A CASE STUDY

- HYPOXIA -

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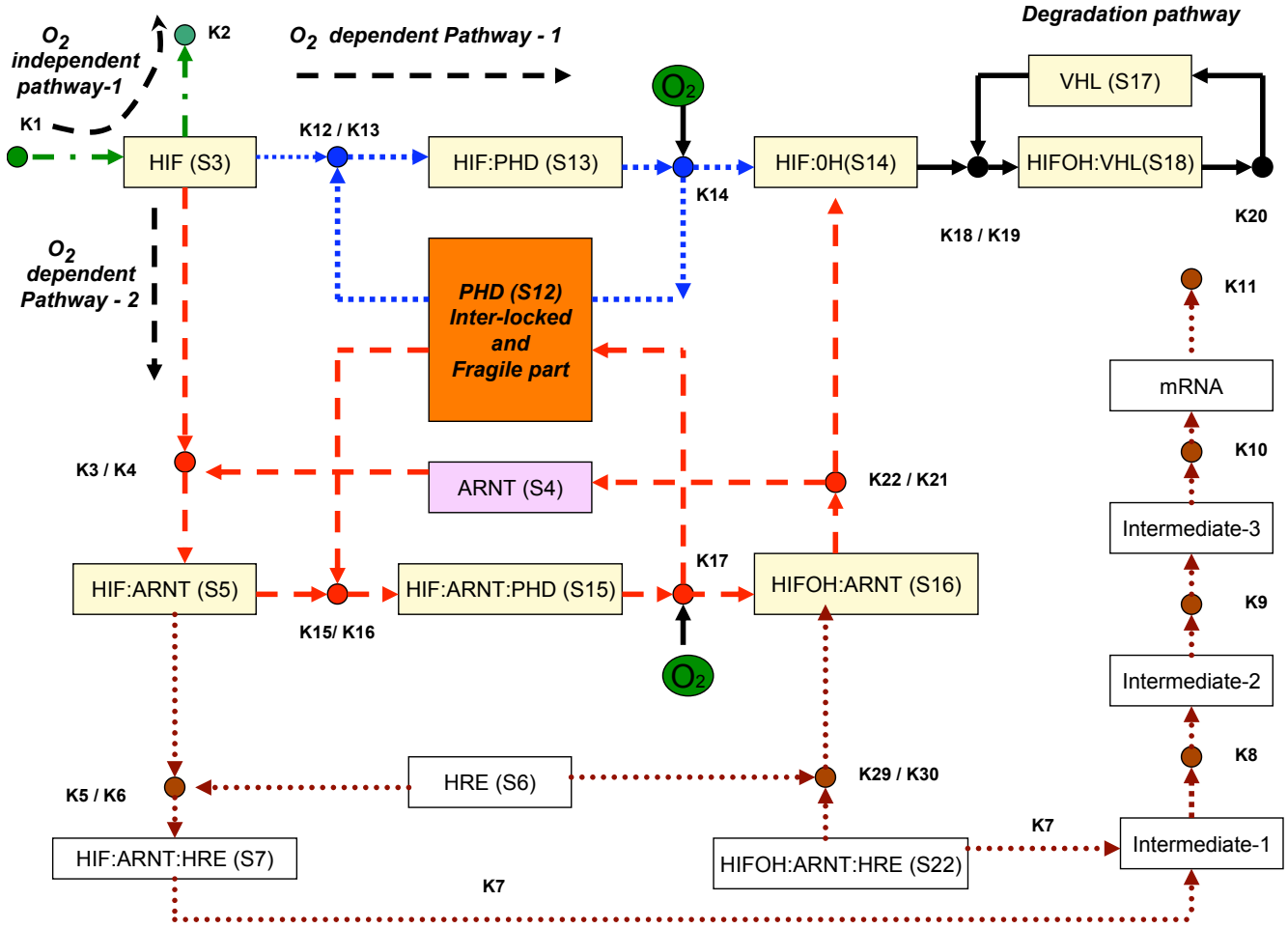
CASE STUDY - HYPOXIA

[YU ET AL. 2007]



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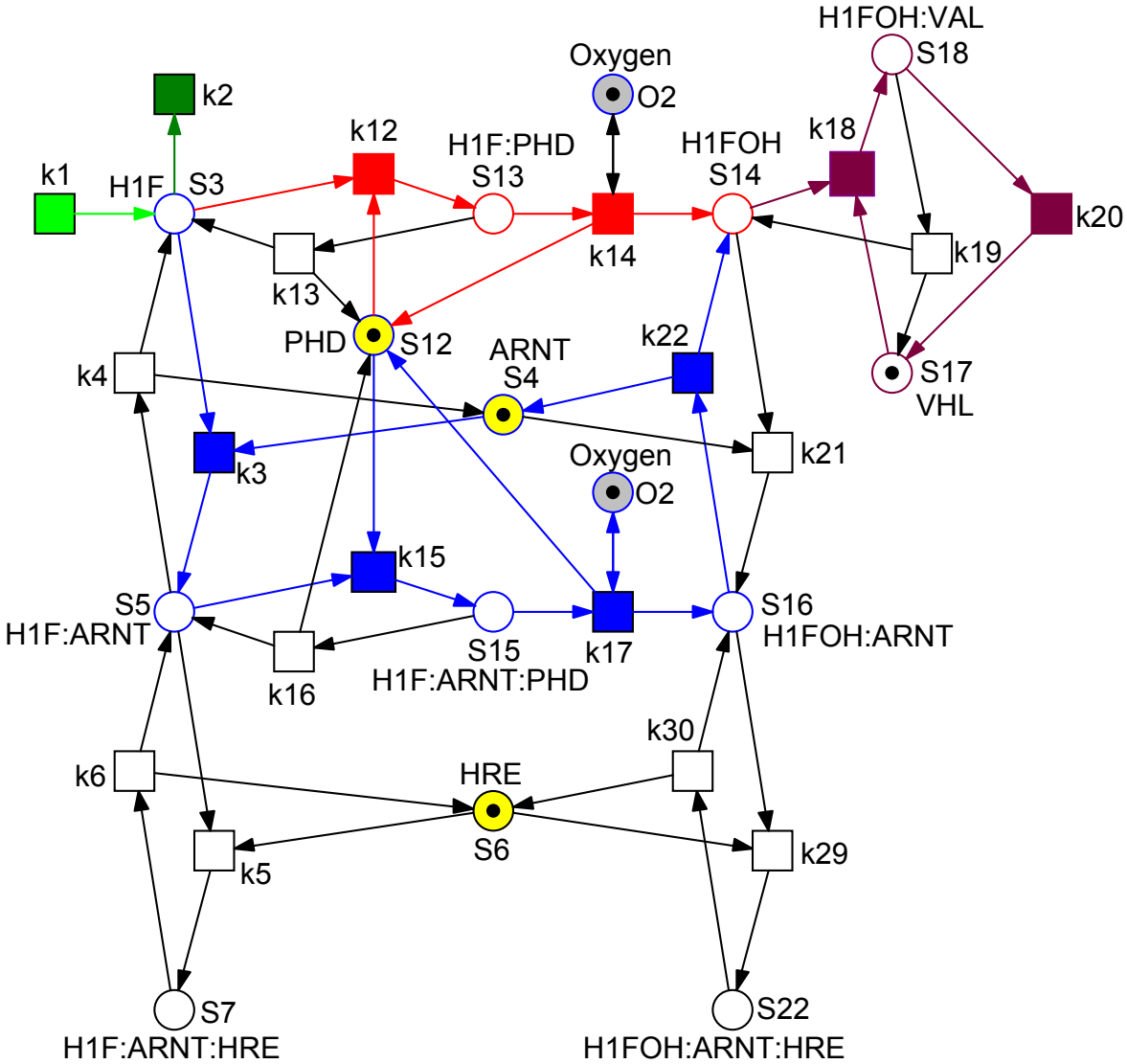
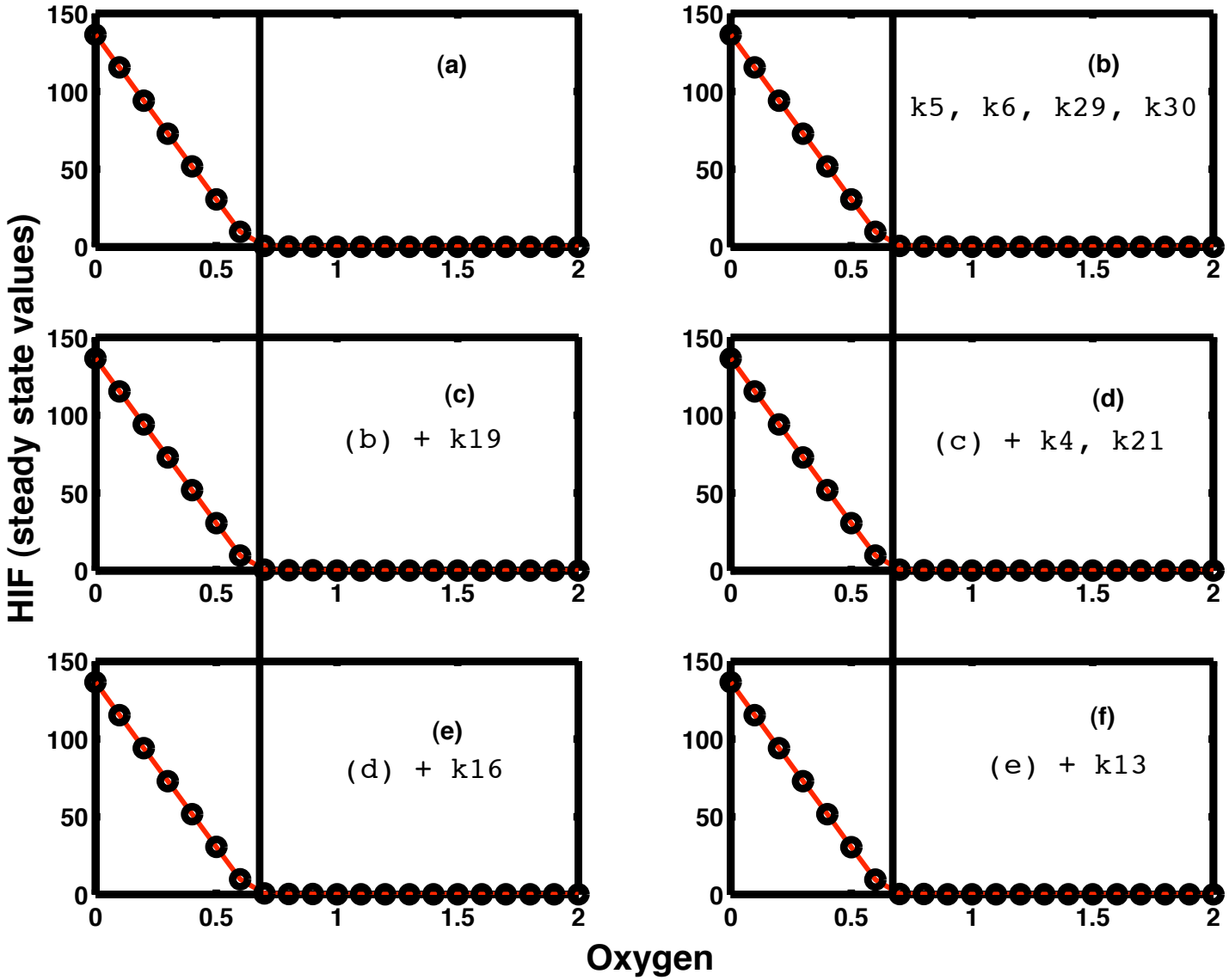
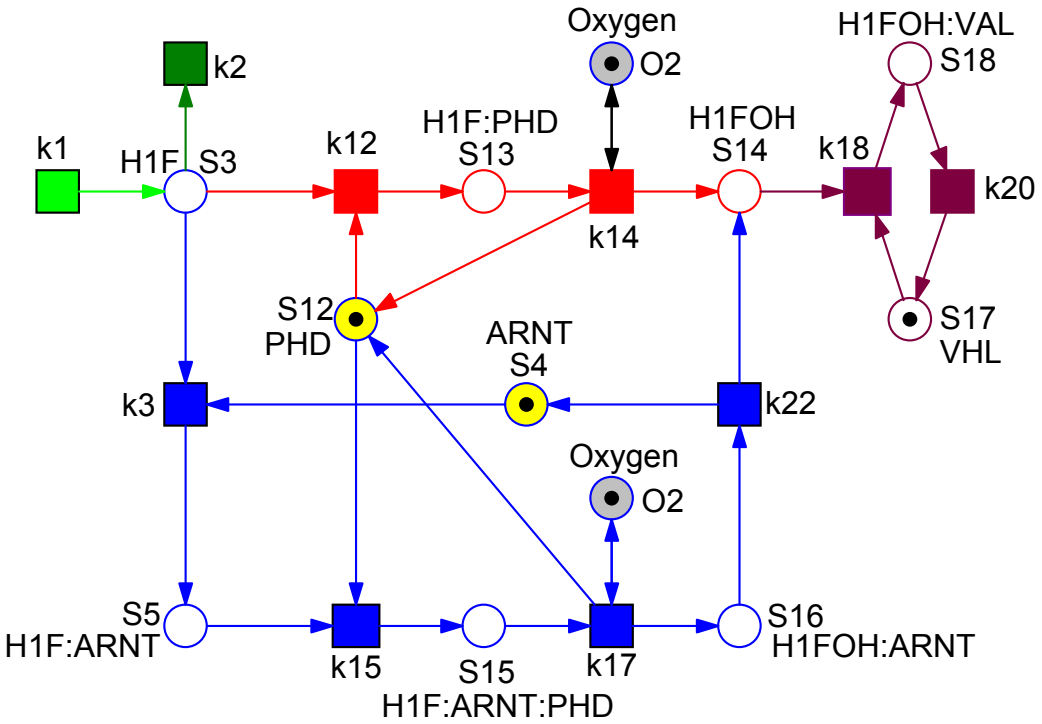
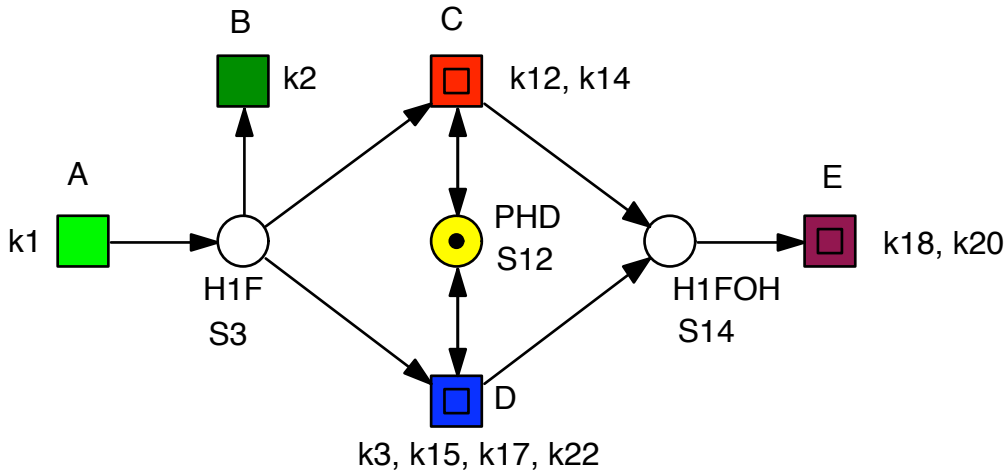
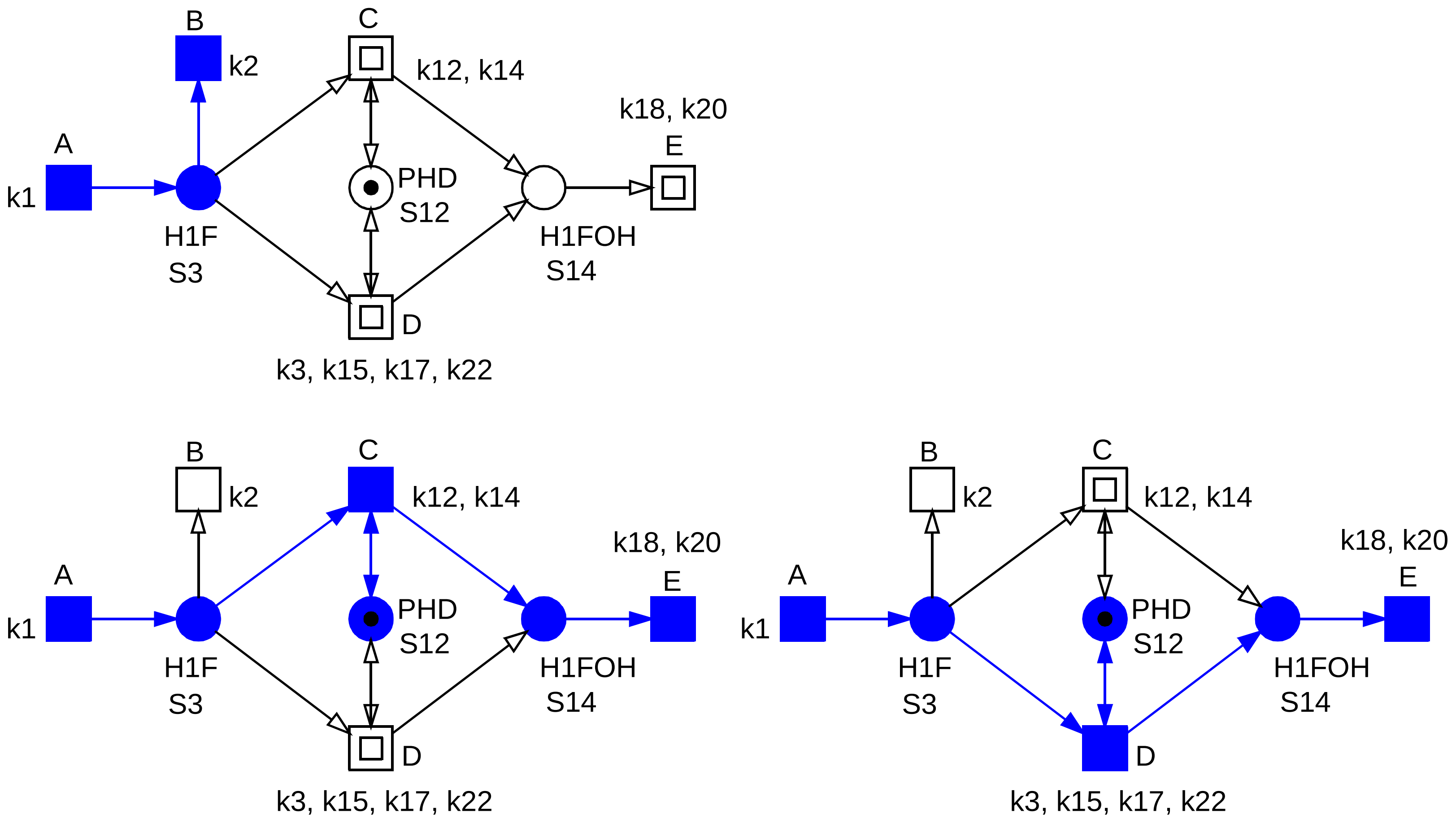
[HEINER; SRIRAM 2010]




HIF (steady state values)
Oxygen
(a)
(b)
k5, k6, k29, k30
(c)
(b) + k19
(d)
(c) + k4, k21
(e)
(d) + k16
(f)
(e) + k13
150
100
50
0
0
0.5
1
1.5
2


Oxygen
O2
H1FOH:VAL
S18
k2
k1
H1F
S3
k12
H1F:PHD
S13
H1FOH
S14
k18
k20
k14
S12
PHD
ARNT
S4
S17
VHL
k3
k22
Oxygen
O2
S5
H1F:ARNT
k15
S15
H1F:ARNT:PHD
k17
S16
H1FOH:ARNT


B
C
k2
k12, k14
A
E
k1
PHD
S12
k18, k20
H1F
S3
H1FOH
S14
D
k3, k15, k17, k22



B
k2
C
k12, k14
k18, k20
E
A
k1
PHD
S12
H1F
S3
H1FOH
S14
D
k3, k15, k17, k22
B
k2
C
k12, k14
k18, k20
E
A
k1
PHD
S12
H1F
S3
H1FOH
S14
D
k3, k15, k17, k22
B
k2
C
k12, k14
k18, k20
E
A
k1
PHD
S12
H1F
S3
H1FOH
S14
D
k3, k15, k17, k22

BUT,

THERE ARE MANY EXAMPLES
WHERE THE TRANSITION SPN -> CPN
COMES WITH COUNTERINTUITIVE EFFECTS.

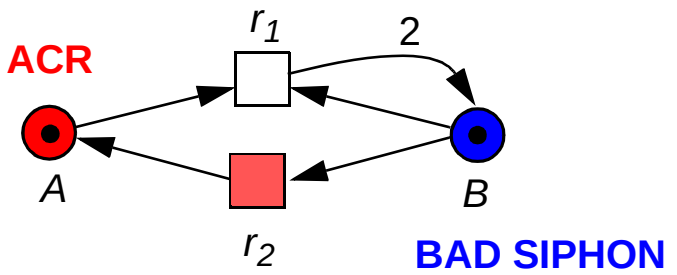
ABSOLUT CONCENTRATION ROBUSTNESS (ACR)

- **ACR: steady state value of variable (place) does not depend on total mass, only on kinetic constants** *-> [SHINAR, FEINBERG 2010]*

- **simple example** **mass-action kinetics**

  r_1: $A + B \rightarrow 2B$ $v_1(r_1) = k_1AB$

  r_2: $B \rightarrow A$ $v_2(r_2) = k_2B$



- **ODEs**

  $dA/dt = v_2 - v_1 = k_2B - k_1AB$

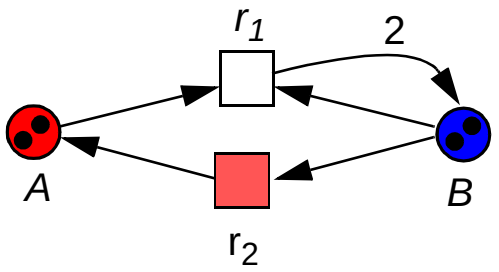
  $dB/dt = v_1 - v_2 = k_1AB - k_2B$

CPI: $m_0(A) + m_0(B) = total$

- **steady state**

  $dA/dt = k_2B - k_1AB = 0$

  $dB/dt = k_1AB - k_2B = 0$



-> *steady_state(A) = k_2/k_1*

steady_state(B) = total - k_2/k_1