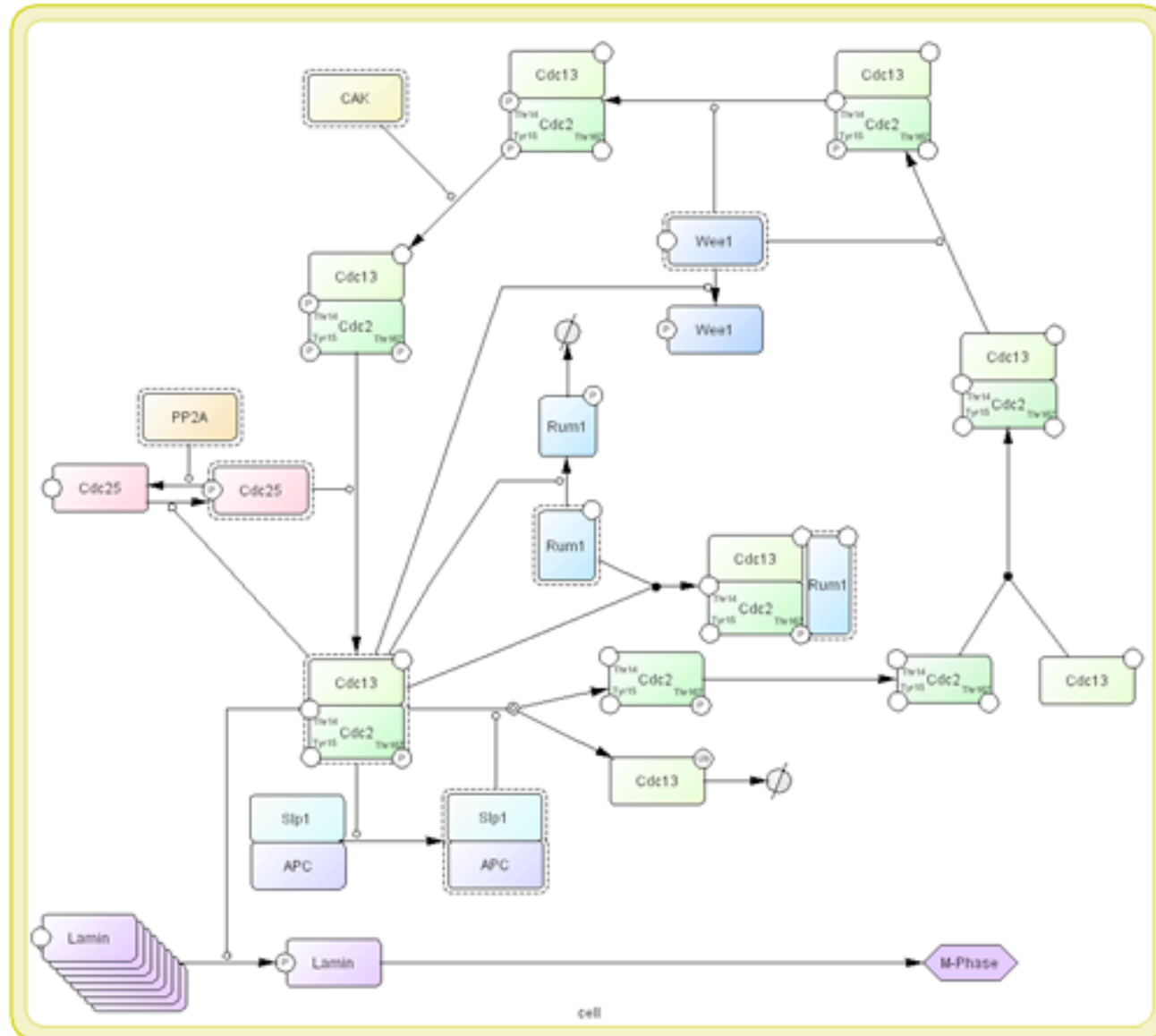
Reduced Notation

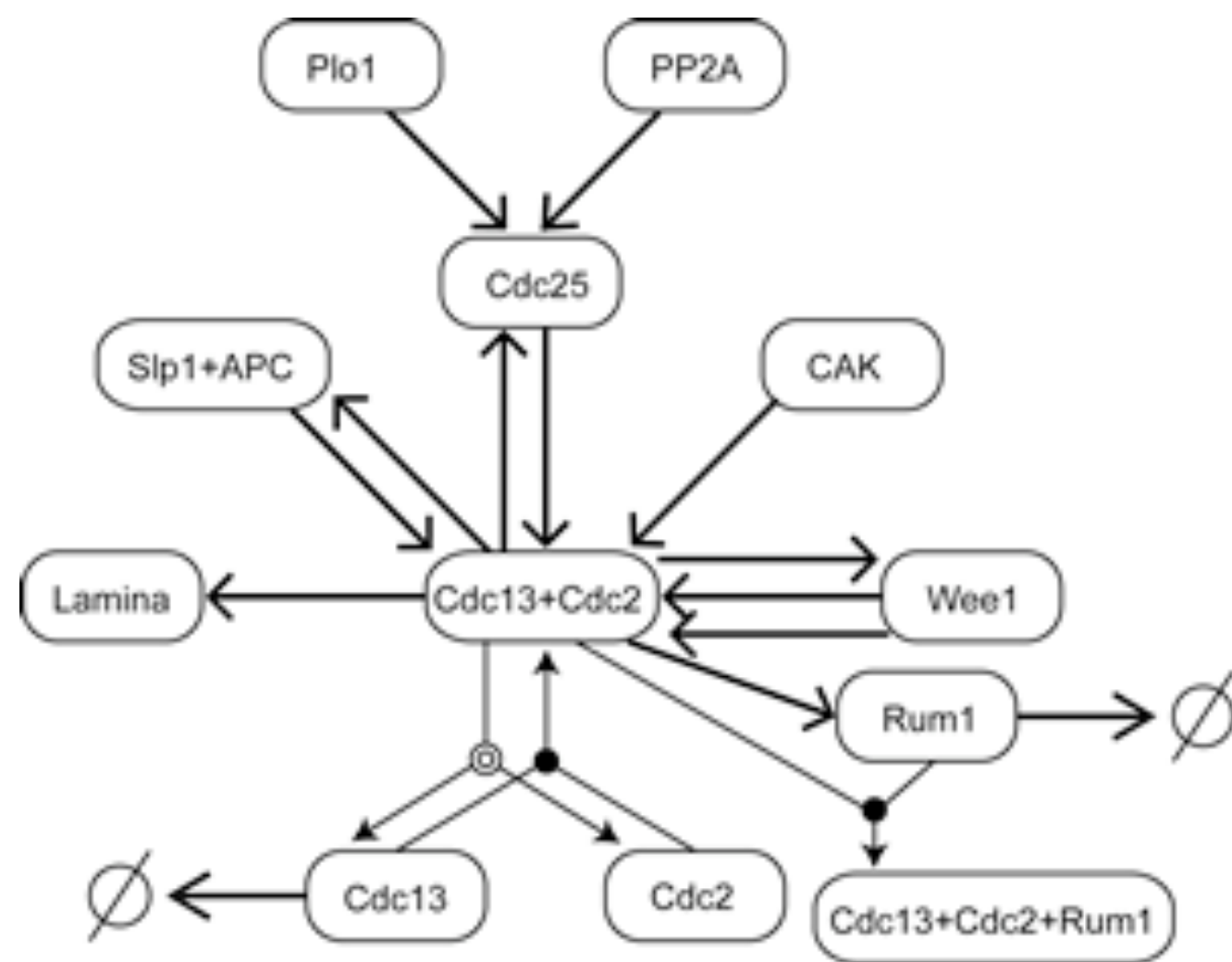


Standard Notation vs Reduced Notation

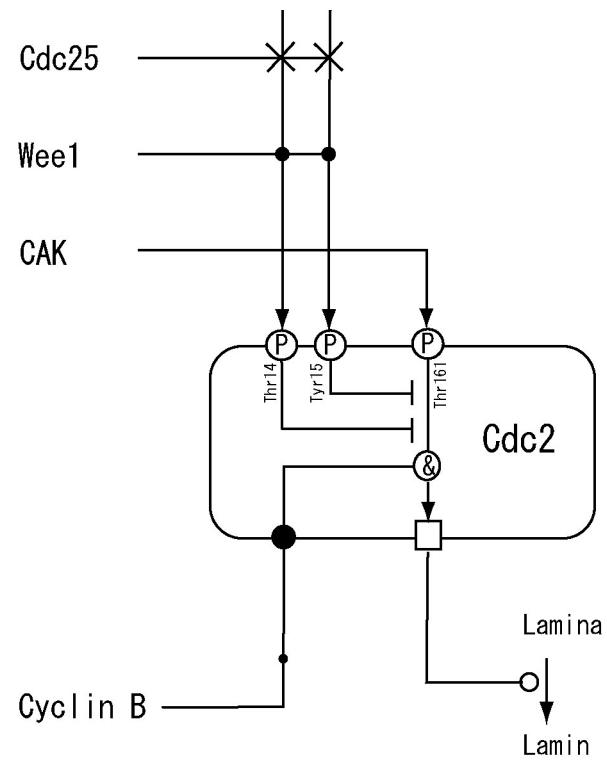


MPF cycle



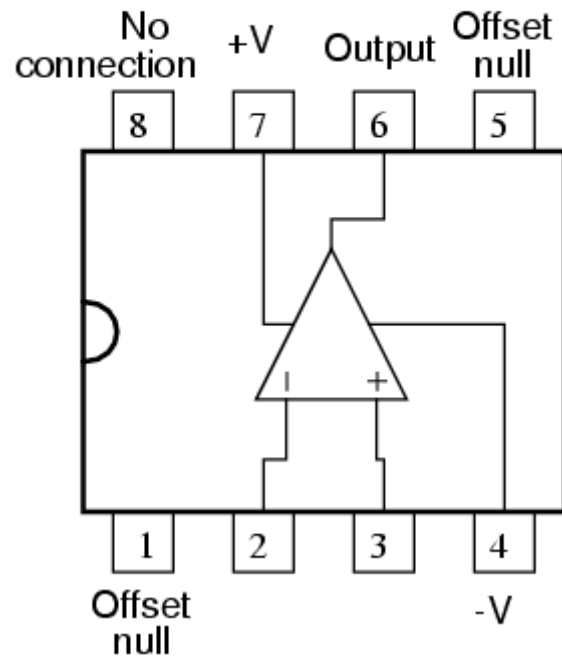


Relationship View

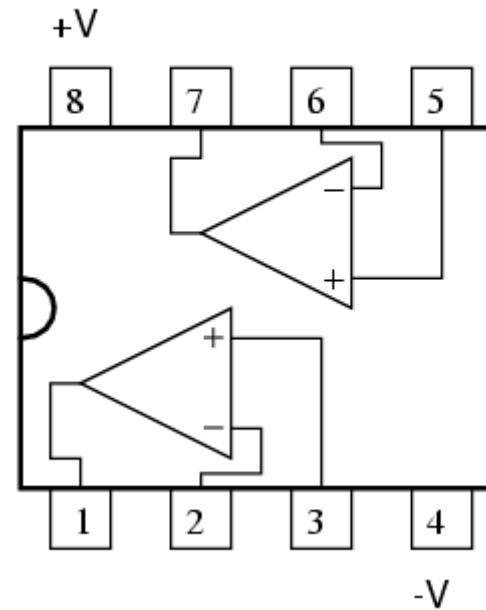


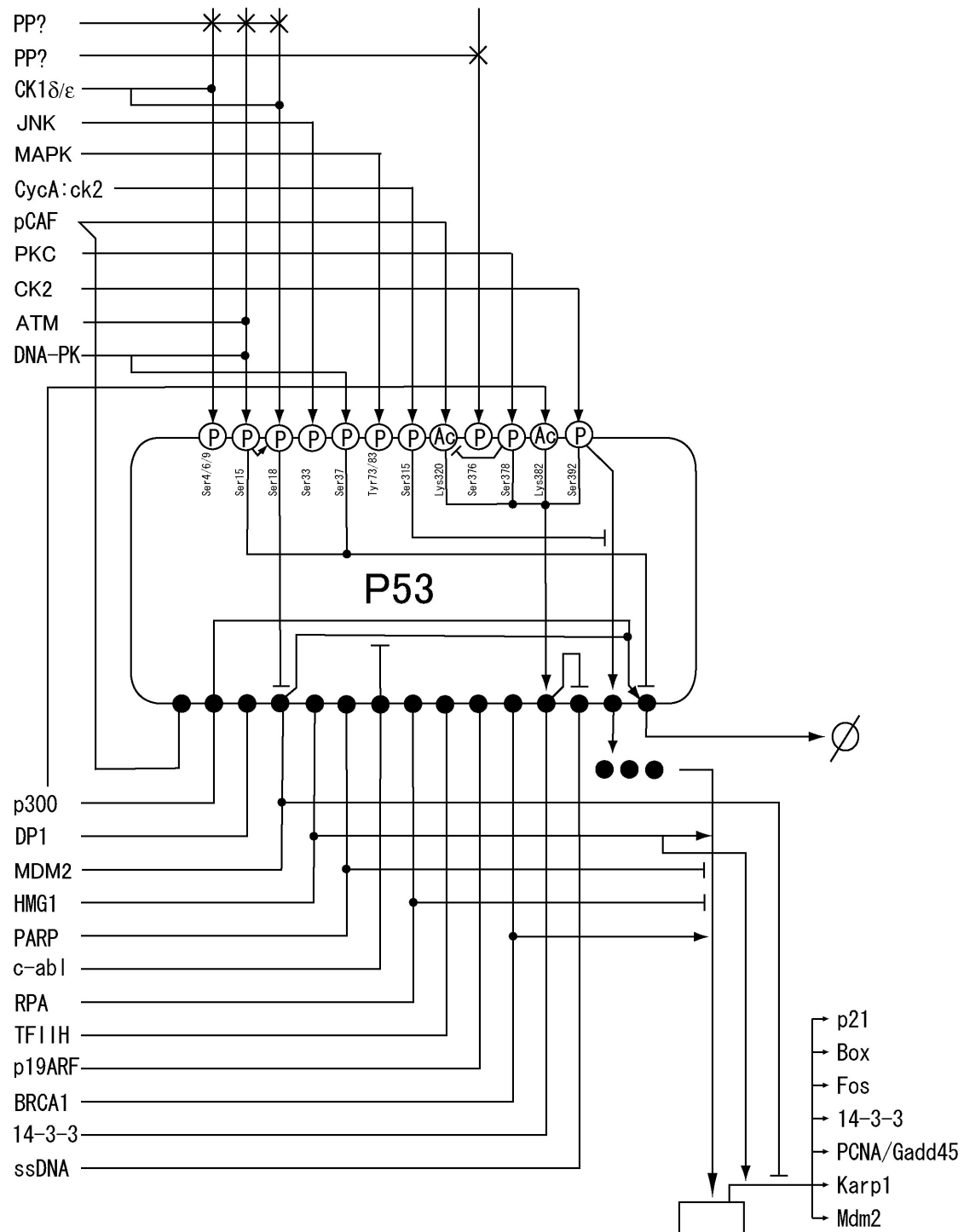
LSI diagram

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

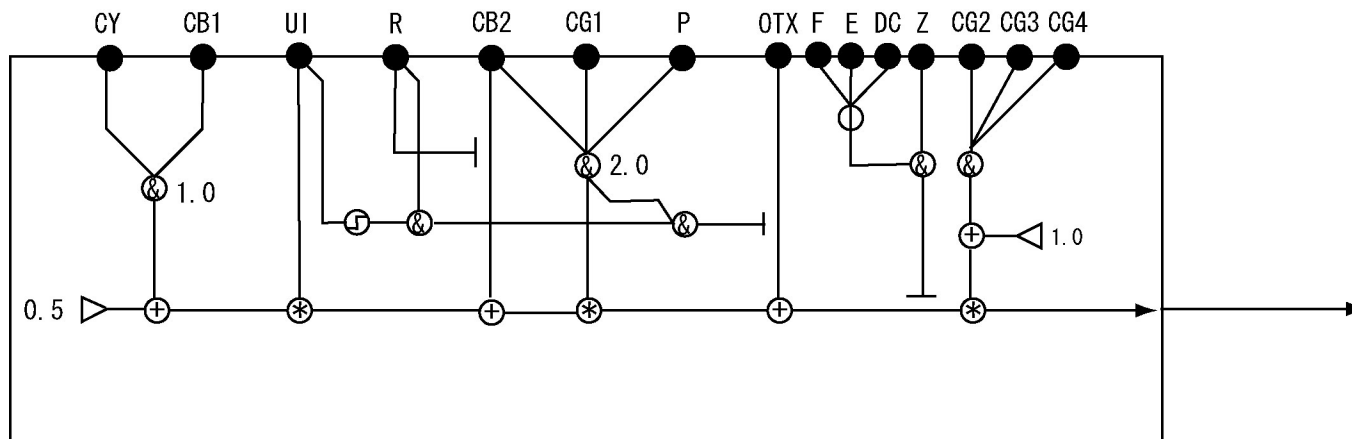


Dual op-amp in 8-pin DIP

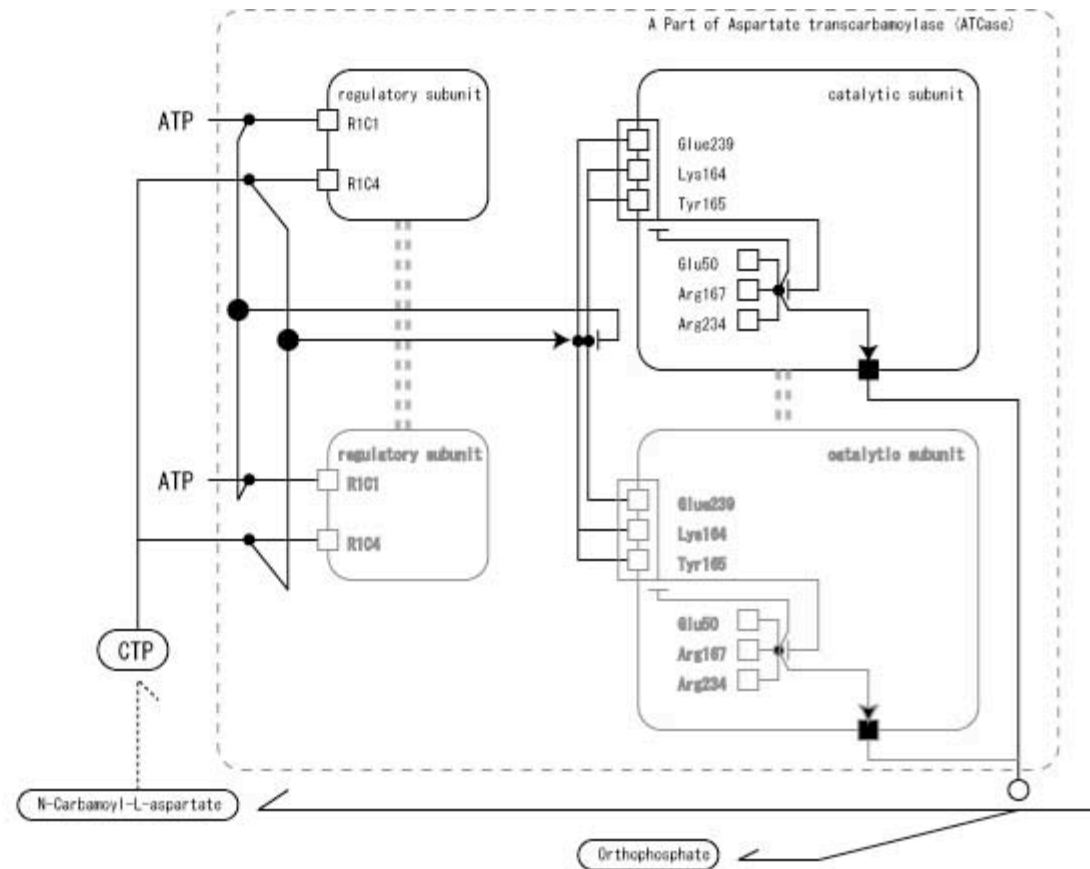
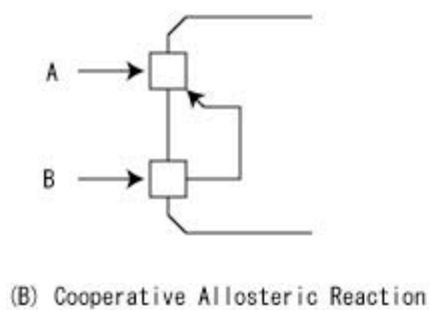
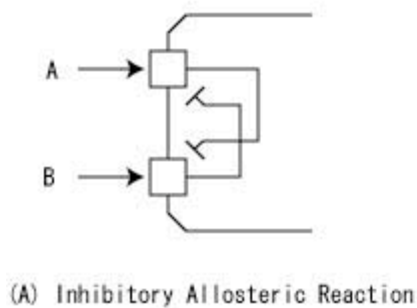




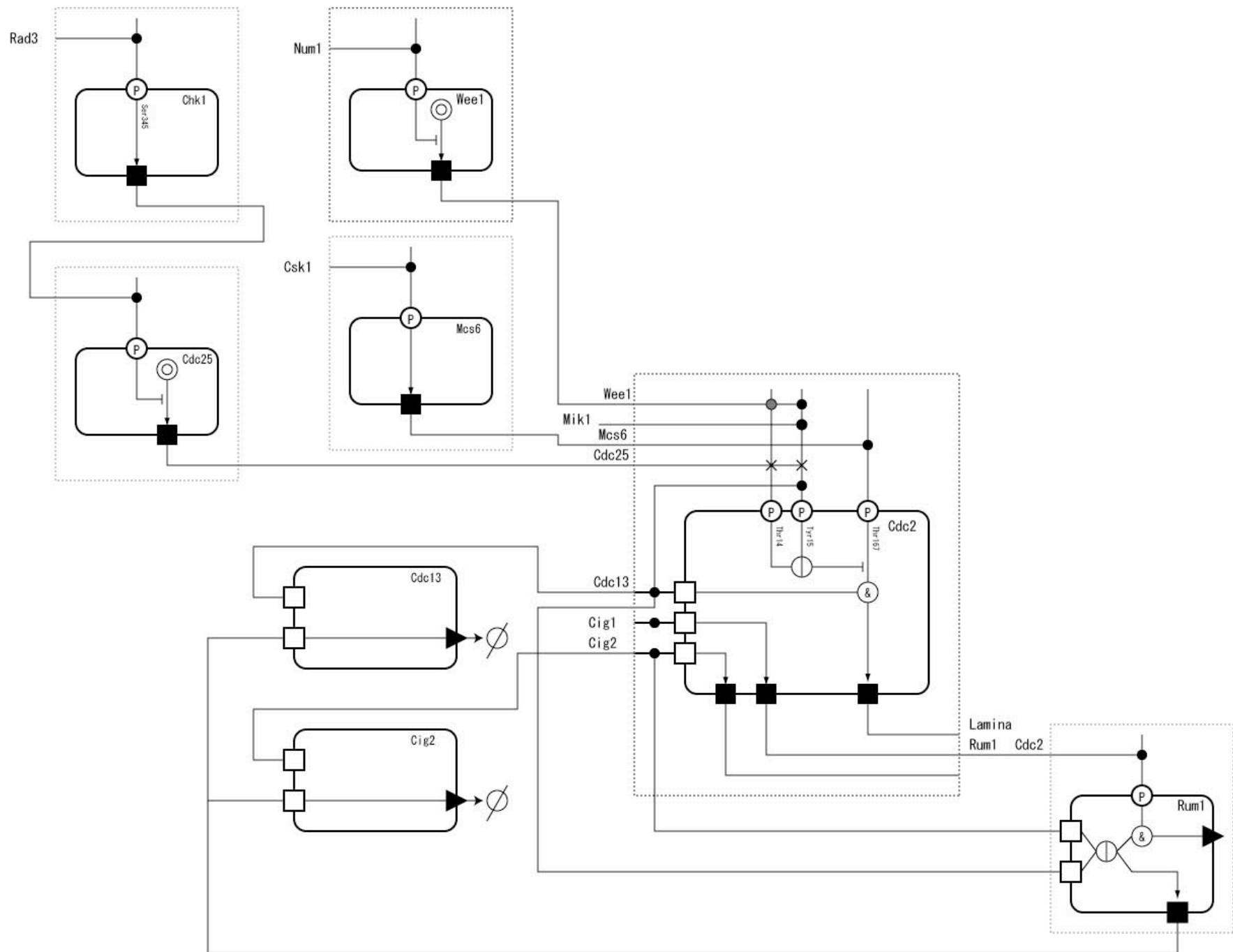
endo16



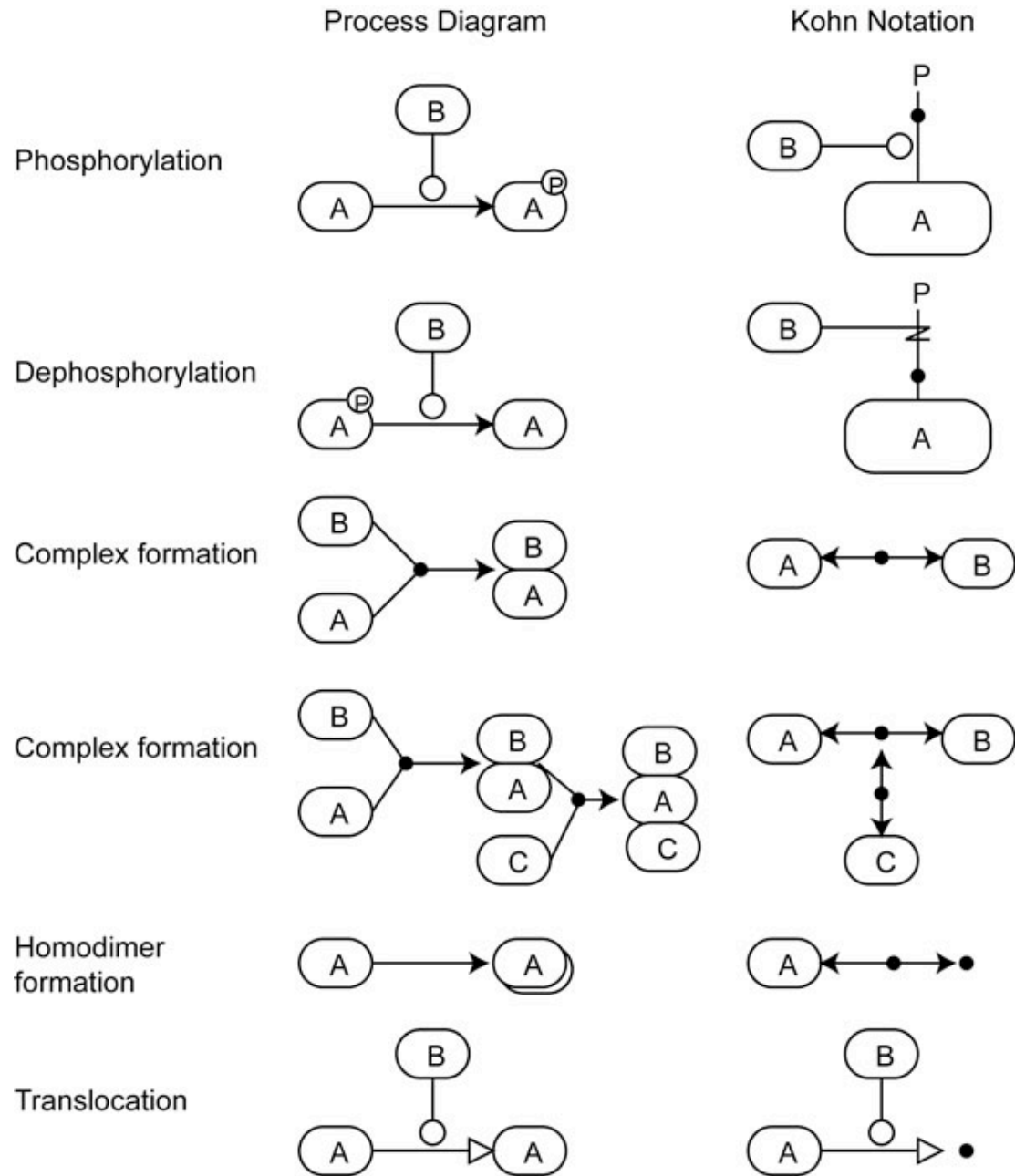
Allosteric Reaction



(C) A Part of Allosteric Reactions in aspartate transcarbamoylase



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

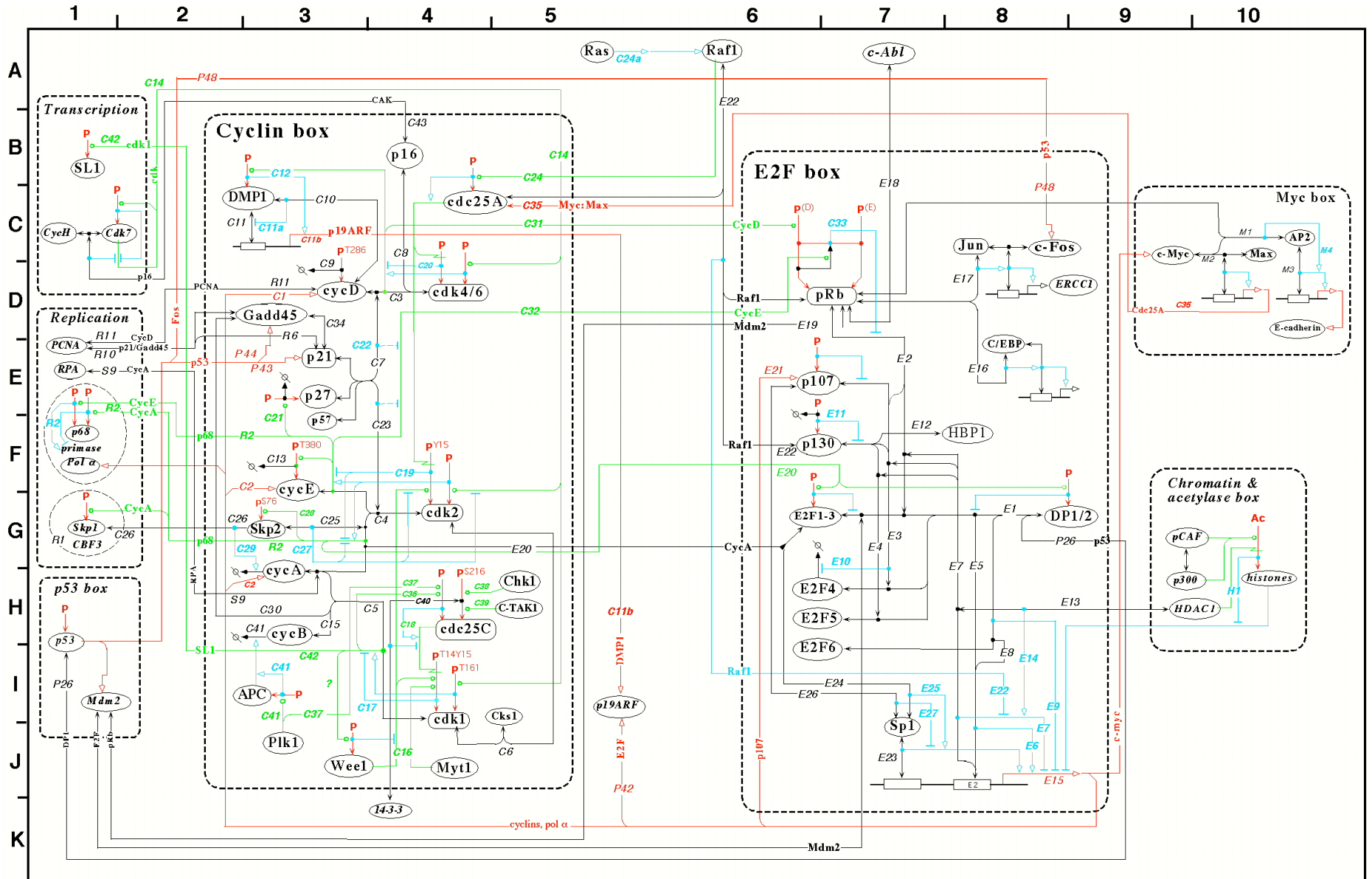


Figure 6A: The Cyclin - E2F cell cycle control system (version 3a - June 8, 1999)