Spatial and nonspatial evolutionary games and their applications

Addendum: Valorization

Valorization is "the process of value creation from knowledge, by making it applicable and available for economic or societal utilization, and by translating it in the form of new business, products, services, or processes". Examples of valorization include publications in (academic or non-academic) journals, software programs, patents, ready-to-use models and systems, suggestions to society, organizations or companies, etc. In this addendum we describe the valorization opportunities that result from this thesis. Through the following three perspectives we demonstrate how this thesis can be of value for societal development.

Social relevance of the research Applying three different game-theoretical models, we addressed three specific biological problems that are of a societal and economic relevance.

The model of the predator-prey game (Chapter 2) relates to the use of the predatory mites (*Acari: Phytoseiidae*) for biological pest control of the fruit-tree red spider mites (*Acari: Tetranychidae*) which feed on and damage apple trees. Traditionally chemicals are used to control pest directly (Uboh et al., 2011), but it is shown that these chemicals have many side effects. For example, chemicals that reside in the agricultural ecosystems not only contaminate the environment, but may also cause human diseases like cancer (Mostafalou and Abdollahi, 2013). Instead, using biological pest control (in agriculture) meets the societal demand for healthy environmental conditions. Moreover, understanding the predator-prey interactions (for problems at hand) helps to develop effective biological pest-control techniques, which may also bring economic benefits. For example, better understanding of the interactions between the predatory mites (*Acari: Phytoseiidae*) and the fruit-tree red spider mites (*Acari: Tetranychidae*) may help farmers to use the predatory mites as a biological pest management. Alternatively, one can intervene in the behavior of the prey/pest by artificially changing the factors like temperature or light, such that the apple trees remain undamaged.

The model describing interaction/competition among microbial species (Chapter 4) addresses mechanisms of microbial diversity. There is no doubt that microbial diversity proves

to be very important to humans. Besides, this model also includes one type of the quorum sensing mechanism that relates to virulence, i.e., the ability of a pathogen to infect a host. The understanding of how bacteria coordinate and turn on their group behavior (as attacking the host) can be very useful for developing new techniques that prevent pathogenicity (Jayaraman and Wood, 2008). Antibiotics are what we use now to kill bacteria. However, these are becoming less effective (World Health Organization, 2017) because killing bacteria with (traditional) antibiotics selects for resistant mutants. Novel treatment strategies may focus on interfering the bacterial quorum sensing mechanisms such that the bacteria become less virulent. Such a treatment strategy may be more effective in controlling infectious diseases and would be beneficial to the society. Our model mimics a simple case of quorum sensing, but more complex mechanisms of quorum sensing can be studied as well.

The chapter on tumorigenesis (Chapter 5) addresses the eco-evolutionary dynamics of metastatic castrate-resistant prostate cancer. Understanding these dynamics will be very helpful in designing effective cancer treatment. The standard metastatic cancer therapy is to kill as many cancer cells as possible by applying the maximum tolerable dose (MTD) of drugs. Initially, this approach is often successful in reducing the tumor burden, but it inevitably fails due to evolution of resistant cancer phenotypes. The MTD focuses only on decreasing the tumor mass but it ignores the evolution of the tumor composition. However, an effective treatment should also take into account how the cancer responds both in terms of tumor mass and its composition. Moreover, such an effective treatment requires lower doses of drugs (than the standard treatment does) and as such treatment becomes less expensive. This more adaptive treatment is expected to lengthen patients' lives and therefore has a high potential of being beneficial for society.

Target groups of the research results The results of this research, as summarized in Chapter 6, can be of interest to various target groups, but mainly to oncologists, cancer biologists, microbiologists and those working in pest control. For game theorists the models developed in this thesis are interesting from the application perspective.

Products that the research holds promise to The main products that resulted from this thesis are software toolboxes for modeling biological interactions which can be applied to a wide range of domains. We expect that the availability of more and more data on for example pest control or tumorigenesis will allow us to tune and validate our models as the codes in the toolboxes can be flexibly adjusted. So far, these toolboxes are still in a testing phase but we expect that in due time these can be utilized commercially for making accurate predictions.