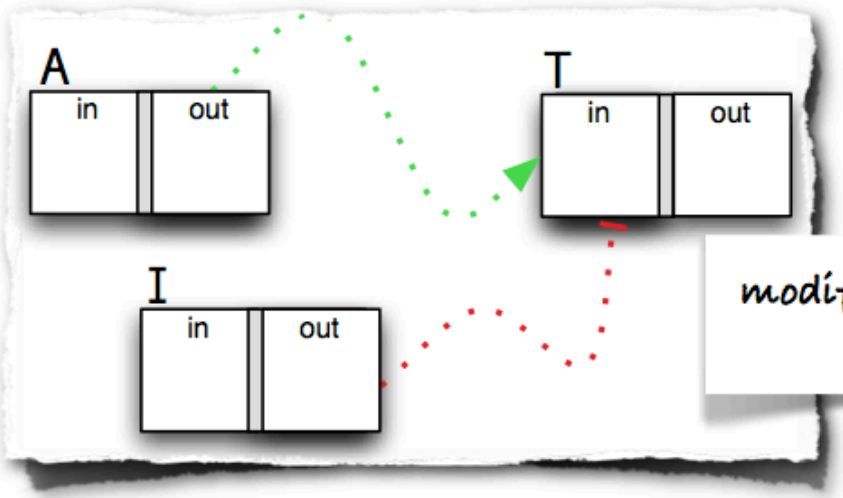
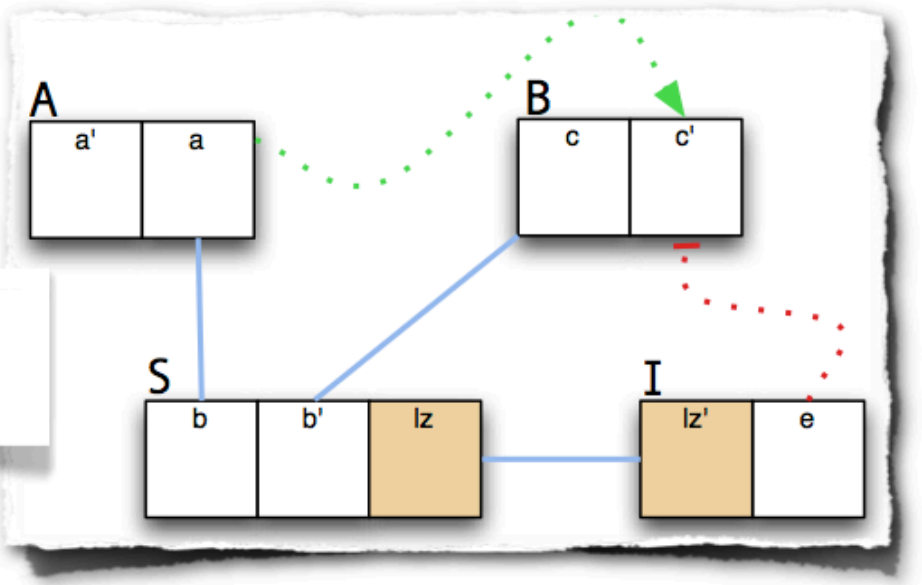
sbm 2: synbio of protein networks



ppi: common

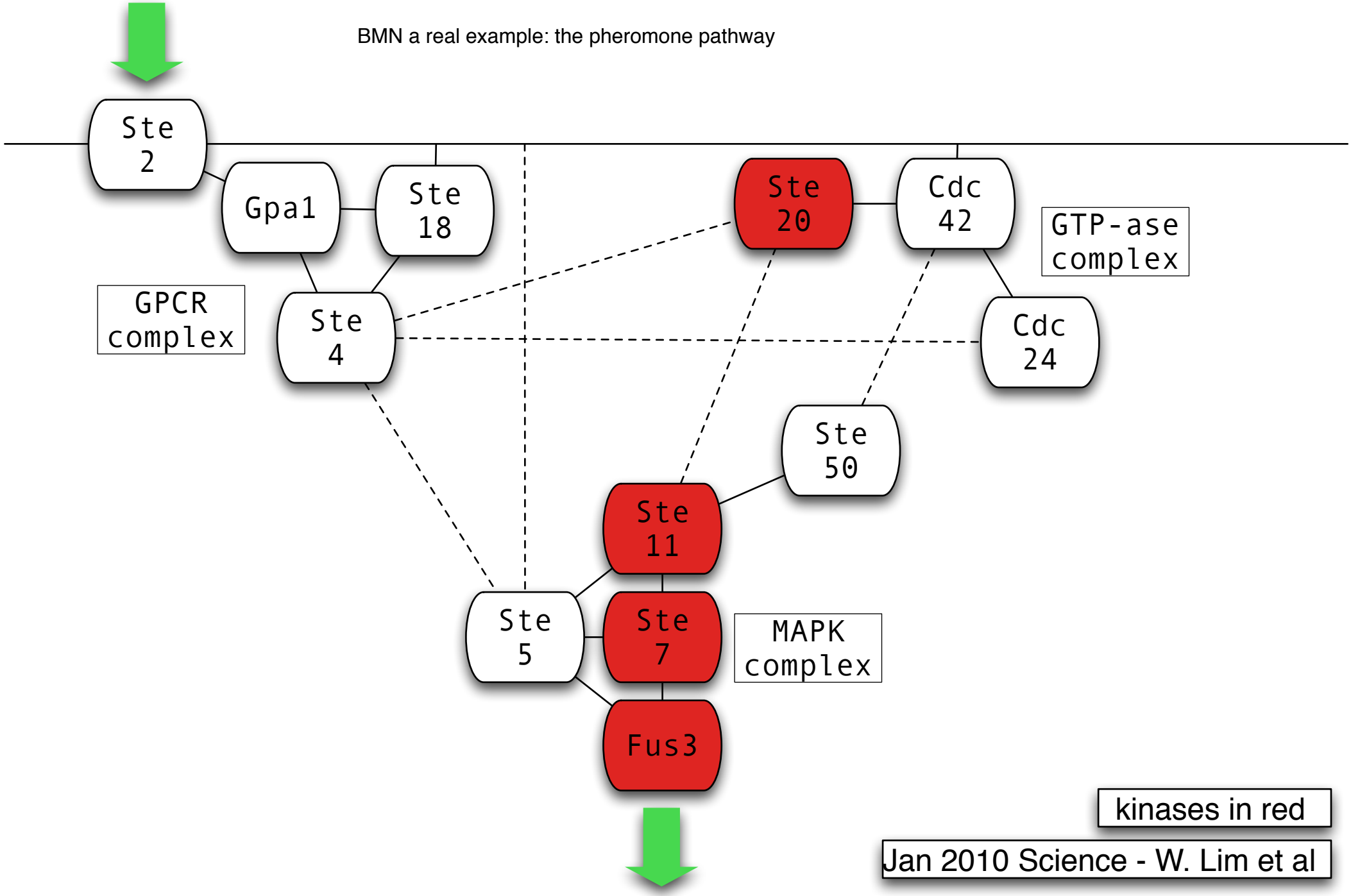
motives

modification triplet/polarized agents

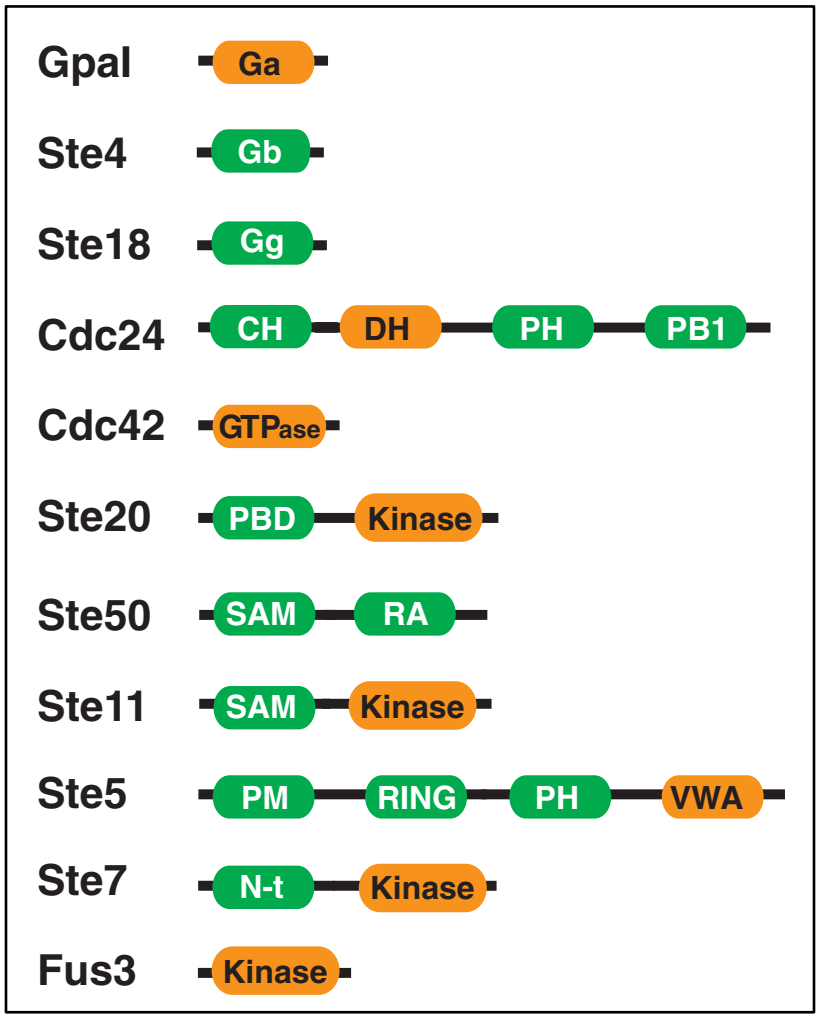


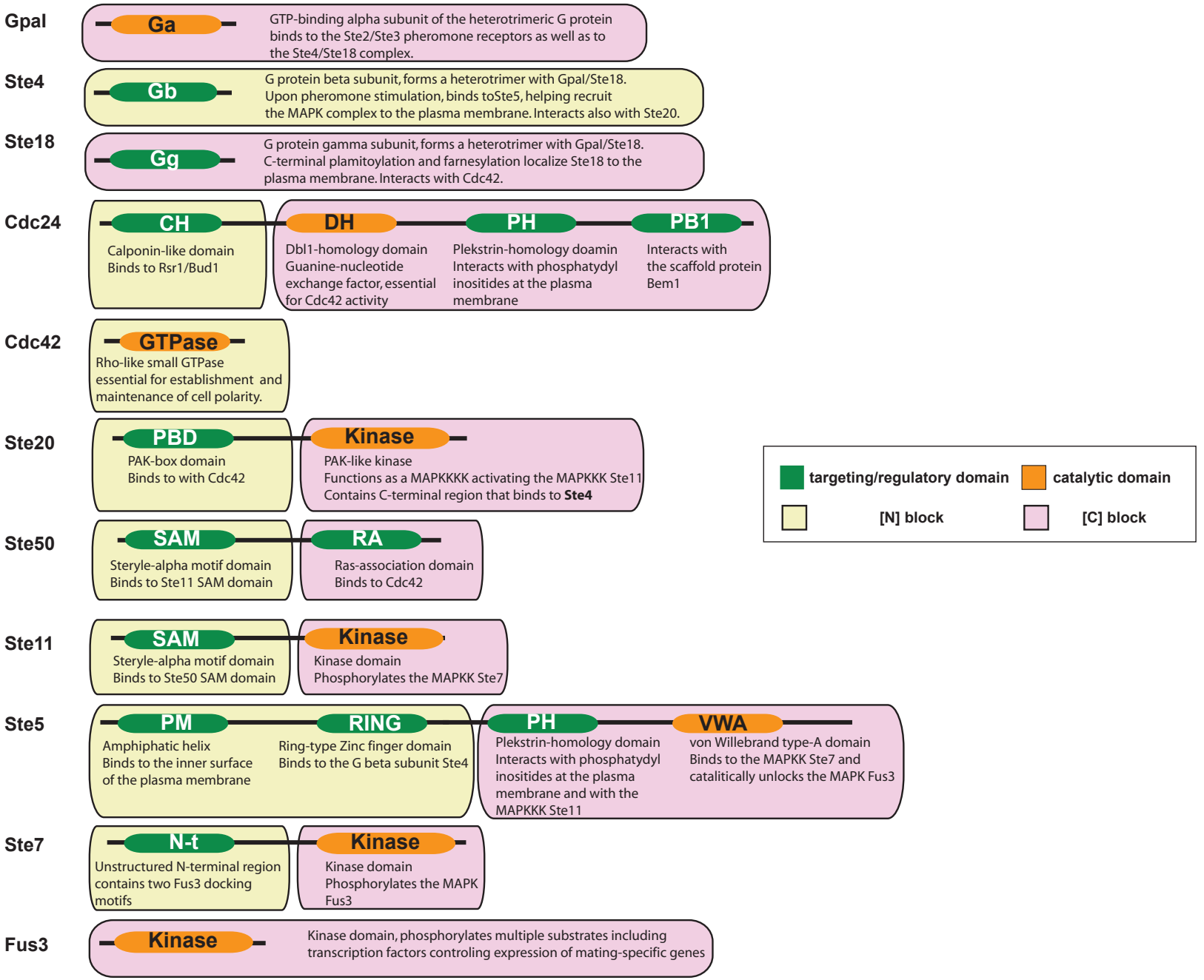
scaffolds/beyond the "simple" modification triplet

BMN a real example: the pheromone pathway

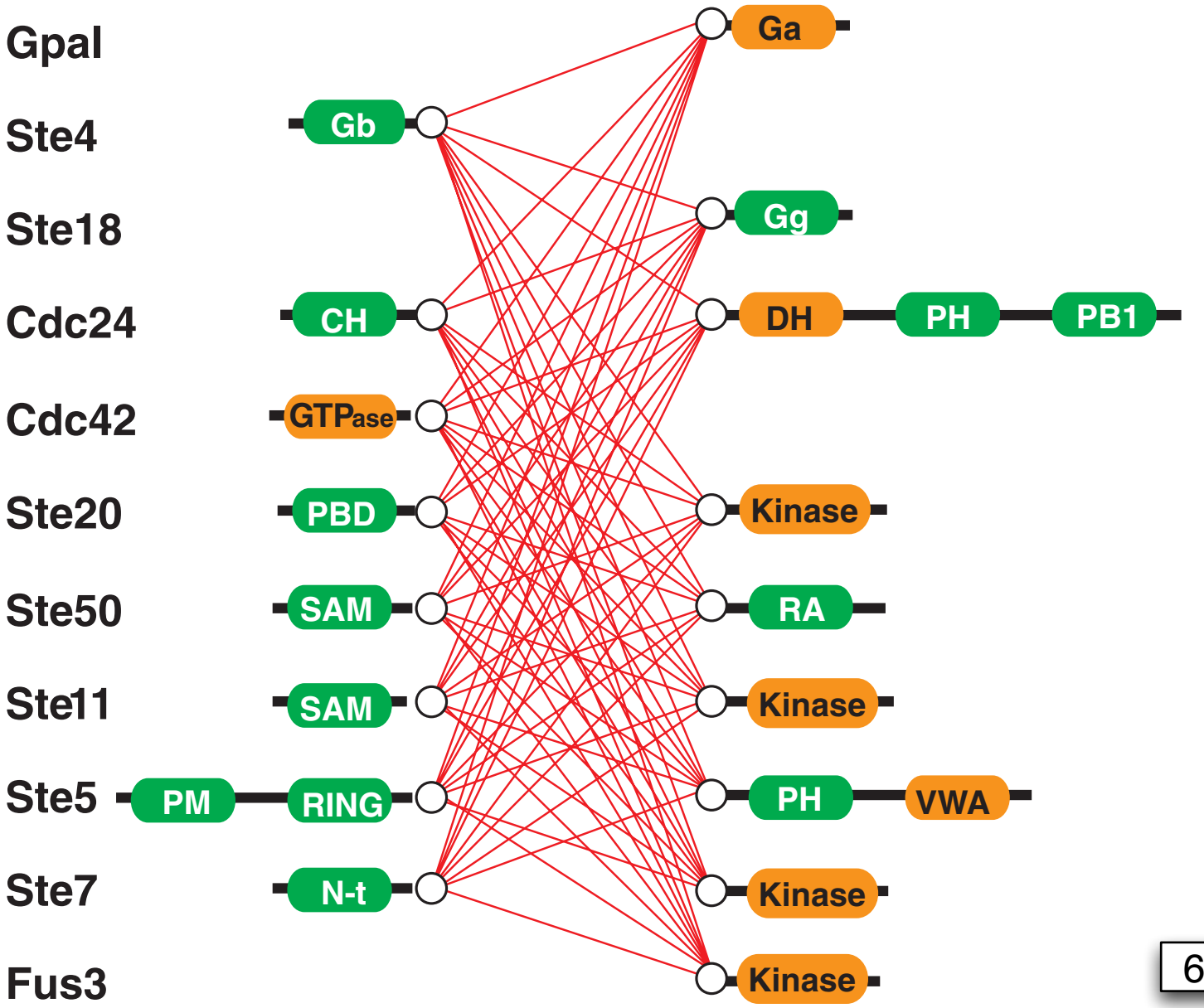


modularity 1 - domain split



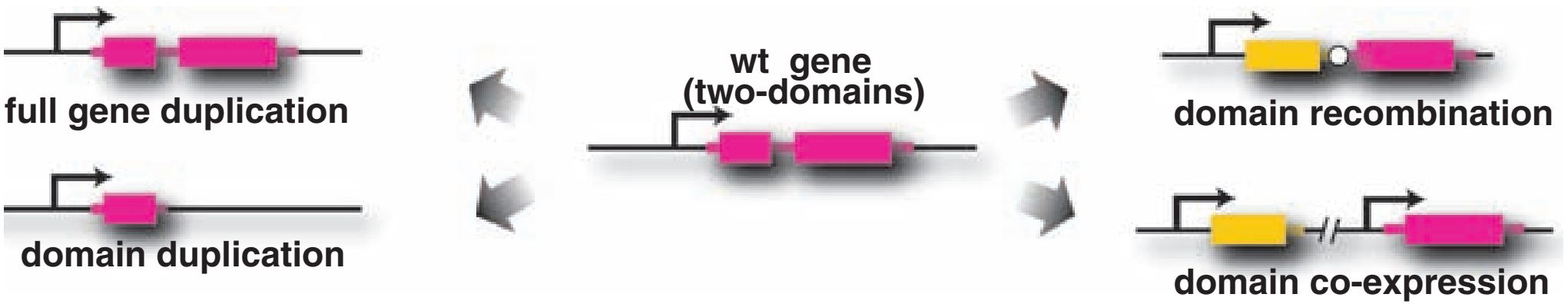

Gpal
Ga
GTP-binding alpha subunit of the heterotrimeric G protein binds to the Ste2/Ste3 pheromone receptors as well as to the Ste4/Ste18 complex.
Ste4
Gb
G protein beta subunit, forms a heterotrimer with Gpal/Ste18. Upon pheromone stimulation, binds toSte5, helping recruit the MAPK complex to the plasma membrane. Interacts also with Ste20.
Ste18
Gg
G protein gamma subunit, forms a heterotrimer with Gpal/Ste18. C-terminal plamitoylation and farnesylation localize Ste18 to the plasma membrane. Interacts with Cdc42.
Cdc24
CH
Calponin-like domain Binds to Rsr1/Bud1
DH
Dbl1-homology domain Guanine-nucleotide exchange factor, essential for Cdc42 activity
PH
Plekstrin-homology doamin Interacts with phosphatydyl inositides at the plasma membrane
PB1
Interacts with the scaffold protein Bem1
Cdc42
GTPase
Rho-like small GTPase essential for establishment and maintenance of cell polarity.
Ste20
PBD
PAK-box domain Binds to with Cdc42
Kinase
PAK-like kinase Functions as a MAPKKKK activating the MAPKKK Ste11 Contains C-terminal region that binds to Ste4
Ste50
SAM
Steryle-alpha motif domain Binds to Ste11 SAM domain
RA
Ras-association domain Binds to Cdc42
Ste11
SAM
Steryle-alpha motif domain Binds to Ste50 SAM domain
Kinase
Kinase domain Phosphorylates the MAPKK Ste7
Ste5
PM
Amphiphatic helix Binds to the inner surface of the plasma membrane
RING
Ring-type Zinc finger domain Binds to the G beta subunit Ste4
PH
Plekstrin-homology domain Interacts with phosphatydyl inositides at the plasma membrane and with the MAPKKK Ste11
VWA
von Willebrand type-A domain Binds to the MAPKK Ste7 and catalitically unlocks the MAPK Fus3
Ste7
N-t
Unstructured N-terminal region contains two Fus3 docking motifs
Kinase
Kinase domain Phosphorylates the MAPK Fus3
Fus3
Kinase
Kinase domain, phosphorylates multiple substrates including transcription factors controling expression of mating-specific genes
targeting/regulatory domain
catalytic domain
[N] block
[C] block

modularity 2 - domain recombination

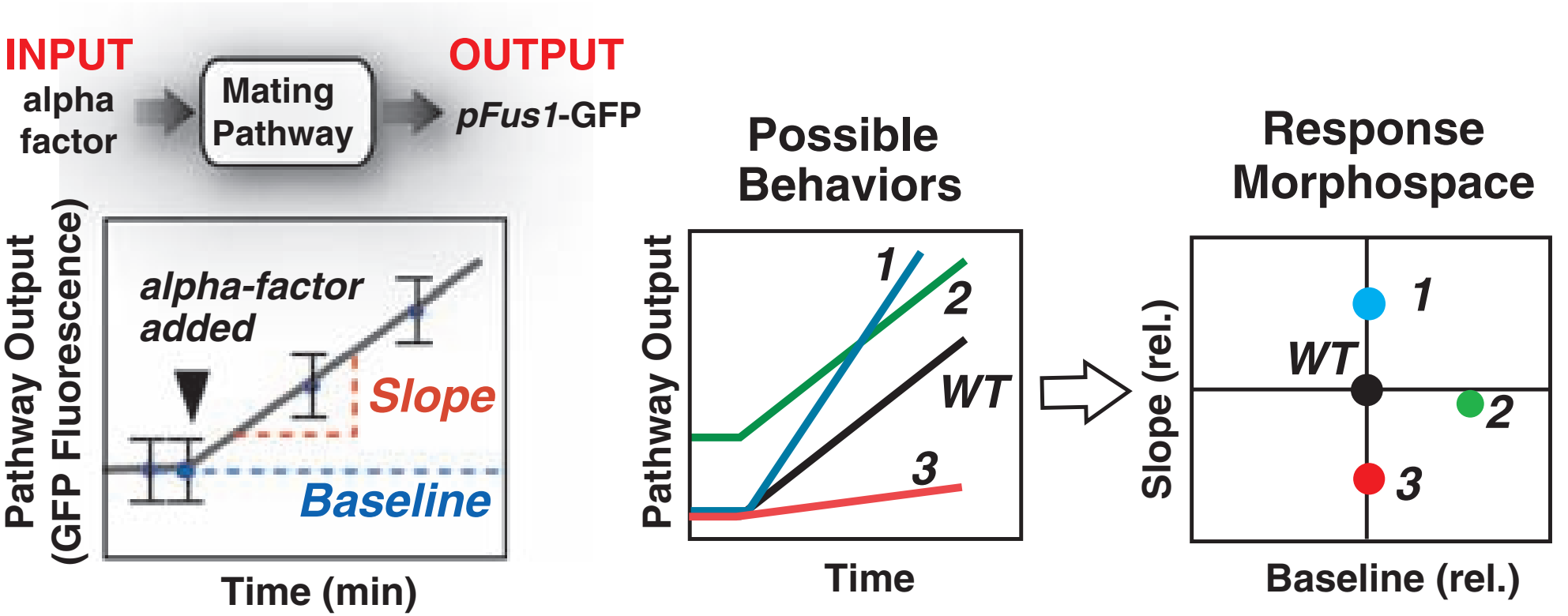


66 synthetics?

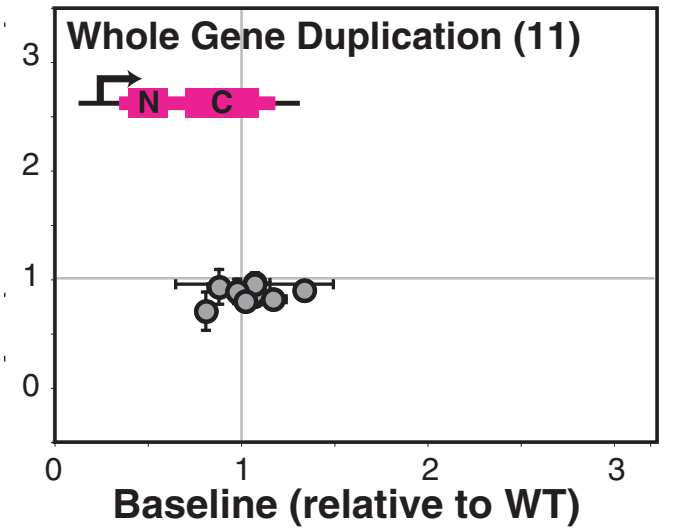
Types of Genetic Changes Analyzed in this Study

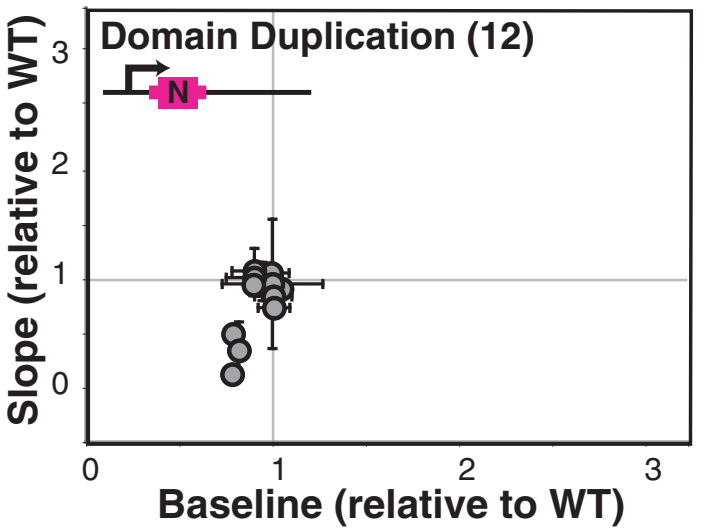


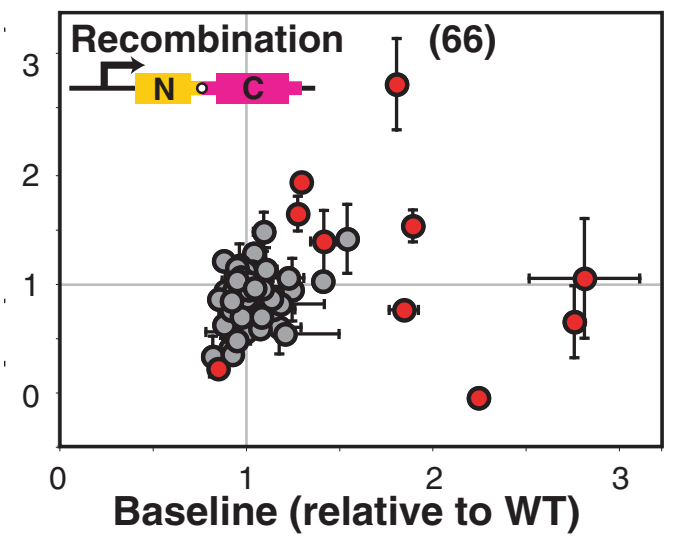
morphospace

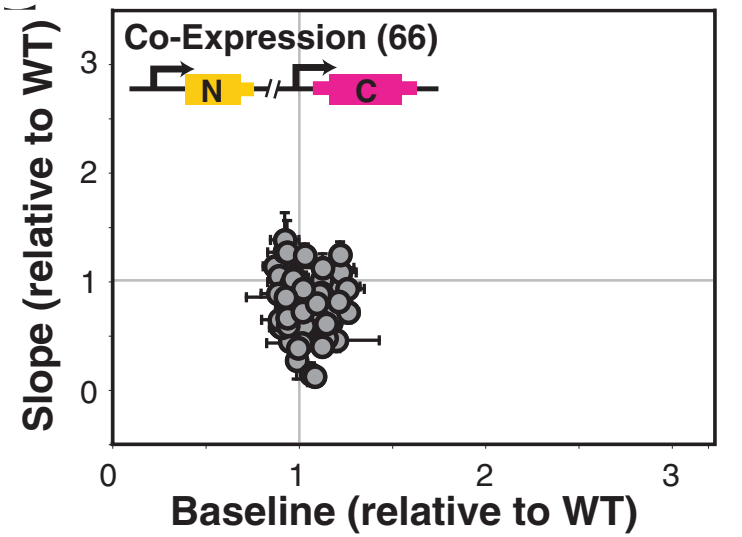


results - signalling

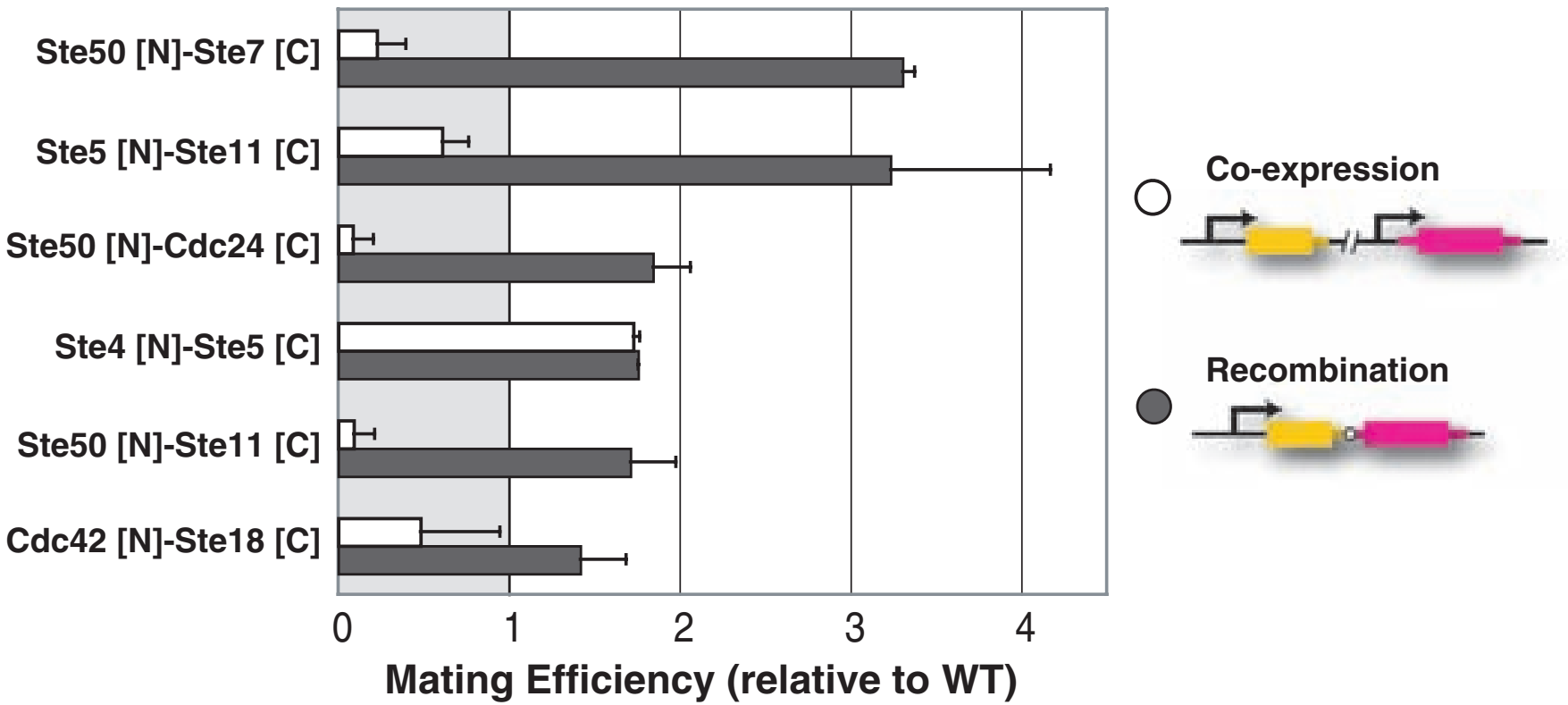






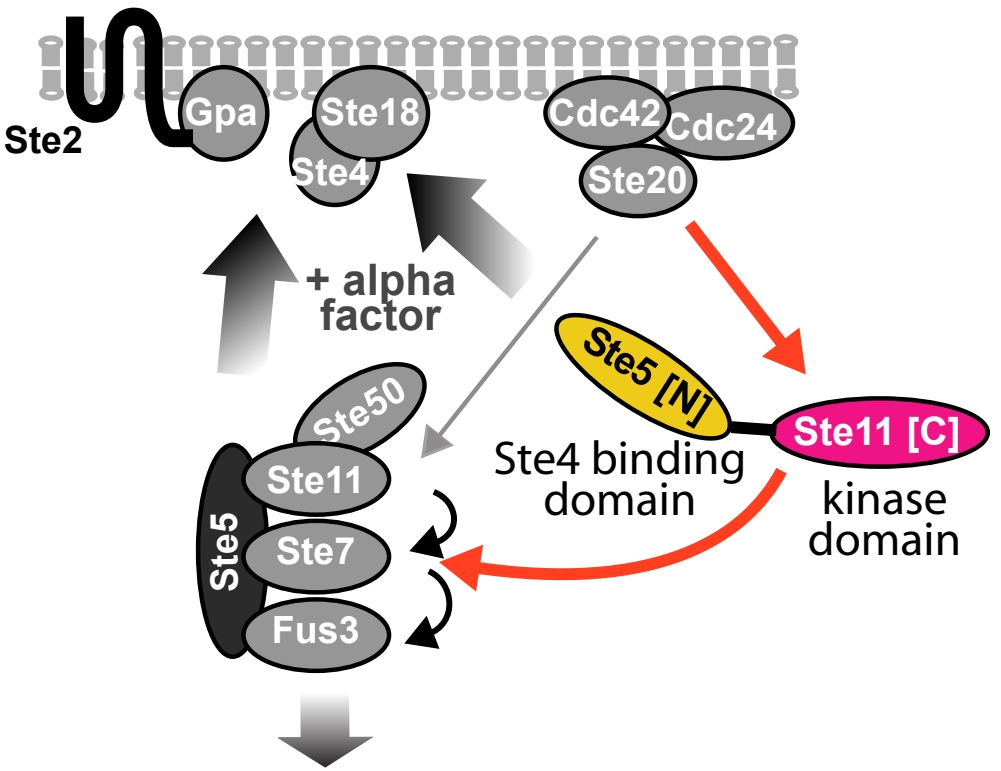


results - mating

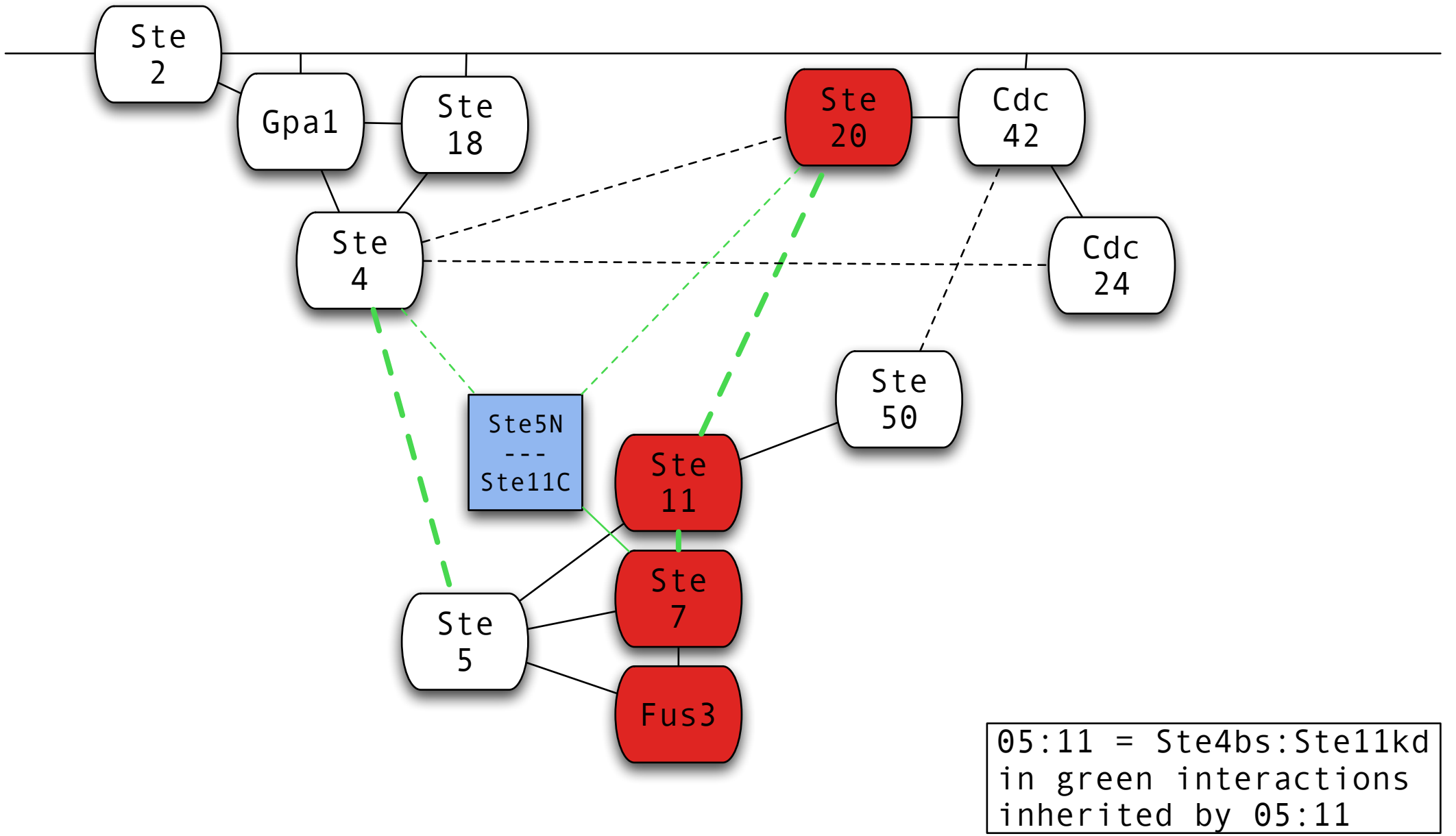


Ste5 [N]-Ste11 [C]

Model: Fusion provides additional route for alpha-factor dependent Ste11--> Ste7 signaling

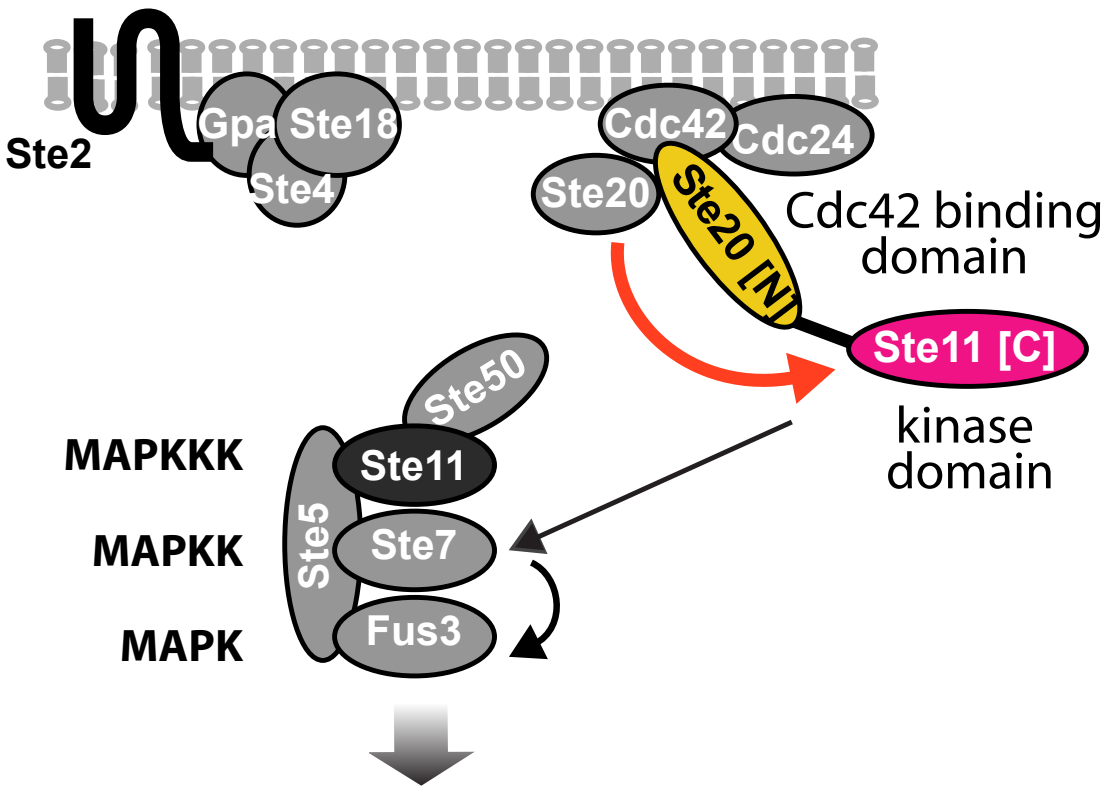


the blind watch making game



Ste20 [N]-Ste11 [C]

Model: Constitutive recruitment of Ste11 (MAPKKK) kinase domain to polarity complex primes activation by Ste20 (MAPKKKK)



Ste50 [N]-Ste20 [C]

Model: Constitutive recruitment of Ste20 (MAPKKKK) kinase domain to MAPK complex leads to constitutive pathway activation