The influence of the network structure on tumor growth

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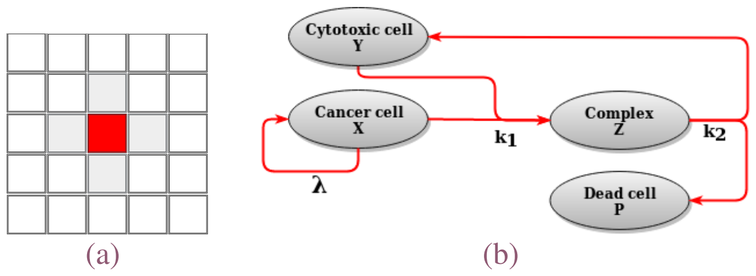
Abstract

The quantitative research study was conducted to examine the influence of the network structure on tumor growth based on measurements of first passage times (FTP). The model of cancer cells' development, based on the kinetic reactions of the Michaelis-Menten model, was modeled on networks: regular and small world. The main focus was on the tumor dynamics performed on the regular network, in particular, how model parameters (rate of tumor cells' proliferation and cytotoxic cells' concentration) affect the rate of tumor growth. The following effects have been observed: The probability of stopping cancer development decreases as the cyctotoxic cells' concentration decreases and the rate of tumor cells' proliferation increases. Presence of long range links in the system reduces FTP to areas of the network at any distance from the center and decreases the percentage of networks, where the cancer development has been inhibited. In small world models, the number of long range links in the system dominates over any other parameter, until some threshold value then it saturates.

Mathematical model

The mathematical model of local interaction between tumor and cytotoxic cells is given by the catalytic Michaelis-Menten scenario Eq. (1) [1]. Cytotoxic cells Y and cancer cells X bind together at rate k_1 to form a complex ZX + ZY. The complex decays at a rate k_2 to a dead cell P, regenerating the original cytotoxic cell. Dead cells are removed from the system after 1 iteration. In addition to that, cancer cells may proliferate spontaneously at a rate λ.

$$\mathrm{X} + \mathrm{Y} \xrightarrow{k_1} \mathrm{ZX} + \mathrm{ZY} \xrightarrow{k_2} \mathrm{Y} + \mathrm{P}$$
$$\mathrm{X} \xrightarrow{\lambda} 2\mathrm{X} \qquad (1)$$



(a) (b)

Figure 1: The von Neumann (left) neighborhoods. Schematic diagram of cell dynamics for tumor growth (right).

Networked model

In a network representation the model given by Eq. (1) is in the form of two-dimensional Euclidean lattice (300×300). Each node represents a cell (empty, cancer, cytotoxic, complex or dead) while edges stands for connections between cells, see Fig 2. The new state of each cell is determined by the current state of the cell and the states of the cells in its direct neighborhood (von Neumann neighborhood, see Fig. 1a), for small world model cancer cells might have one additional neighbour via the long range connection.

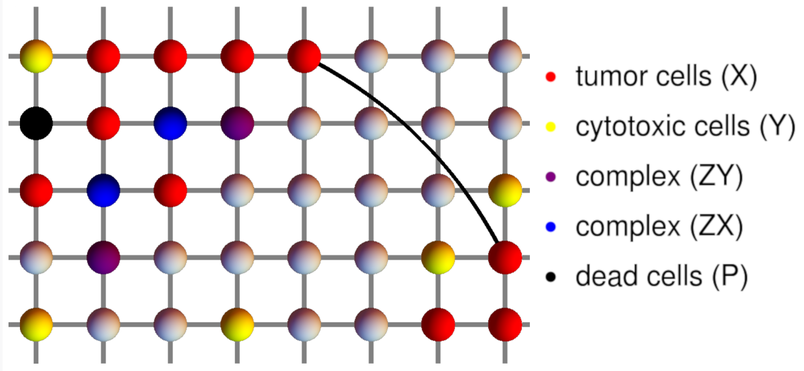
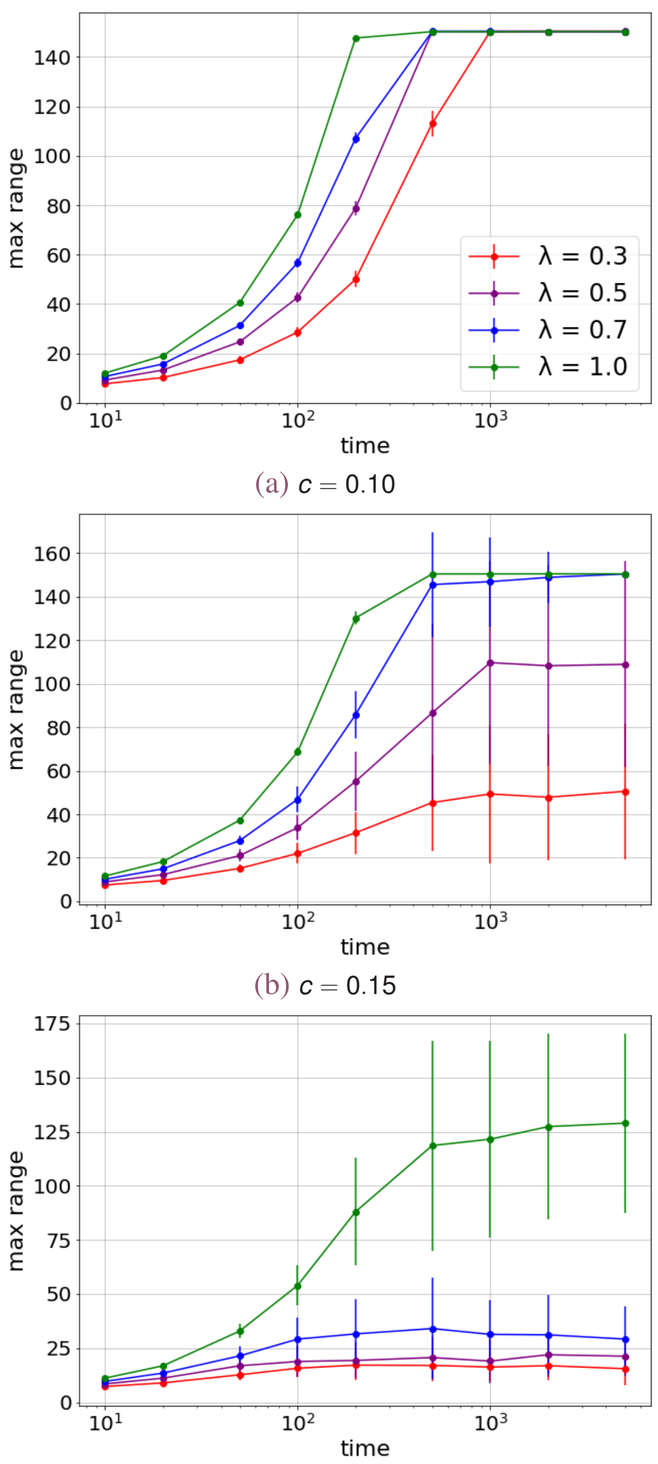


Figure 2: Graph representation of the model system Eq. (1).

Tumor range as a function of time



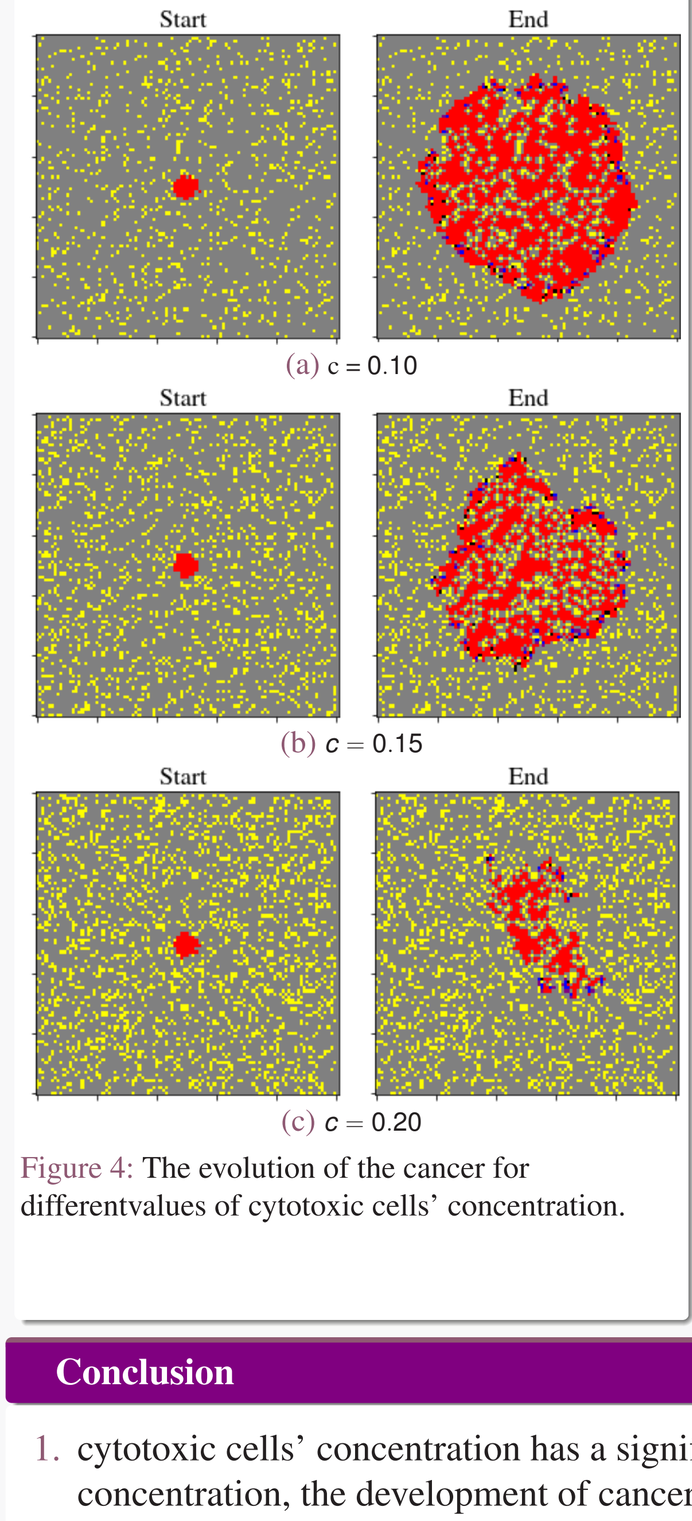
(a) $c = 0.10$

(b) $c = 0.15$

(c) $c = 0.20$

Figure 3: The range of tumor as a function of time for different values of cytotoxic cells' concentration. Error bars are normalized standard deviation values.

Tumor development



(a) c = 0.10

(b) $c = 0.15$

(c) $c = 0.20$

Figure 4: The evolution of the cancer for differentvalues of cytotoxic cells' concentration.

Regular network vs small world model

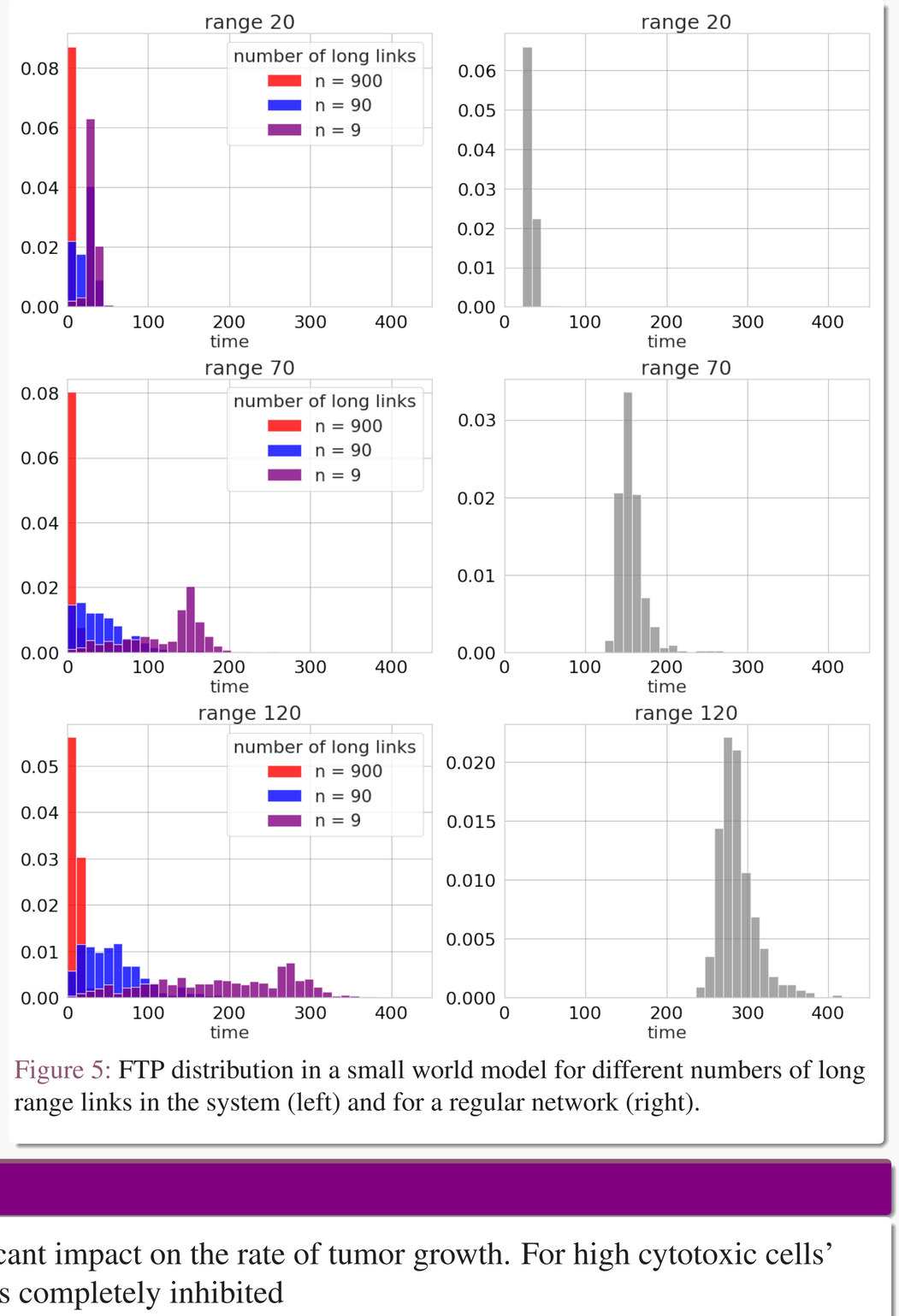


Figure 5: FTP distribution in a small world model for different numbers of long range links in the system (left) and for a regular network (right).

Conclusion

1. cytotoxic cells' concentration has a significant impact on the rate of tumor growth. For high cytotoxic cells' concentration, the development of cancer is completely inhibited
2. presence of long range links in the system significantly reduces FTP
3. in small world models number of long range links dominates over any other parameter
4. for a small number of long links in the system, two peaks can be distinguished. The first peak, caused by the presence of long range links, corresponds to the occurrence of metastatics, the second corresponds to the tumor that growths locally

References

A. Fiasconaro, A. Ochab–Marcinek , B. Spagnolo, E. Gudowska–Nowak, Monitoring noise-resonant effects in cancer growth influenced by external fluctuations and periodic treatment, Eur. Phys. J. B65, 435–442 (2008)

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