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Spatial cumulant models enable spatially informed treatment strategies in theoretical cancer systems

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Cancer cells can interact with each other by, for example, exchanging signalling molecules and competing for resources such as space and nutrients. Such cell-cell interactions have been identified as factors that drive eco-evolutionary dynamics of cancer cell populations. Consequently, these interactions have been proposed as treatment targets, where the general premise is that treatments can perturb cell-cell interactions and, by extension, disease trajectories.

We recently identified a need to formulate cancer cell population models that include cell-cell interactions and (1) are mathematically tractable (analytical), (2) are spatio-temporally resolved, and (3) maintain cell discreteness. In this presentation, I describe an approach to achieve (1-3) using spatial cumulant models (SCMs). SCMs are spatially resolved population models that are translated from a specific family of individual-based models, namely spatio-temporal point processes (STPPs).

Following a mathematical manipulation that involves a perturbation expansion around mean-field equations, SCMs approximate two STPP-generated summary statistics: first-order spatial cumulants (densities) and second-order spatial cumulants (spatial covariances). We exemplify how SCMs can be used in mathematical oncology by modelling theoretical cancer cell populations comprising interacting growth factor-producing and non-producing cells.

Our results demonstrate that SCMs can capture STPP-generated population density dynamics, even when mean-field population models (MFPMs), fail to do so. From both MFPM and SCM equations, we derive treatment-induced death rates required to achieve non-growing cell populations. When testing these treatment strategies in STPP-generated cell populations, our results demonstrate that SCM-informed strategies outperform MFPM-informed strategies in terms of inhibiting population growths. We thus demonstrate that SCMs provide a new framework in which to study localised cell-cell interactions, and can be used to describe and perturb STPP-generated cell population dynamics.

We anticipate that the opportunity to analytically derive spatially informed cancer treatment strategies, as enabled via SCMs, will inspire new theoretical and applied mathematical biology research.

Keywords: individual-based models, spatio-temporal point processes, spatial moments, cancer eco-evolution, mathematical oncology

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