An overview of cancer progression and evolutionary accumulation models

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Cancer progression and evolutionary accumulation models have been developed to discover dependencies in the irreversible acquisition of binary traits (e.g., mutations) from cross-sectional data. They have been used in computational oncology and virology but also in widely different problems such as malaria progression. Some of these methods have been applied to data with phylogenetic and longitudinal dependencies in questions including tool acquisition in animals and antimicrobial resistance in tuberculosis. Because of their interest, new methods continue to be developed.

These tools have been used to make predictions about future and unobserved states of the system, identify different routes of, and dependencies in, feature acquisition in subsets of the data, and improve patient stratification and survival prediction based on the evolutionary trajectories and denoising of the data. The rich variety of available models increases their utility as markedly different dependency structures can be compared on the same data. These methods also hold promise to help identify therapeutic targets and improve evolutionary-based treatment approaches.

I will first give an overview of the available methods. Then, using fitness landscapes, and discussing the conflation of lines of descent, path of the maximum, and mutational profiles, I will focus on how and why inferences might not be about the processes we intend, in particular under bulk sequencing.

I will comment on major research opportunities, including translational uses, identifying dependencies that derive from frequency-dependent selection, and the relationship of these methods with phylogenetic comparative methods.

Keywords: cancer progression model, fitness landscape, bulk sequencing, evolutionary accumulation model, epistasis.