Abstract

This paper examines the use of spatial evolutionary games to model the dynamics of tumour development. Models based on replicator equations assume perfect mixing of phenotypes, which greatly simplifies real-world conditions and fails to capture phenomena resulting from local interactions between cells and their environment. Tumours, on the other hand, are characterised by high phenotypic and spatial heterogeneity, which is caused by unequal access to resources, chaotic tumour vascularisation and the presence of multiple cell subpopulations. The aim of the study was to demonstrate the potential of spatial evolutionary games as a tool for modelling tumour development, allowing for the consideration of environmental factors and local clonal evolution.

For the purposes of the study, GaTher3DEvo software was developed, which is currently the only available tool for simulating spatial evolutionary games in two and three dimensions. The programme allows defining irregular game matrices, any number of phenotypes, and spatially diverse resource availability zones. It allows for the analysis of population dynamics over time, both in the form of averaged graphs and spatial results. The software was used to perform calculations and visualise simulation results.

Several models were analysed in the study. The Hawk-Dove model, as the flagship model of evolutionary game theory, was examined both in its classic version and with resources taken into account, and its heterogeneity was analysed. This allowed us to observe the impact of spatial interactions and uneven distribution of phenotypes on the dynamics of the model. Next, a prostate cancer model was simulated, taking into account interactions between hormone-sensitive and hormone-insensitive cell phenotypes, which enabled the analysis of conditions favouring the dominance of particular phenotypes. Next, a model of glioblastoma multiforme was analysed, both with and without blood vessels, which allowed the impact of access to resources and microenvironmental conditions on tumour dynamics to be assessed. The last part of the study was devoted to investigating a double bind model, in which the impact of different treatment strategies (their order) on tumour development was examined, both with and without the arrangement of therapy zones.

The results obtained clearly indicate that spatial structure and local environmental conditions are crucial for modelling tumour dynamics. The phenomenon of local clonal evolution, the possibility of tumour stabilisation with the coexistence of less aggressive phenotypes, and a strong correlation between treatment efficacy and the arrangement of treatment zones were

observed. Spatial analyses have enabled the observation of phenomena that remain beyond the reach of classical models based on replicator equations.

The conclusions of the study show that spatial evolutionary games are a promising tool for modelling the development of cancerous tumours. They not only enable a better understanding of biological processes, but also the creation of new therapeutic strategies based on tumour control rather than its complete elimination.