

A decomposable multi-type Bellman-Harris branching process with mutations. Application in modeling of cancer evolution.

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Abstract

A prominent feature of biological systems is their capacity to adapt and mutation is a key mechanism for achieving adaptation. As a continuation of [3] we propose a decomposable multi-type Bellman-Harris branching process, which incorporates a possibility for mutation.

Metastasis, the spread of cancer cells from a primary tumour to secondary location(s) in the human organism, is the ultimate cause of death for the majority of cancer patients. We consider a metastasized cancer cell population after some medical treatment (e.g. chemotherapy). Arriving in a different environment the cancer cells may change their characteristics concerning lifespan and reproduction, thus they may differentiate into different types. Even if the treatment is effective (resulting in subcritical reproduction of all cancer cell types), however, it is possible during cell division for mutations to occur. These mutations can produce a new cancer cell type that is adapted to the treatment (having supercritical reproduction). Cancer cells from this new type may lead to a non-extinction process.

We model the above scenario with the proposed model. Expanding [1] and [2] we investigate relevant quantities such as the probability of extinction of the process until time t and as t approaches infinity, the number of occurred supercritical mutants until time t and as t approaches infinity, the time until the first occurrence of a mutant starting a non-extinction process and the immediate risk for the process to escape extinction. We also propose numerical schemes for performing calculations.

Keywords: Mutations, Decomposable multi-type branching process, Probability of extinction, Waiting time to escape mutant, Immediate risk of escaping extinction

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References

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