Micro and Macro Systems in Life Sciences
Będlewo, 8 -13 June 2015

Mean-field approximation in gene regulation and evolutionary games

Jacek Miękisz
Institute of Applied Mathematics and Mechanics
University of Warsaw

Systems of many interacting entities

- particles, atoms, spins in statistical physics
- bio-molecules in molecular biology
- players in evolutionary game theory

rigorous analytical results, difficult or impossible

numerical simulations, not fundamental

approximations, providing important insights

but often not rigorous

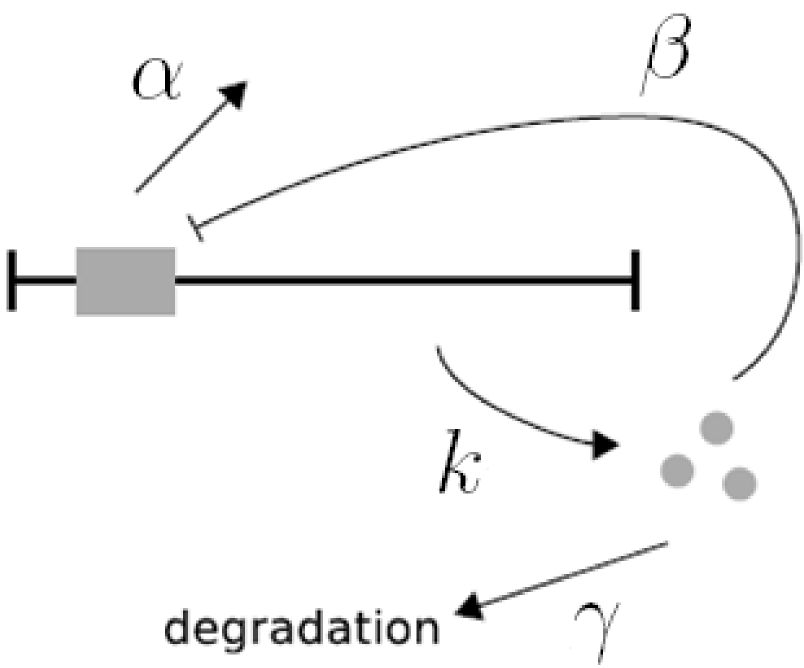
mean – field approximations

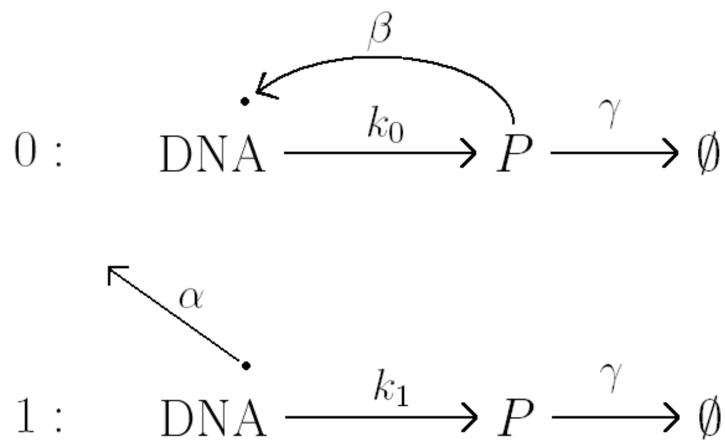
pair approximations

hierarchy of approximations

Self-repressing gen

JM and Paulina Szymańska
Bulletin of Mathematical Biology, 2013





We assume that if at time t there was n protein molecules, then

- probability of production (birth) of one protein molecule at the time interval $(t, t+h)$ is equal to $kh + o(h)$
- probability of degradation (death) of one protein molecule at the time interval $(t, t+h)$ is equal to $\gamma nh + o(h)$
- probability of more than one reaction to take place at the time interval $(t, t+h)$ is equal to $o(h)$.

in time (t,t+h) 0 → 1 with probability nβh

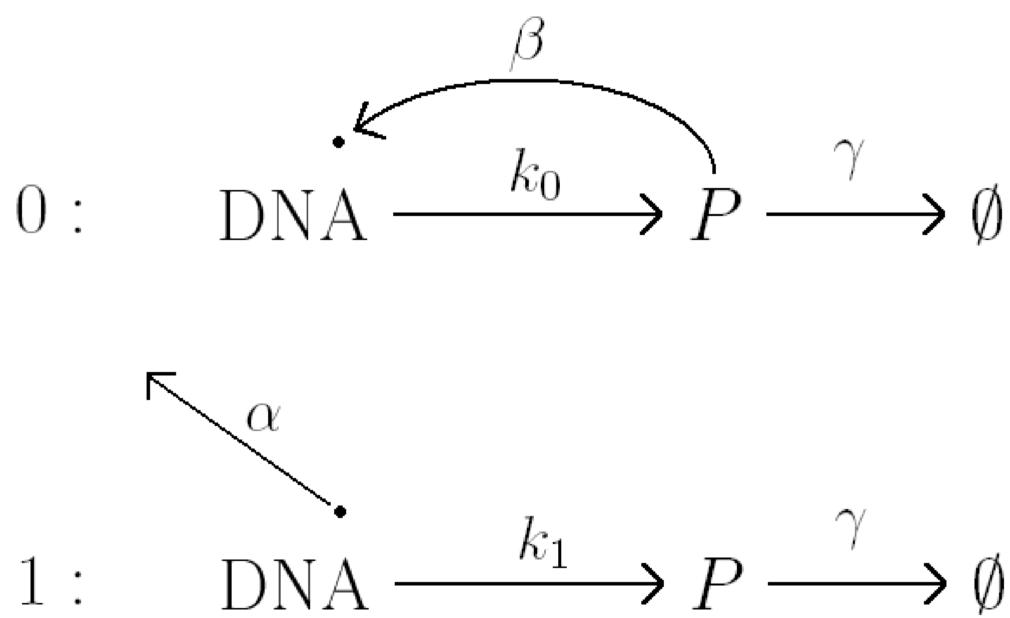
1 → 0 with probability αh

Master equation

$f_0(n,t), f_1(n,t)$ probability that there are n protein molecules in the cell and gen is respectively at state 0 or 1 at time t

$$\frac{df_0(n,t)}{dt} = k_0[f_0(n-1) - f_0(n)] + \gamma[(n+1)f_0(n+1) - nf_0(n)] - \beta \cdot nf_0(n) + \alpha f_1(n)$$

$$\frac{df_1(n,t)}{dt} = k_1[f_1(n-1) - f_1(n)] + \gamma[nf_1(n+1) - (n-1)f_1(n)] + \beta \cdot nf_0(n) - \alpha f_1(n)$$



$K_1 < K_0$

Generating function approach

$$F_0(z,t)=\sum_{n=0}^{+\infty} z^n f_0(n,t) \quad \text{and} \quad F_1(z,t)=\sum_{n=0}^{+\infty} z^n f_1(n,t)$$

$$A_i=\sum_{n=0}^{+\infty} f_i(n),\ i=0,1 \qquad \langle n\rangle_i=\sum_{n=0}^{+\infty} n f_i(n)$$

$$F_i(z=1,t)=A_i(t),\ \ i=0,1$$

$$\frac{\partial F_i}{\partial z}(z,t)_{|z=1}=< n >_i (t)$$

$$\frac{\partial^2 F_i}{\partial z^2}(z,t)_{|z=1}=< n(n-1) >_i (t)$$

$$\frac{df_0(n,t)}{dt} = k_0[f_0(n-1) - f_0(n)] + \gamma[(n+1)f_0(n+1) - nf_0(n)] - \beta \cdot nf_0(n) + \alpha f_1(n)$$

$$\frac{df_1(n,t)}{dt} = k_1[f_1(n-1) - f_1(n)] + \gamma[nf_1(n+1) - (n-1)f_1(n)] + \beta \cdot nf_0(n) - \alpha f_1(n)$$

$$F_0(z,t) = \sum_{n=0}^{+\infty} z^n f_0(n,t) \quad \text{and} \quad F_1(z,t) = \sum_{n=0}^{+\infty} z^n f_1(n,t)$$

$$\frac{\partial F_0(z,t)}{\partial t} = (z-1)\left[k_0 F_0(z,t) - \gamma \frac{\partial F_0(z,t)}{\partial z}\right] - \beta \cdot z \frac{\partial F_0(z,t)}{\partial z} + \alpha \cdot F_1(z,t)$$

$$\frac{\partial F_1(z,t)}{\partial t} = (z-1)\left[k_1 F_1(z,t) - \gamma \frac{\partial F_1(z,t)}{\partial z}\right] + F_1(z,t)\left(\gamma - \frac{\gamma}{z}\right) + \beta \cdot z \frac{\partial F_0(z,t)}{\partial z} - \alpha F_1(z,t)$$

$$\frac{\partial}{\partial z}\frac{\partial F_i}{\partial t}_{|z=1} = \frac{d < n >_i}{dt}$$

In the stationary state we obtain a system of algebraic equations for moments

$$A_0 + A_1 = 1$$
$$\beta \langle n \rangle_0 - \alpha A_1 = 0$$
$$k_0 A_0 - \gamma \langle n \rangle_0 - \beta \langle n^2 \rangle_0 + \alpha \langle n \rangle_1 = 0$$
$$k_1 A_1 - \gamma \langle n \rangle_1 + \gamma A_1 + \beta \langle n^2 \rangle_0 - \alpha \langle n \rangle_1 = 0$$

The above system is not closed, equations for lower moments involve higher moments

How to close it ?

Self-consistent mean-field approximation

$$\frac{df_0(n,t)}{dt} = k_0[f_0(n-1) - f_0(n)] + \gamma[(n+1)f_0(n+1) - nf_0(n)] - \beta\, n f_0(n) + \alpha f_1(n)$$

$$\frac{df_0(n)}{dt} = k_0[f_0(n-1) - f_0(n)] + \gamma[(n+1)f_0(n+1) - nf_0(n)] - \beta\, \frac{< n >_0}{A_0} f_0(n) + \alpha f_1(n)$$

We use again generating function and obtain a closed system of equations

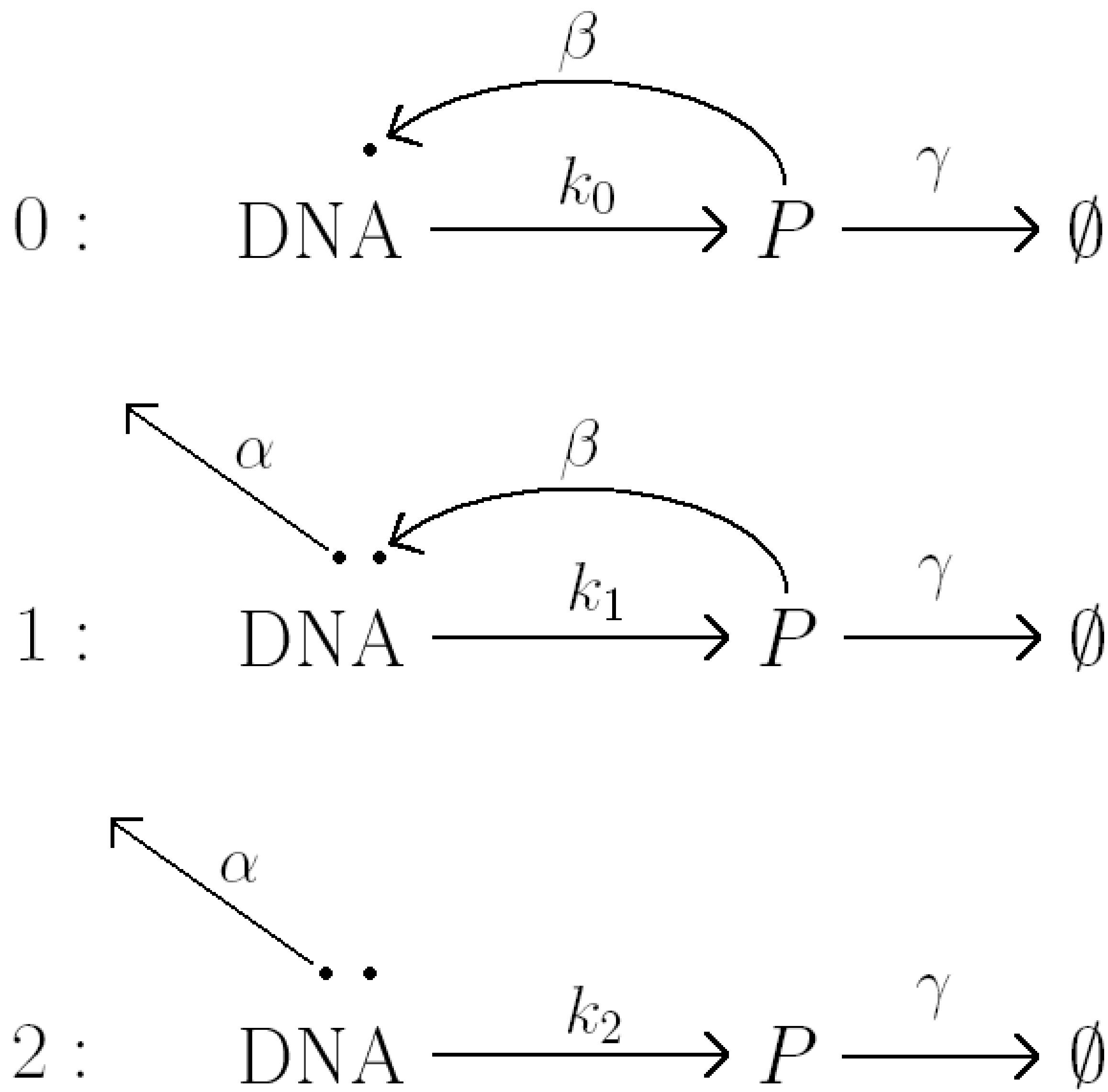
$$A_0 + A_1 = 1$$

$$\beta \langle n \rangle_0 - \alpha A_1 = 0$$

$$k_0 A_0 - \gamma \langle n \rangle_0 - \beta \frac{\langle n \rangle_0}{A_0} \langle n \rangle_0 + \alpha \langle n \rangle_1 = 0$$

$$k_1 A_1 - \gamma \langle n \rangle_1 + \gamma A_1 + \beta \frac{\langle n \rangle_0}{A_0} \langle n \rangle_0 - \alpha \langle n \rangle_1 = 0$$

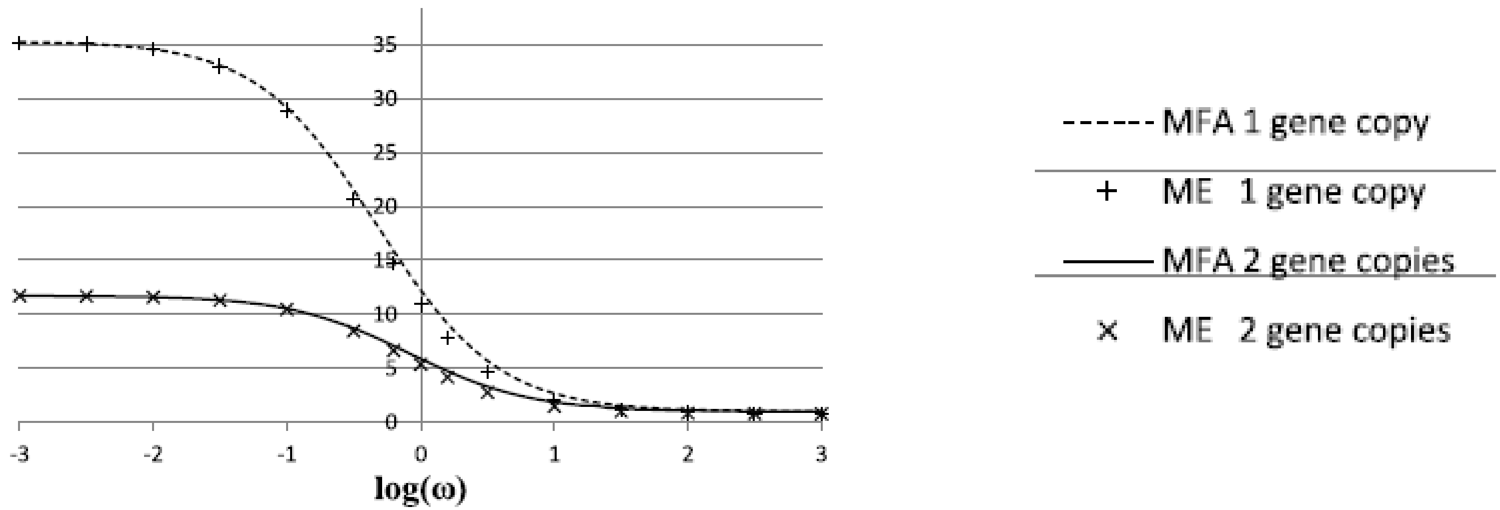
Two gene copies



We obtained formulas

for expected values and variance of n

Bulletin of Mathematical Biology 2013, JM and Paulina Szymańska



Fano Factor = variance/expected value as a function of $\omega = \frac{\alpha}{\gamma}$

Self-activating gene

in time $(t,t+h)$ $1 \rightarrow 0$ with probability αh

$0 \rightarrow 1$ with probability $(\beta_0 + \beta n^2)h$

$K_0 = 0$

mean-field equation has 3 solutions, one corresponds to an unstable state

Prisoner's Dilemma on random graphs

joint work with Jakub Łącki, Michał Matuszak, Bartosz Sułkowski

Players: two suspects
Strategies: Cooperation, Defection
Payoffs: reduction of a sentence

	Cooperation	Defection
Cooperation	3	0
Defection	5	1

The only Nash equilibrium is (Defection,Defection)

Erdos-Renyi graphs

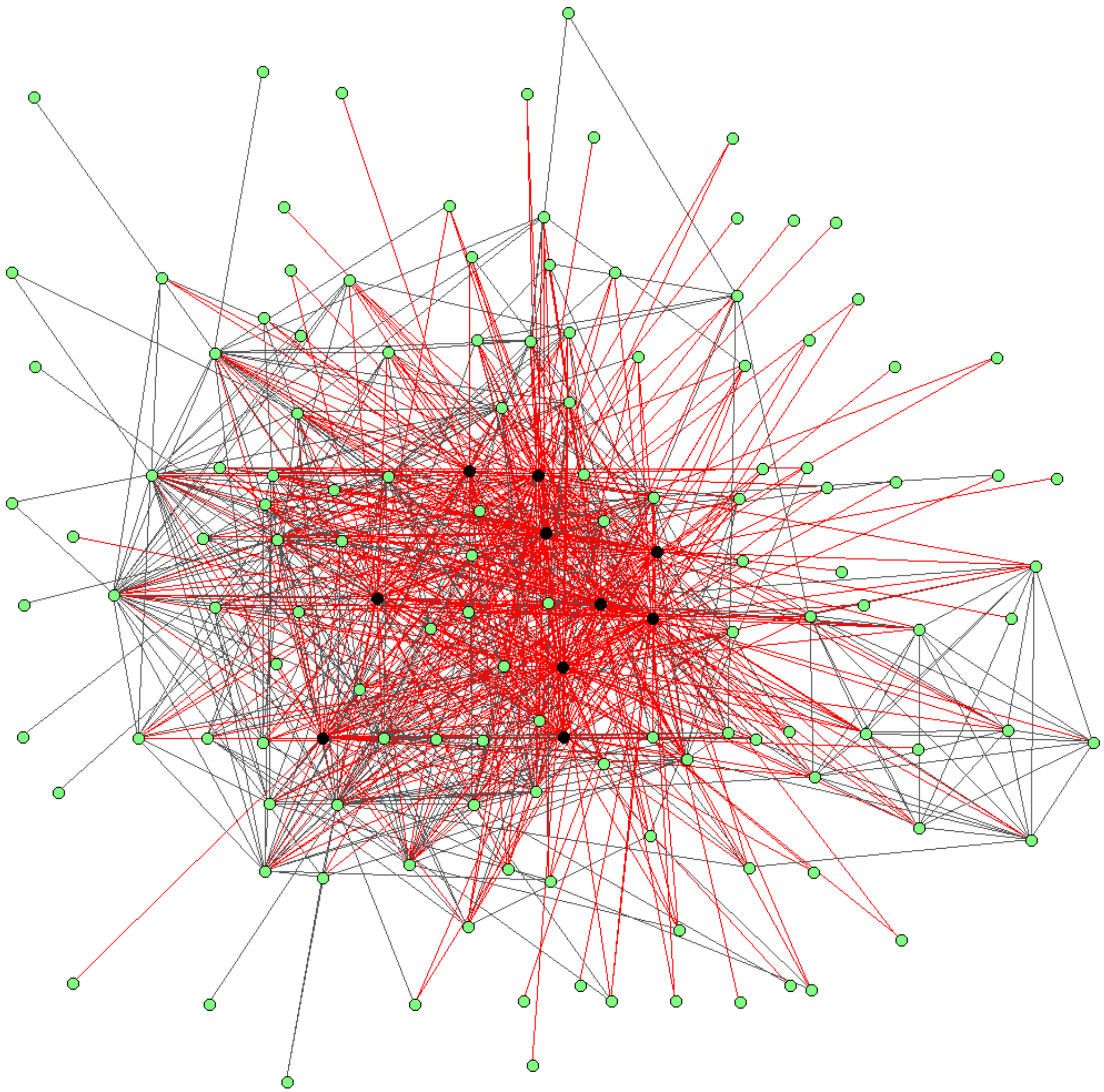
Each pair of vertices is connected with probability ε

Vertex degree distribution is Poissonian

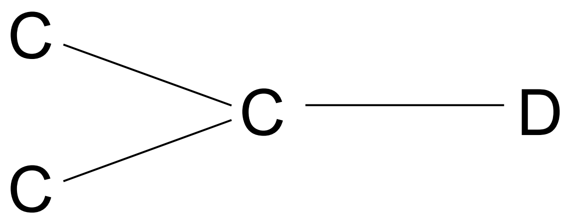
Scale-free Barabasi-Albert graphs

Preferential attachment

Vertex degree distribution ~ k^{-3}



imitation dynamics



	C	D
C	3	0
D	5	1

left players get 3
middle player 6
right player 5

D changes to C

with probability ε players make mistakes

	C	D
C	1	0
D	T	0

	C	D
C	$1-\gamma$	$-\gamma$
D	$T-\gamma$	$-\gamma$

γ - linking cost

imitation dynamics

fraction of cooperators in the stationary state

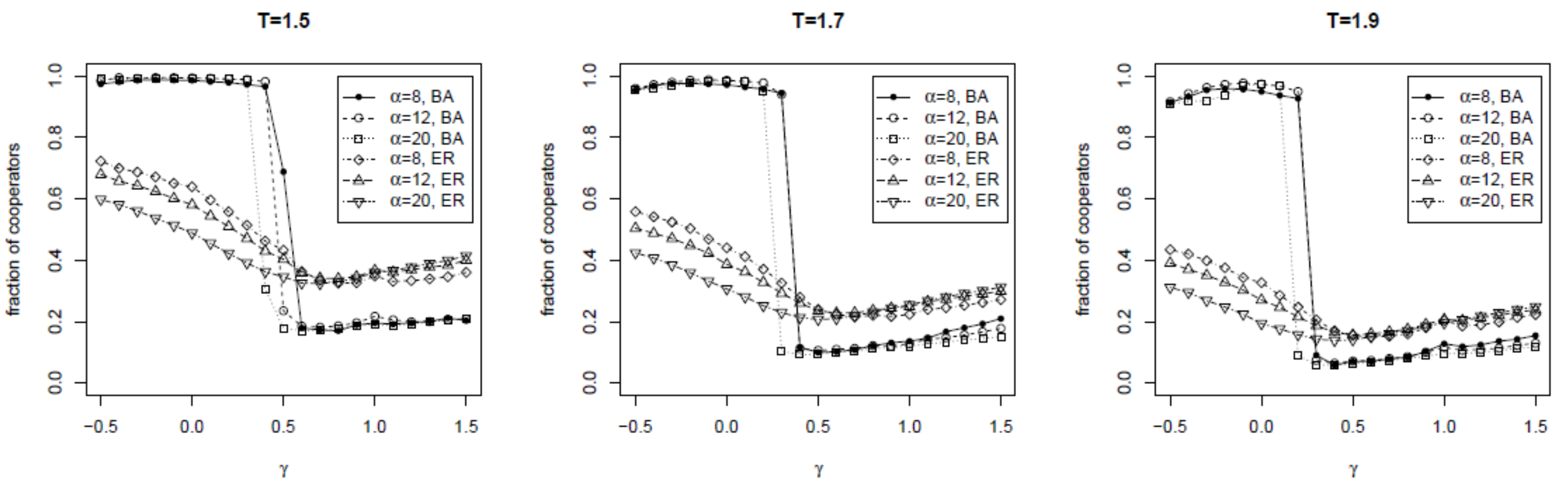


FIG. 2. Fractions of cooperators depending on the cost of maintaining a link.

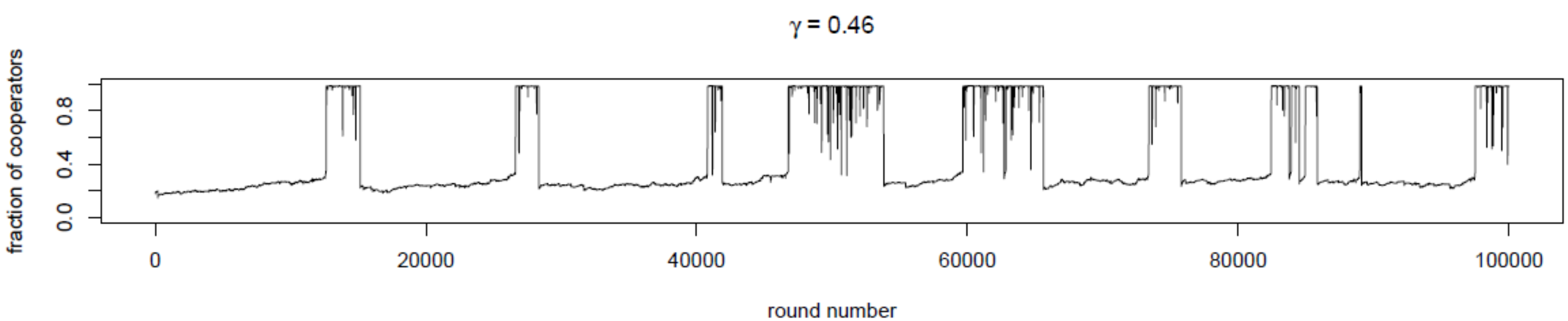


FIG. 4. Fractions of cooperators after each round in sample simulations for different values of γ. Barabási-Albert network, $T = 1.5$, average connectivity equal to 12.

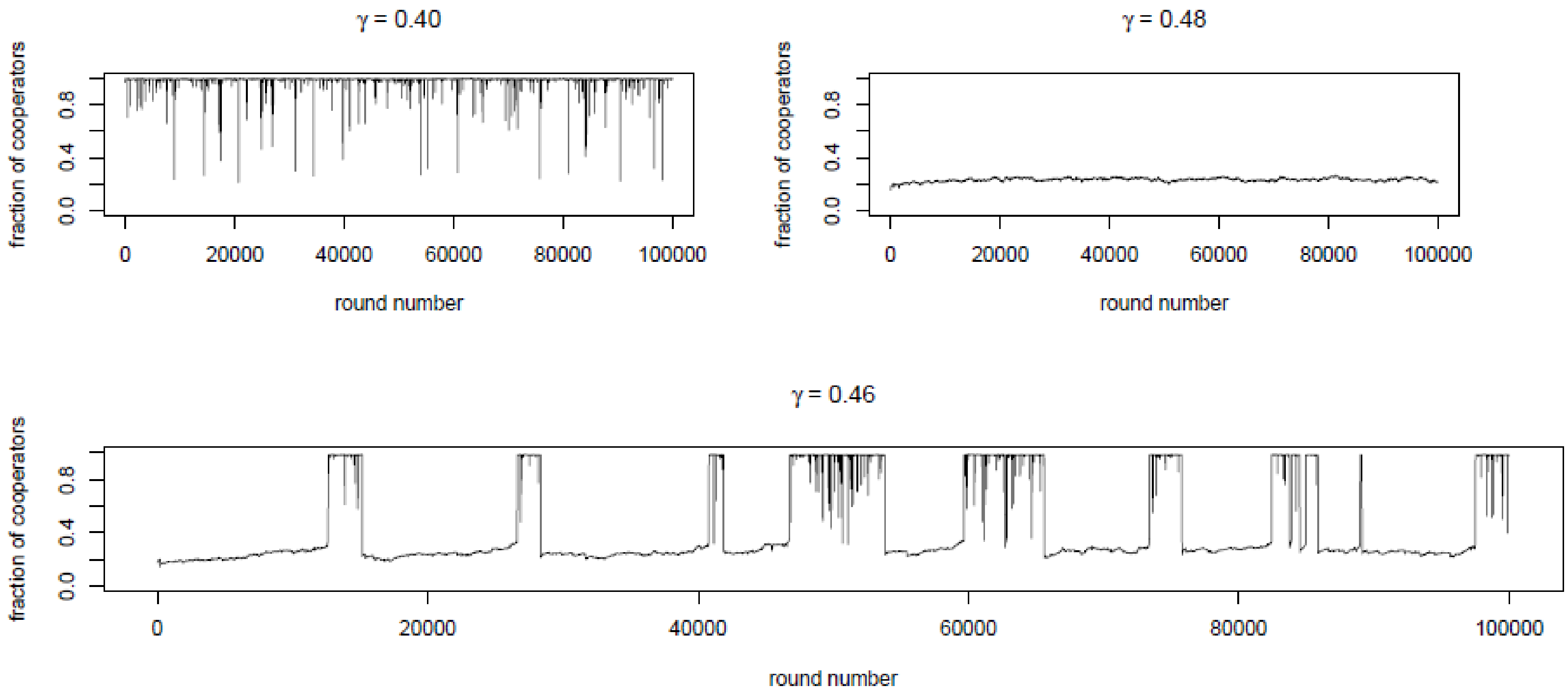


Figure 3: Fractions of cooperators after each round in sample simulations for different values of γ. Barabási-Albert network, $T = 1.5$, average connectivity equal to 12.

thank you for your attention

more on

www.mimuw.edu.pl/~miekisz