THESES OF THE DOCTORAL DISSERTATION

Statistical physics of *in vitro* 2D cell motility and virus spreading, and *in silico* 3D collective motion

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The objective of the research

Cell motility and factors influencing it, including virus spreading, are among the most investigated fields in biological physics. I present my work on these two topics, and complete it with the modeling of collective motion of cells and other organisms.

In my doctoral dissertation I show an imaginative experimental setup allowing us to investigate the virus propagation on a hundred thousand „individuals". Using a cell culture in a Petri dish with low original rate of infection (PFU) has the advantage that one can observe the spreading of infection and the emerging pattern in a high number of cells.

Microglia cells play an essential role in the defensive mechanism of the central nervous system. Change in microglia cell motility has great importance both in the fundamental understanding of brain processes and in medicine. In our research our goal was to investigate the change *in vitro* the cell motility. We investigated ATP-ase activity, because ATP is one of the most important signalling molecule of microglia cells.

The understanding of the collective motion of organisms is an important goal of biological research. The two-dimensional Vicsek et al. model (1995) shows the emerging of collective motion from randomly moving particles without a leader. This model uses one simple interaction between the self propelled particles, and this minimal assumption is enough to observe ordered motion of particles.

This model was designed to investigate small simulation steps compared to the radius of interaction. In this case the phase transition from disordered to ordered state is second order. We investigated if the difference in the simulation steps or in the mode of noise (scalar/vectorial) can change the behavior of the model. These differences suggest that there may be significant change in the behavior of the model also in three dimensions. My research objective was to map the similarities and differences between the two and three dimensional model.

New scientific results

In my doctoral dissertation I show an imaginative experimental setup allowing us to investigate the virus propagation on a hundred thousand „individuals”. Our experimental result was modelled in numerical simulations for the deeper understanding of the dynamics of the infection. We conclude the following.

a) The developing clusters of infected cells were found to be fractal-like, with a 1,78 fractal dimension which is different from the result of the standard percolation model.

b) The cluster size follows a power law distribution.

c) Both the fractal dimension and the cluster size distribution has a better agreement with our model than with the percolation model. Our newly introduced model takes into account the specificities of the astroglial cell culture to a minimal degree only, thus it is likely that our observations can be applicable to other real systems.

I studied the motility of microglia cells during the spreading of virus infection in the astroglia cells co-cultured in the same dish. We investigated low density astroglia culture, and also confluent astroglia layer. I developed a computer program, called Cell Track to help the investigation and analysis of cell motility.

d) The average velocity of microglia cells were smaller and the number of resting cells were higher in the infected cultures than in the control experiments.

e) We found that the ecto-ATP-ase activity was increased due to the infection.

f) The motility of microglia cells in infected cultures were more persistent as compared to the control experiments.

I extended the two-dimensional Vicsek et al. model [Vicsek T et al. 1995] of self-propelled particles to three dimension. I proved that the earlier found phenomena in two dimensions didn't change in three dimensions.

g) We did not observe any symmetry breaking in the small velocity regime, the model results were free

from artificial impacts of the boundary condition thus the results have physical relevance to the biological systems.

h) Ordered movement emerges without a leader in the system of initially randomly moving and randomly placed particles. The phase transition was found to be continuous, i.e., second order in the low velocity regime.

i) We studied the model also in the high velocity regime, where we found artificial symmetry breaking both in diffusion and in the direction of average speed of particles. In this velocity regime artificial boundary condition causes the emerging density waves and the first order phase transition.

Publications relevant to the doctoral dissertation

Papers:

Gönci B, Németh V, Balogh E, Szabó B, Dénes Á, et al. (2010) Viral Epidemics in a Cell Culture: Novel High Resolution Data and Their Interpretation by a Percolation Theory Based Model. *PLoS ONE* 5(12): e15571. doi:10.1371/journal.pone.0015571

Gönci B, Nagy M and Vicsek T (2008) Phase transition in the scalar noise model of collective motion in three dimensions. *Eur. Phys. J. Special Topics* 157:53-59 DOI: 10.1140/epjst/e2008-00630-2

Posters:

Környei Zs, Németh V, Gönci B, Kittel Á, Szabó B, Orsolits B, Mészáros Z, Boldogkői Zs, Kovács K, Madarász E, Vicsek T and. Dénes Á (2012) *Microglial responses to virus infection.* FENS forum 2012

Németh V, Dénes Á, Gönci B, Kittel Á, Szabó B, Orsolits B, Boldogkői Zs, Kovács K, Vicsek T and Környei Zs (2010) *Microglial responses to virus infection.* IBRO International Workshop.

Gönci B, Nagy M and Vicsek T (2007) *Phase transition in the scalar noise model of collective motion in three dimensions.* StatPhys23, IUPAP 23. International Conference on Statistical Physics, 2007.