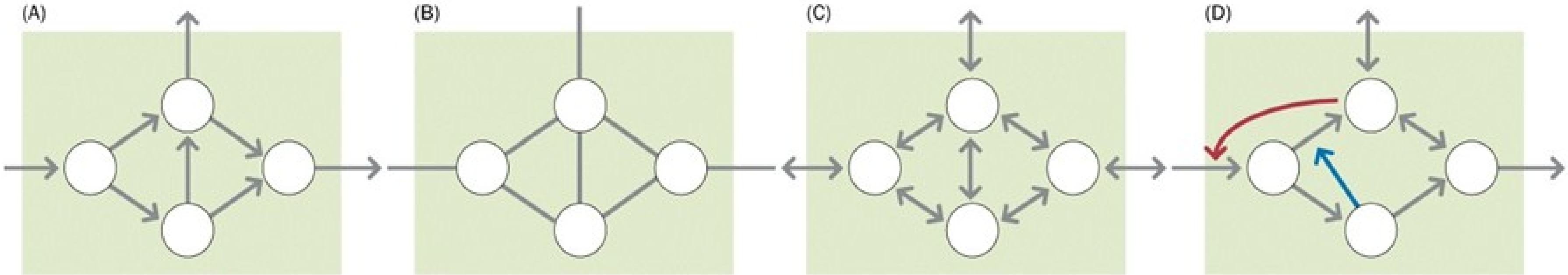
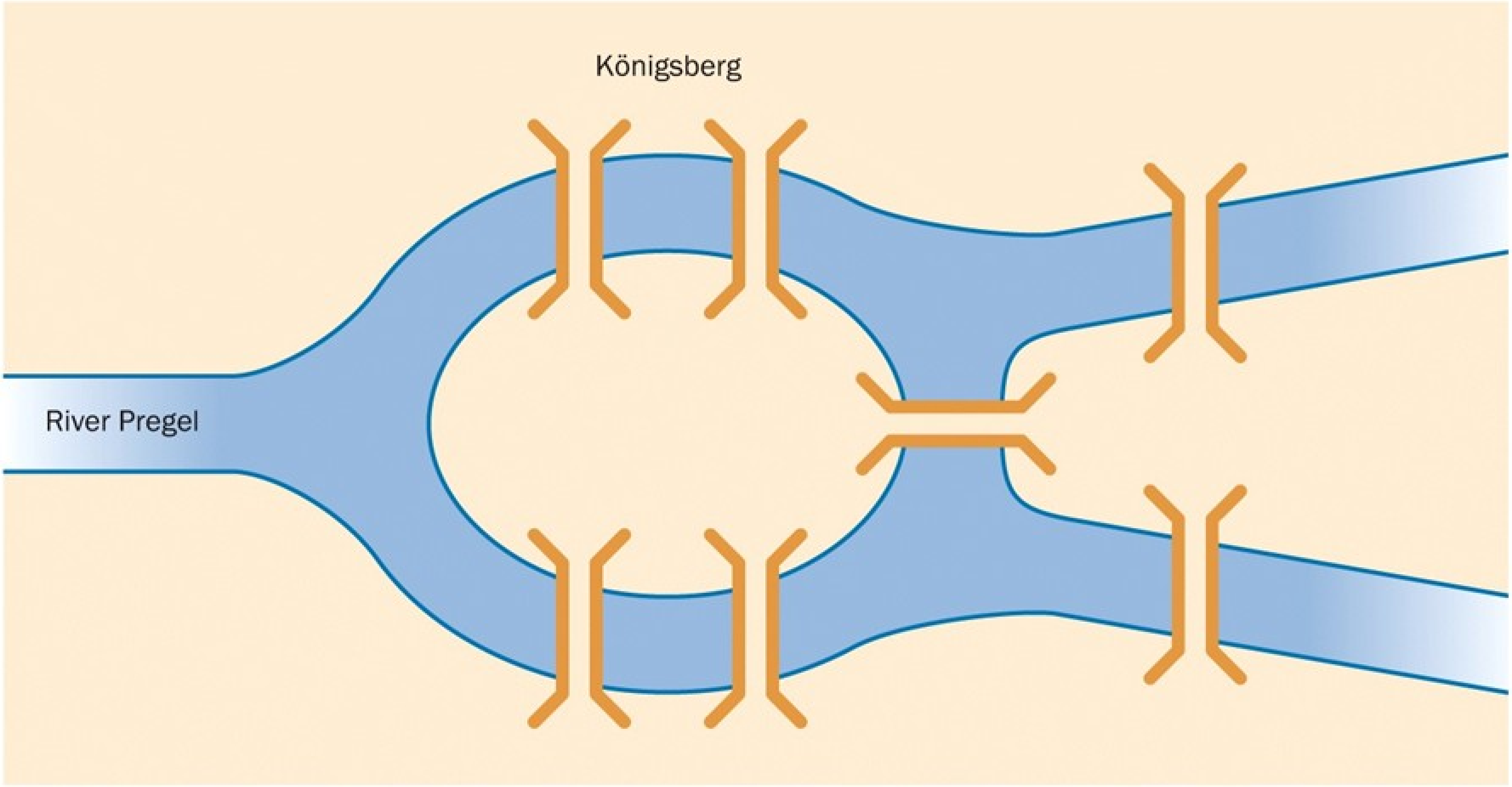
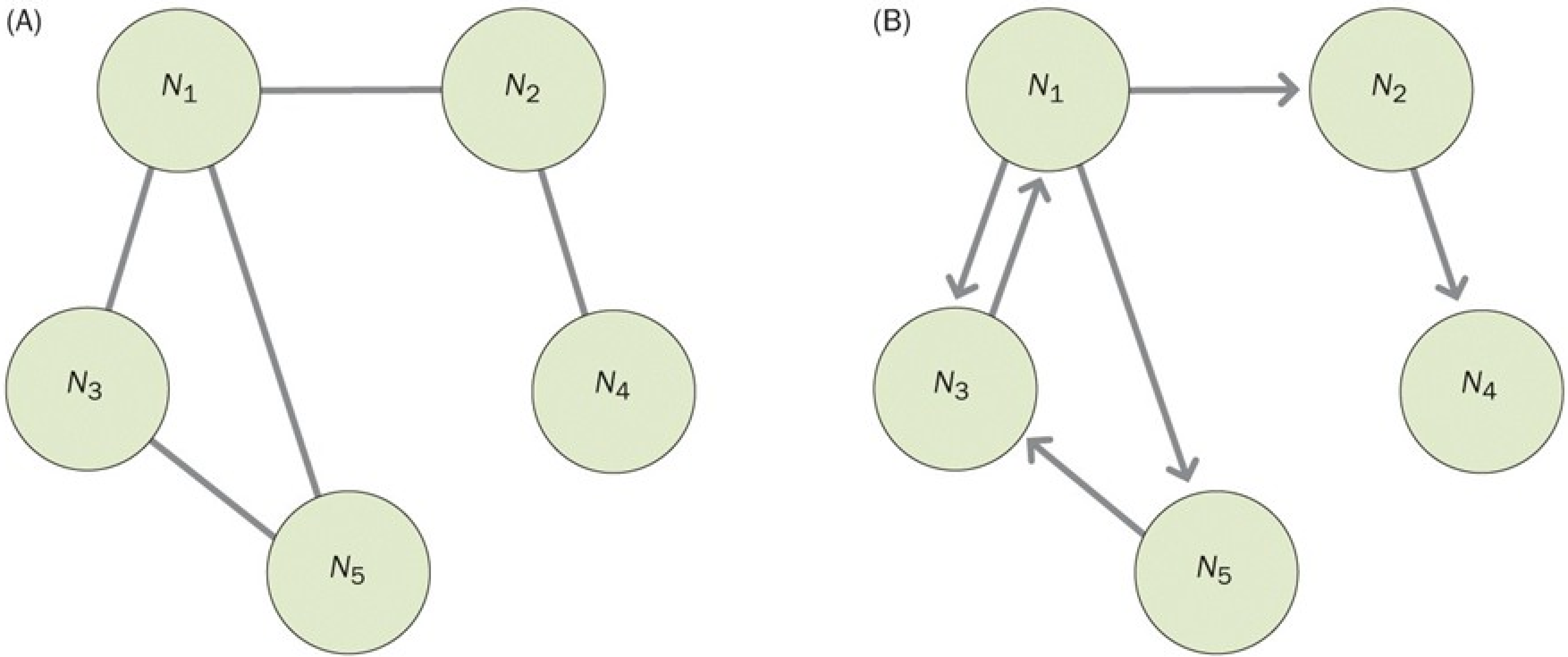
Eberhard O. Voit

A First Course in Systems Biology

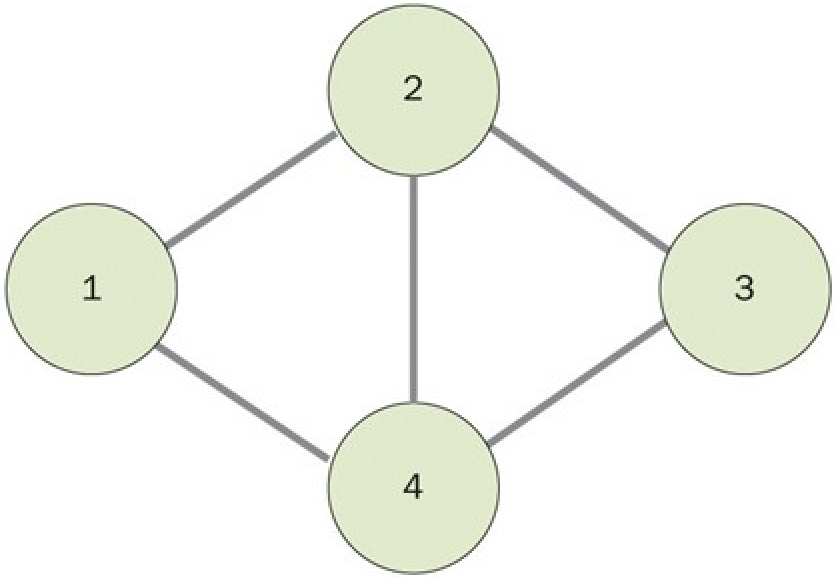
Chapter 3
Static Network Models

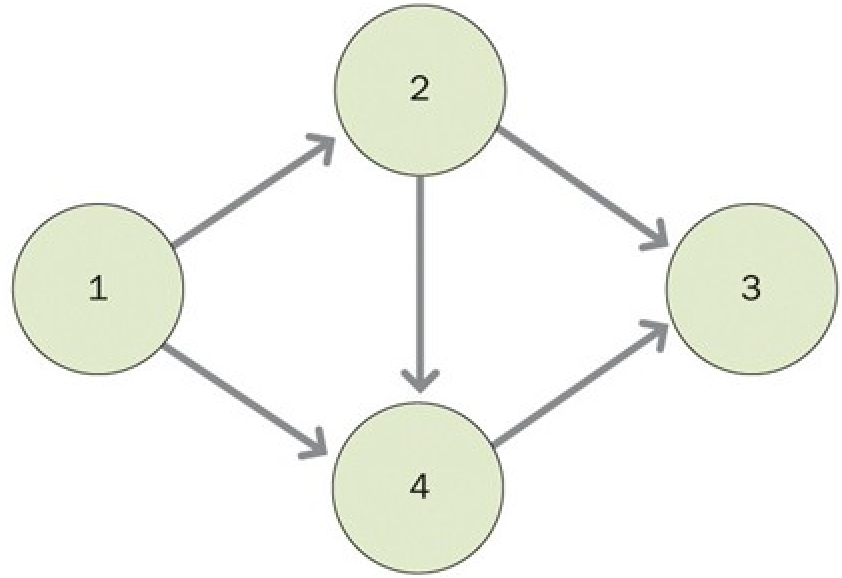

(A)
(B)
(C)
(D)


Königsberg
River Pregel



(A)
N_1
N_2
N_3
N_4
N_5
(B)
N_1
N_2
N_3
N_4
N_5

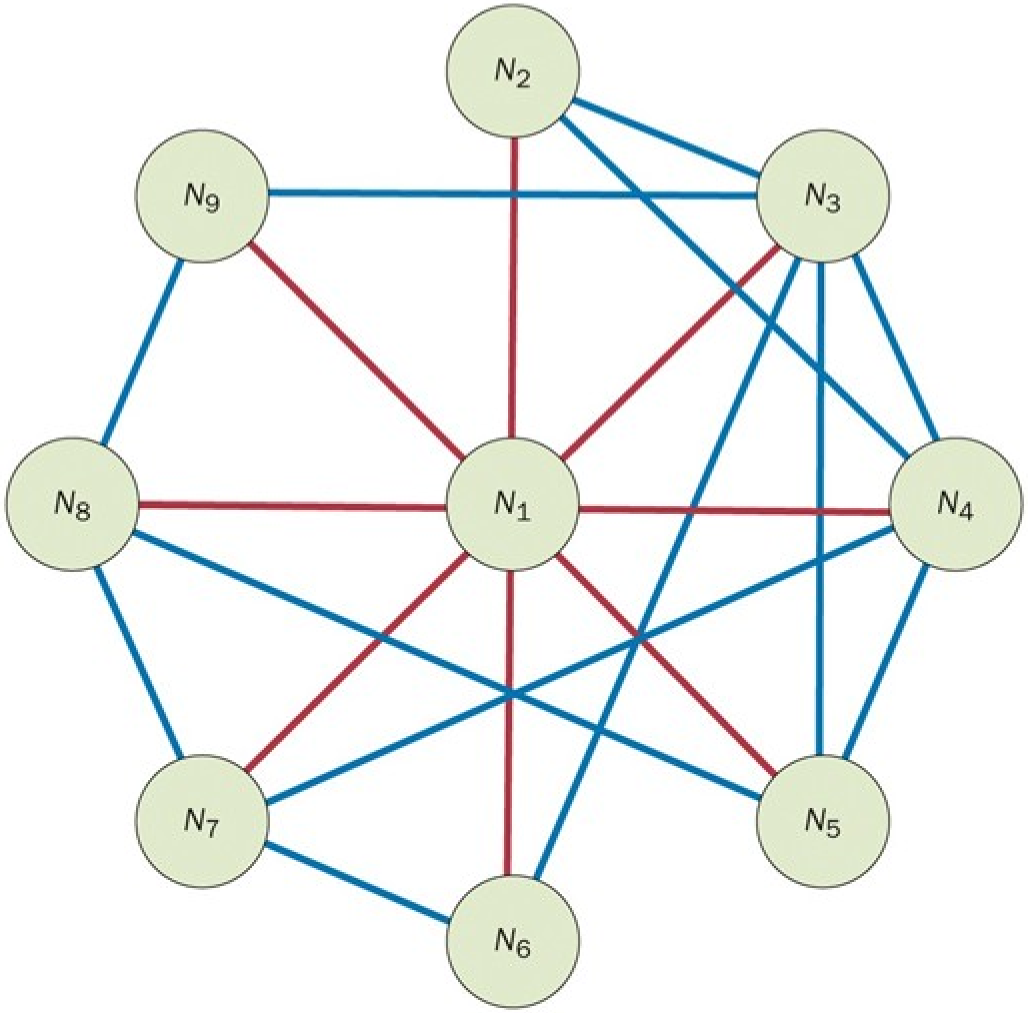




$$\mathbf{A} = \begin{bmatrix} 0 & 1 & 0 & 1 \\ 1 & 0 & 1 & 1 \\ 0 & 1 & 0 & 1 \\ 1 & 1 & 1 & 0 \end{bmatrix}$$

$$\mathbf{A} = \begin{bmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$

Clustering coefficient: Characterizing density of edges associated with a node

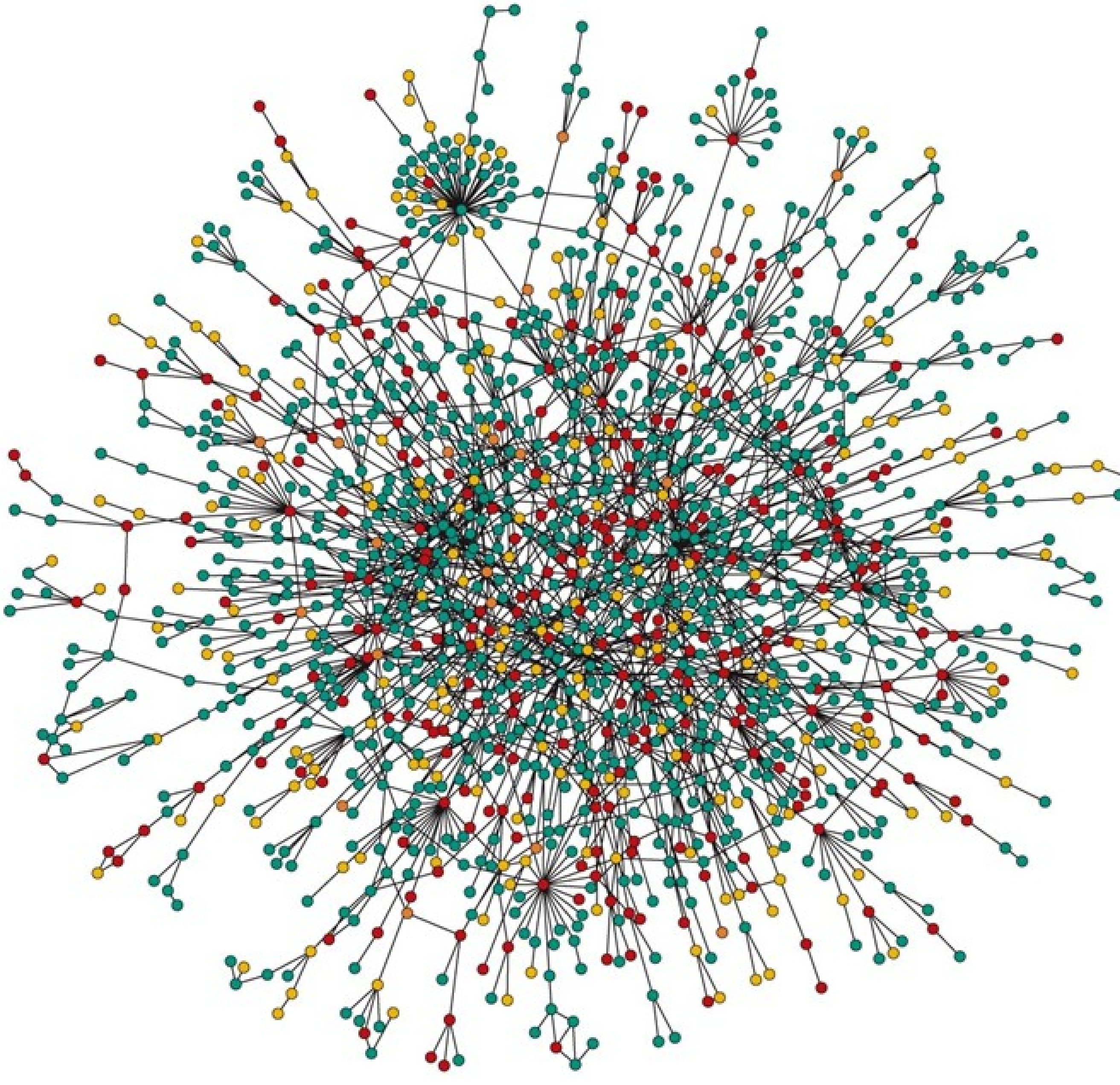


UG: $\mathbf{C_N = 2e/k(k-1)}$

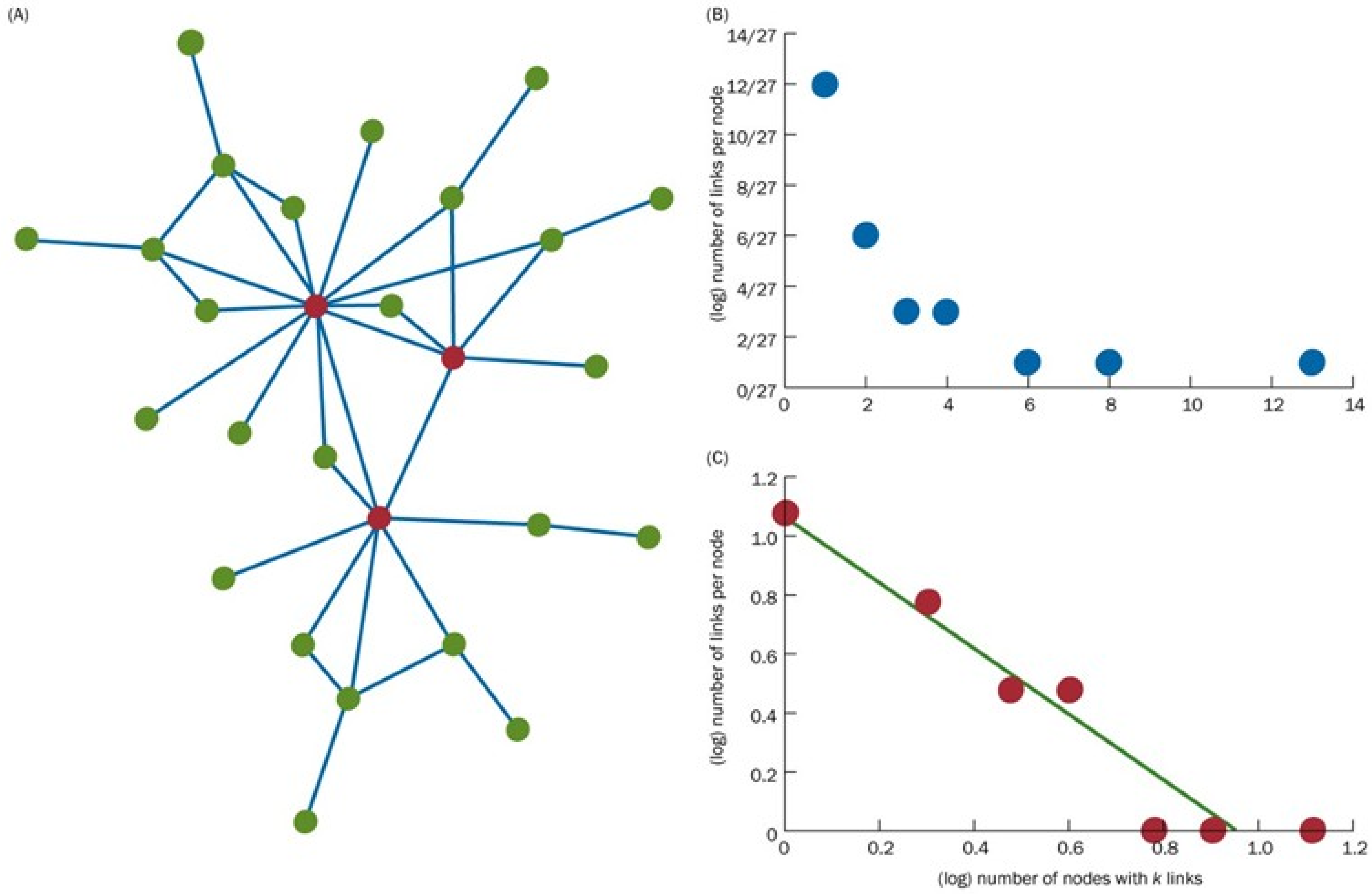
DG: $\mathbf{C_N = e/k(k-1)}$

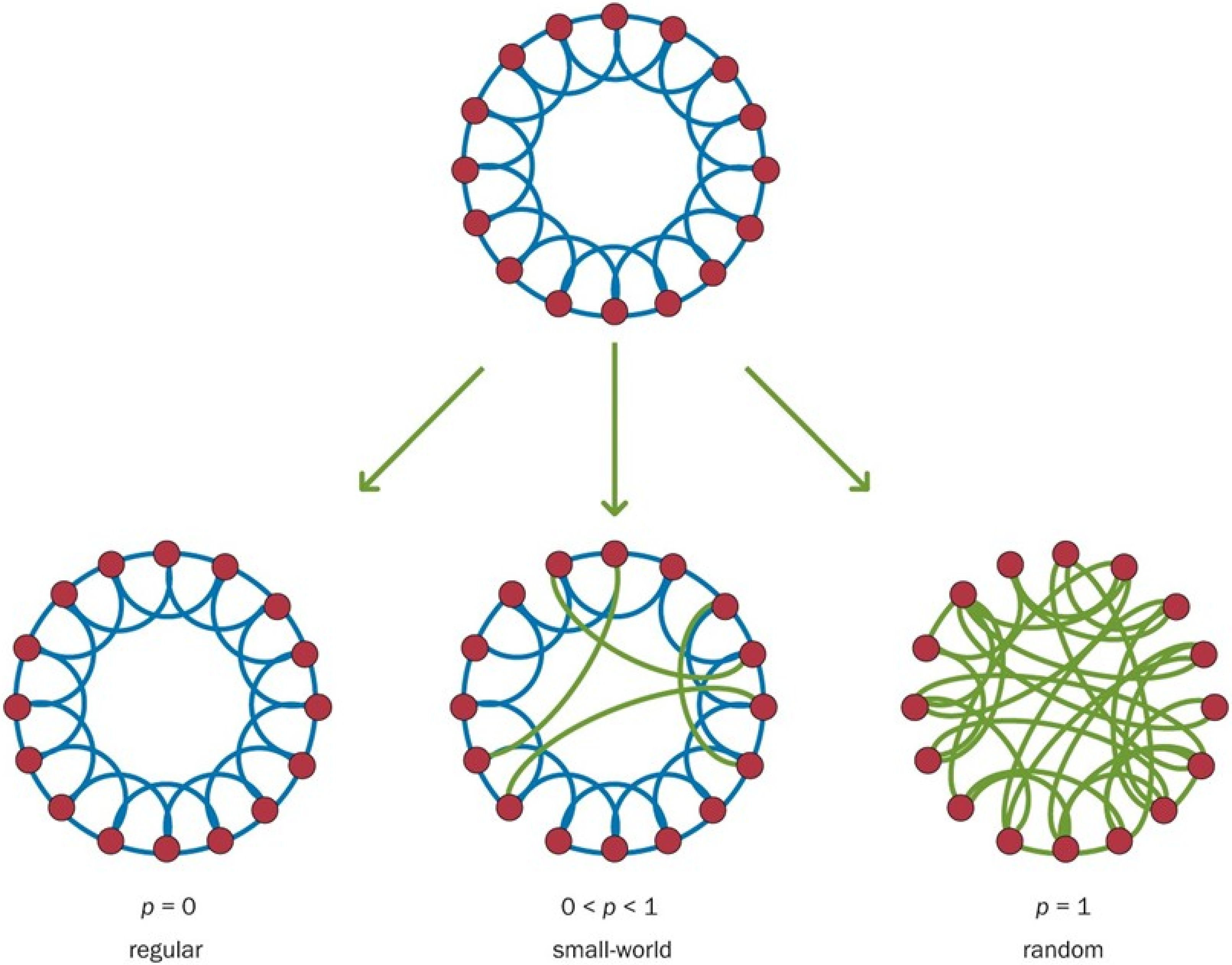
(k is degree)

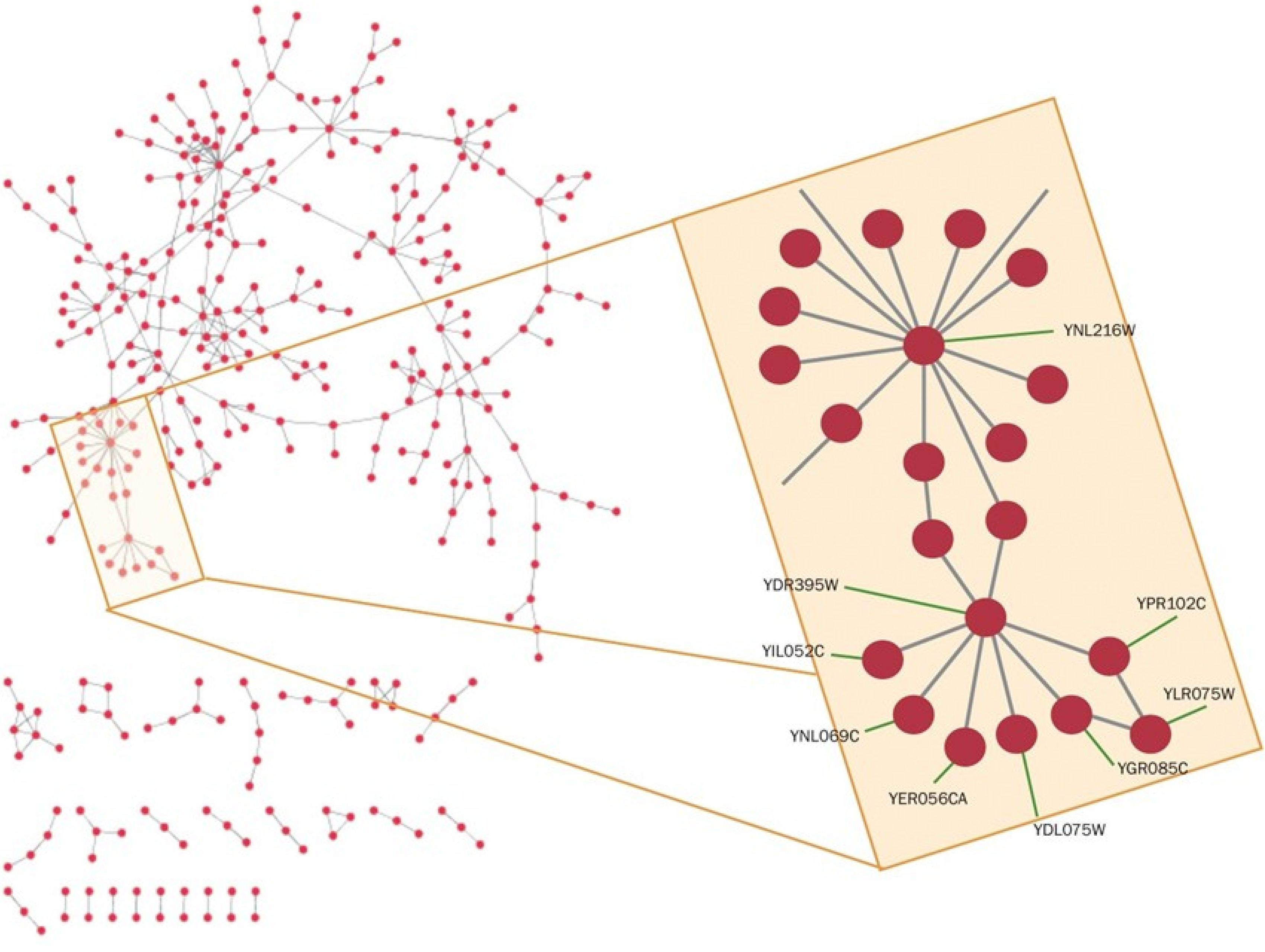
$$C_G = \frac{1}{m}\sum_{N=1}^{m} C_N$$

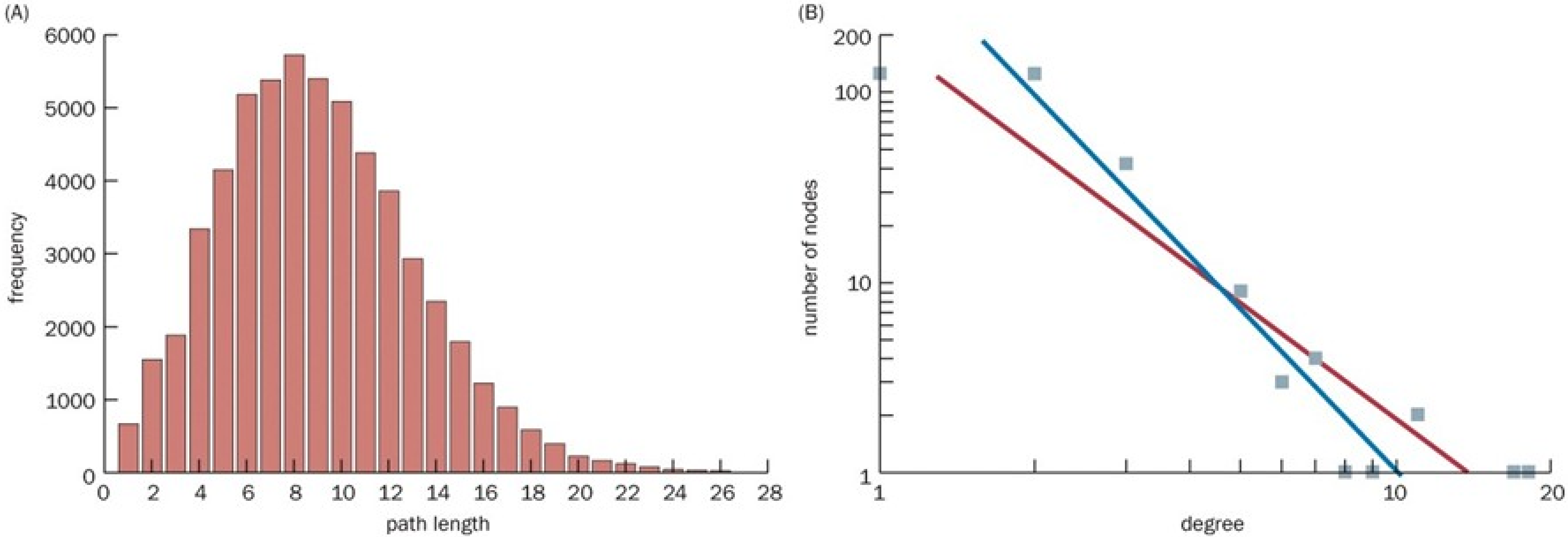


Power-law and degree distribution: $P(k) \propto k^{-\gamma}$



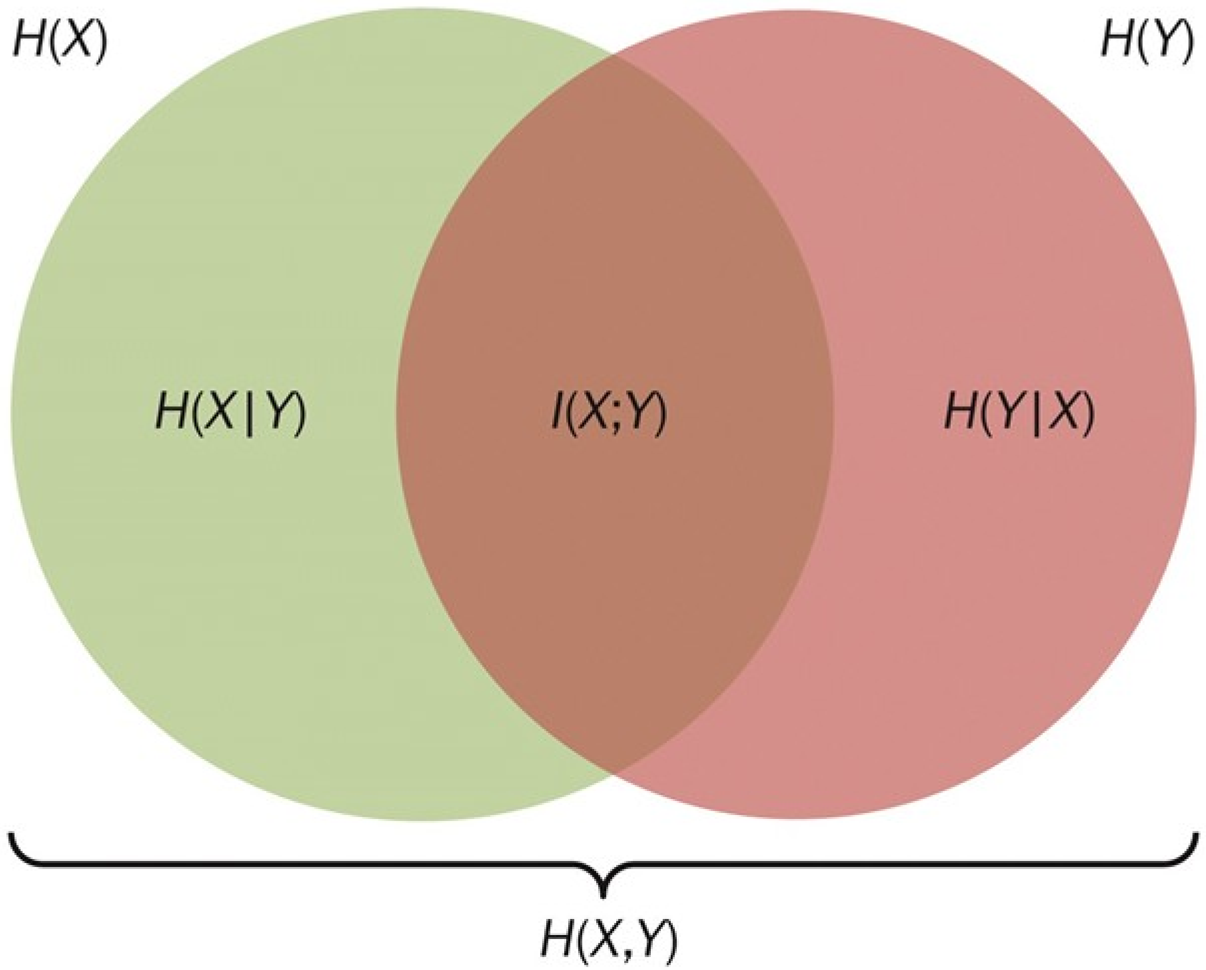

p = 0
regular
0 < p < 1
small-world
p = 1
random


YNL216W
YDR395W
YPR102C
YIL052C
YLR075W
YNL069C
YGR085C
YER056CA
YDL075W



(A)
6000
5000
4000
3000
2000
1000
0
frequency
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
path length
(B)
200
100
10
1
number of nodes
1
10
20
degree

Mutual information I(X;Y) in terms of entropies H(X), H(Y) and conditional entropies H(X|Y) and H(Y|X)



Bayes' theorem

(Also called Bayes' law/formula/rule)

When prior knowledge is available, Bayes' theorem allows computation of probability of an event.

$$P(A \mid B) = \frac{P(B \mid A)P(A)}{P(B)}$$

Note: P(B) is non-zero.

Where:

- P(A) and P(B) are (independent probabilities of observing events A and B,
- P(A|B) is the 'conditional probability' (*ie*, prob. of observing A when B happens), and
- P(B|A) is the 'conditional probability' (*ie*, prob. of observing B when A happens).

$$P(B \mid A) = \frac{P(B \text{ and } A)}{P(A)}$$

$$P(B \mid A)P(A) = P(B \text{ and } A) = P(A \text{ and B}) = P(A \mid B)P(B)$$

$$P(A \mid B) = \frac{P(A \text{ and B})}{P(B)} = \frac{P(B \mid A)P(A)}{P(B)}$$

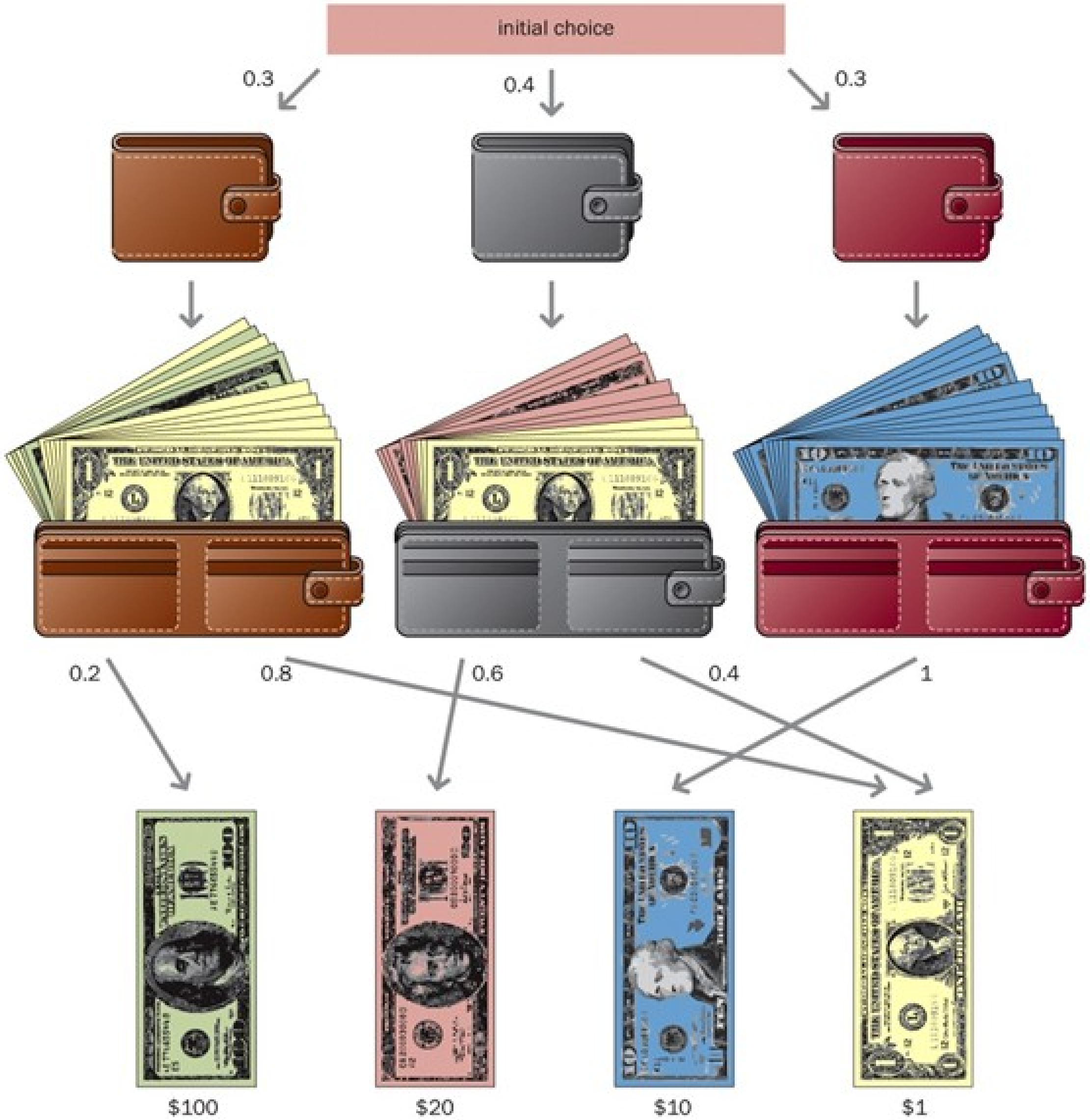
$$P(A \mid B) = \frac{P(B \mid A)P(A)}{P(B)}$$

Prior probability: P(A), the initial belief in A

Posterior probability: P(A|B), is the probability of A given evidence B

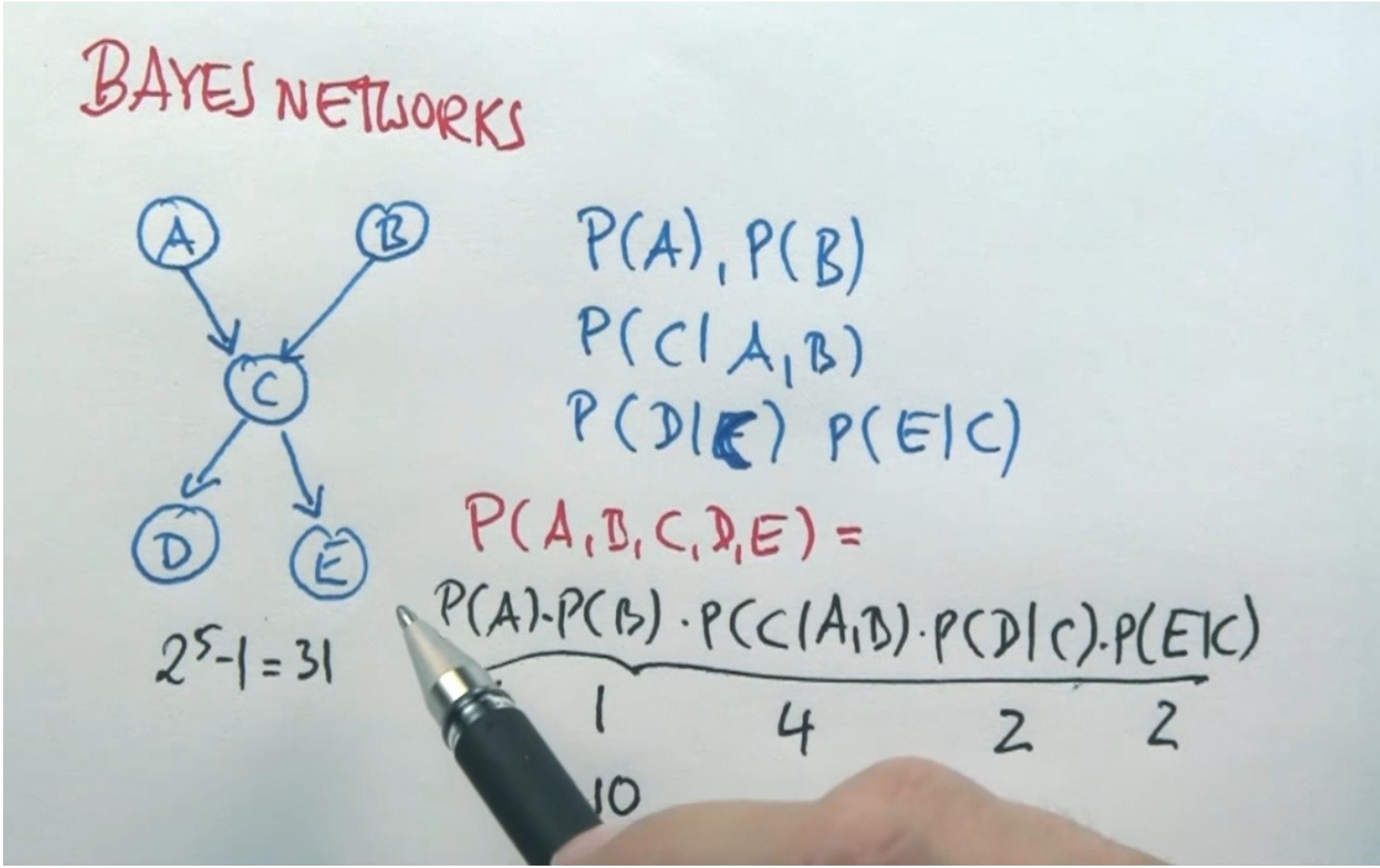
Support B provides for A: P(B|A)/P(B)

Bayesian reconstruction of interaction networks

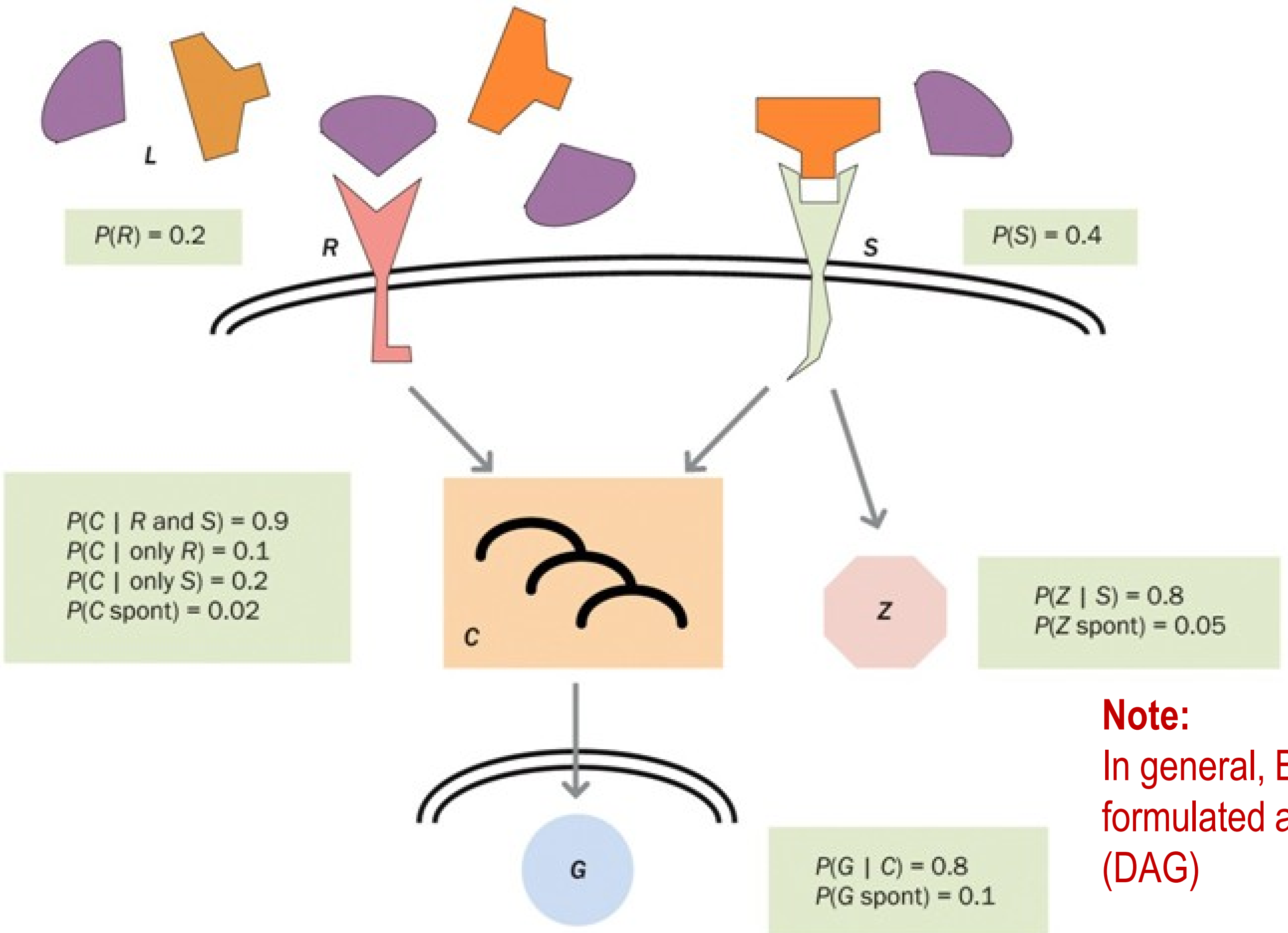


Probabilities:

P($100) = 0.06
P($20) = 0.24
P($10) = 0.3
P($1) = 0.4


BAYES NETWORKS
A
B
C
D
E
2^5-1 = 31
P(A), P(B)
P(C|A,B)
P(D|C) P(E|C)
P(A,B,C,D,E) =
P(A)·P(B)·P(C|A,B)·P(D|C)·P(E|C)
1
4
2
2
10

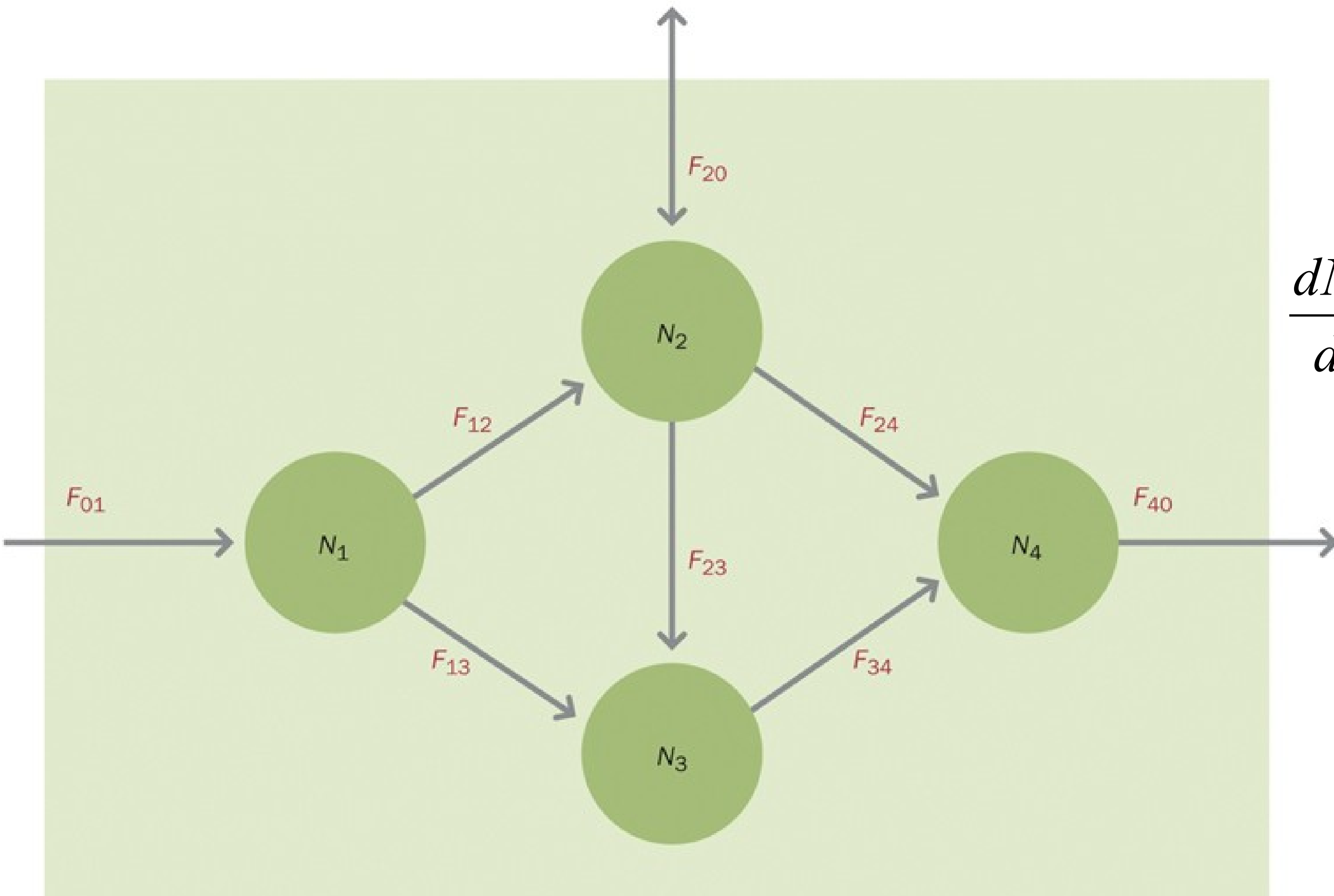
Signaling networks



Note:
In general, Bayesian network is formulated as a directed acyclic graph (DAG)

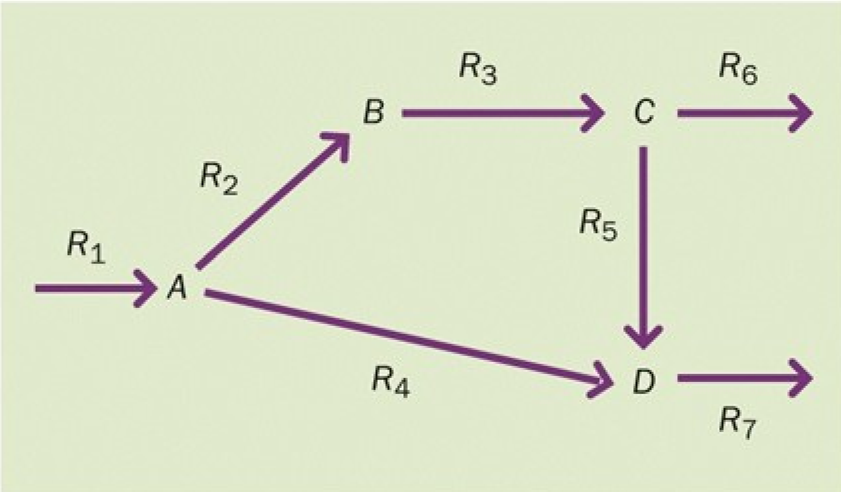
$$P(\text{G, C, R, S are "on"}) = P(G \mid C).P(C \mid \text{R and S}).P(R).P(S)$$
$$= 0.8 * 0.8 * 0.2 * 0.4$$
$$= 0.0576$$

Stoichiometric networks



$$\frac{dN_3}{dt} = F_{13} + F_{23} - F_{34} = 0,$$

$$\Rightarrow F_{13} + F_{23} = F_{34}$$



$$
\mathbf{N} = \begin{array}{c} \\ \end{array}
\begin{array}{ccccccc} R_1 & R_2 & R_3 & R_4 & R_5 & R_6 & R_7 \end{array}
$$

$$
\mathbf{N} = \begin{bmatrix} 1 & -1 & 0 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 & -1 & 0 \\ 0 & 0 & 0 & 1 & 1 & 0 & -1 \end{bmatrix} \begin{matrix} A \\ B \\ C \\ D \end{matrix}
$$

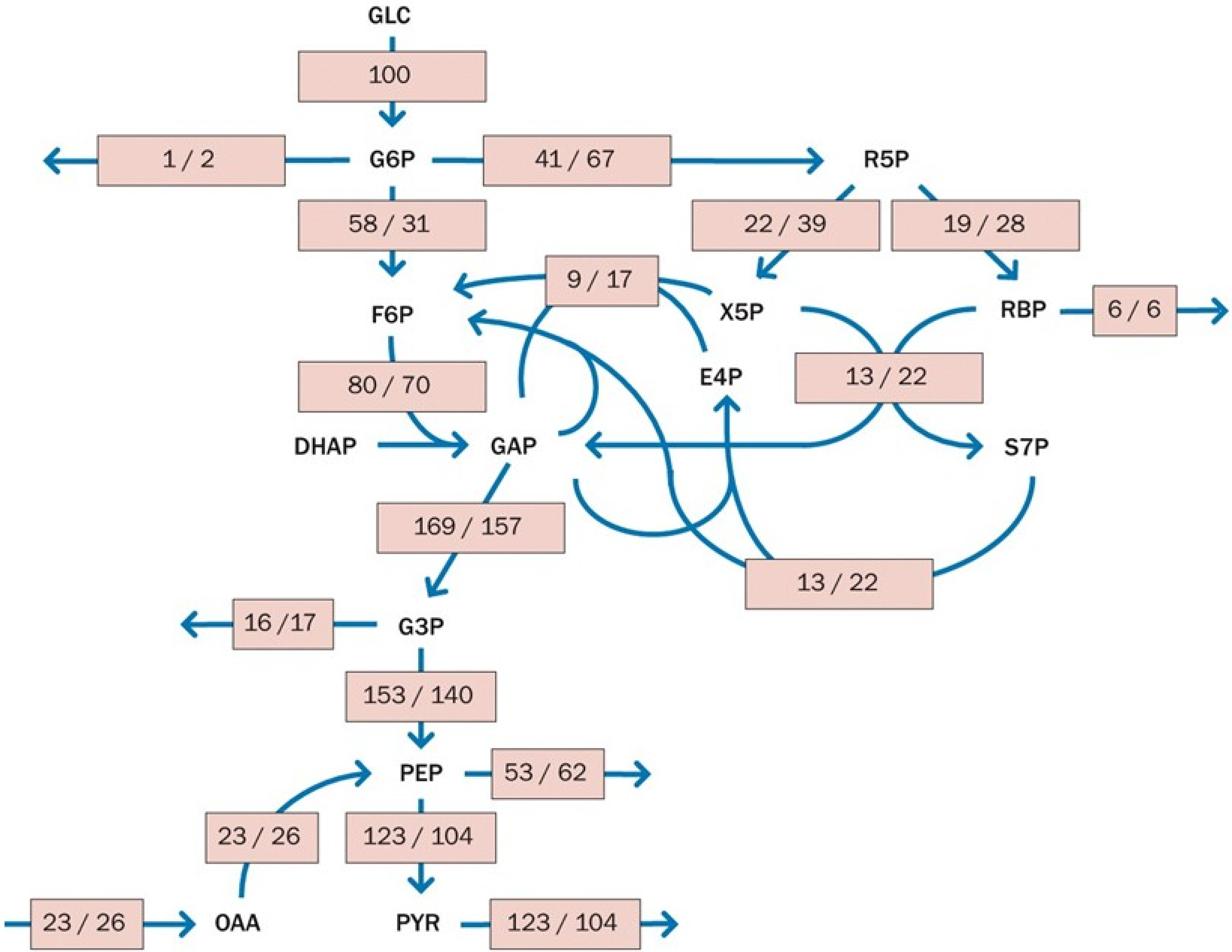
$$\dot{\mathbf{S}} = \mathbf{NR}$$

Stochiometric Analysis:

Flux Balance Analysis is widely used with biologically motivated constraints using *constrained optimization*.

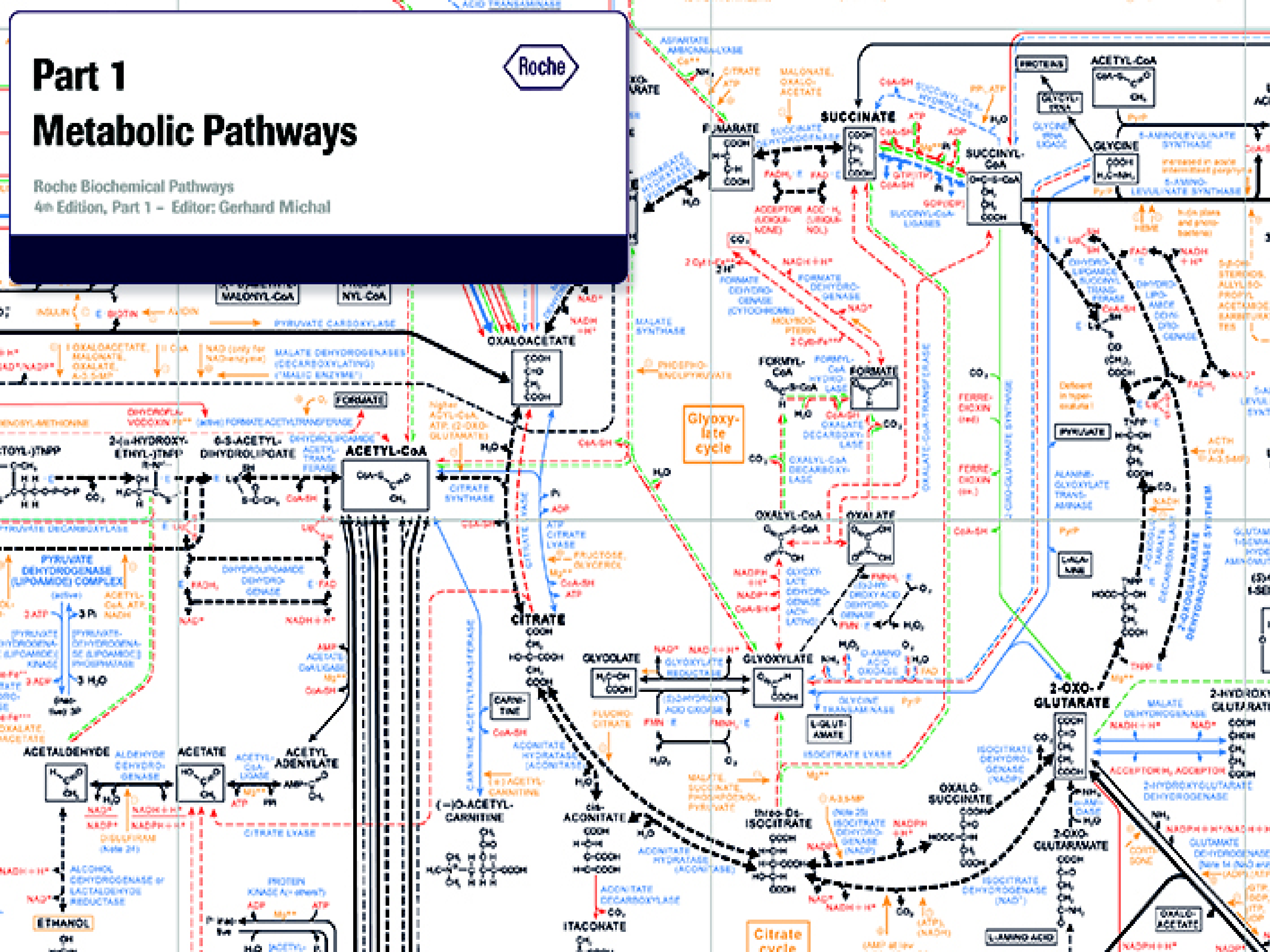
N: Stochiometric matrix of generic flux matrix

R: Fluxes between pools

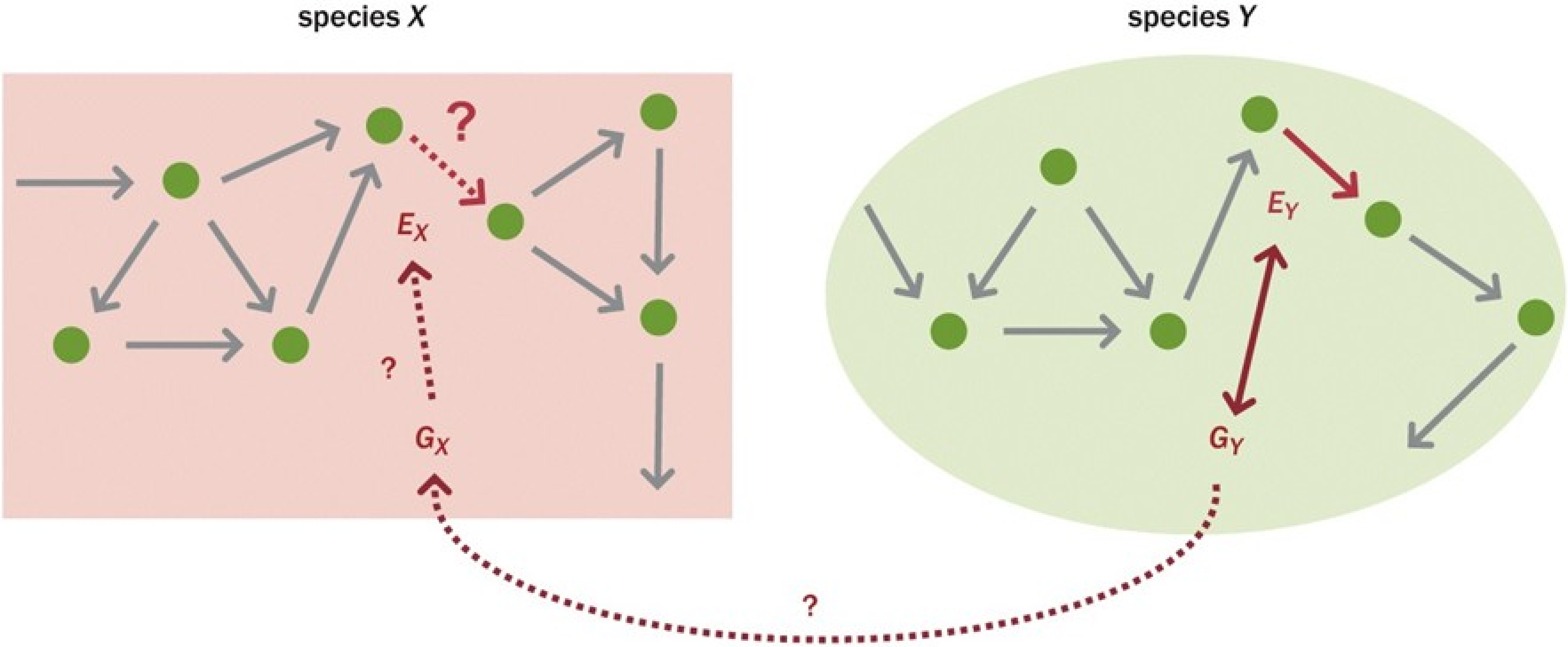

GLC
100
G6P
1 / 2
41 / 67
R5P
58 / 31
22 / 39
19 / 28
9 / 17
F6P
X5P
RBP
6 / 6
E4P
13 / 22
80 / 70
DHAP
GAP
S7P
169 / 157
13 / 22
G3P
16 / 17
153 / 140
PEP
53 / 62
23 / 26
123 / 104
23 / 26
OAA
PYR
123 / 104

Part 1
Metabolic Pathways

Roche Biochemical Pathways
4th Edition, Part 1 – Editor: Gerhard Michal



Metabolic network reconstruction



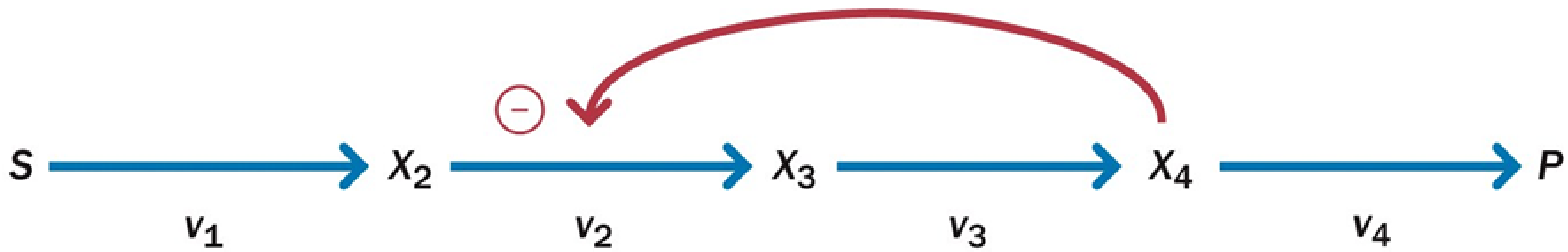
Note:
KEGG and MetaCyc databses are useful

Metabolic Control Analysis

Characterizes small perturbations in a metabolic pathway that operates at steady state.

It uses:
- **Elasticities**
- **Control coefficients**
  - Pathway flux
  - Concentration

Note: Flux control coefficients sum to 1 and concentration control coefficients sum to 0.



S
X2
X3
X4
P
v1
v2
v3
v4
−