**(Benchmarking) A framework for detecting periods of positive growth and the effect of driver candidates during tumor progression from multiple or single tumors**

Abstract

Real-time evolution is observed in many evolving systems like viruses and bacteria. Similarly, each tumor can be treated as a unique “experiment” of an evolving system where cells accumulate hundreds of mutations, affecting genes involved in different biological process such as cell proliferation and development. The mutational outcome is observed after the sequencing of the cell population. With the current advances of sequencing technologies, we have thousands of sequenced cancer samples, expected to be increased by a log-scale. Meanwhile, whole cancer genomes are getting sequenced at deeper depths (>300x coverage). [[what is the prob. ? ID drivers w/o recurr.? just from freq.?]] In this environment we have developed a framework that considers mutational frequencies from sequenced samples in cancer while aiming to model periods of positive growth, suggest driver candidates and their respective effect, for single or multiple tumors, without relying on recurrence. [[reword - but this is our pt. ]]First, we tested our model using simulations where we were able to predict the driver position[[need to def]] and effect. [[more about model]]Then, we applied our model to 993 linear tumors from the Pancancer Analysis of Whole Genomes consortium (PCAWG). Our results shed light to the dynamics of tumor progression indicating which biological processes are significantly affected. Interestingly, different types of mutations appear to have varying effects on tumor growth. Promoter mutations seem to have an upgraded[[wd]] role in regulating the expression of cancer genes, while nonsense mutations seem to positively affect only tumor suppressor genes. Finally, we implemented our model on a deep-sequenced acute myeloid leukemia tumor. Our growth and driver peaks aligned very well with missense mutations from known cancer genes,[[validating our driver disc? should we move up?]] while our analysis suggested the potential presence of additional driver candidates. Granted current and future advances in sequence depth and numbers, our framework aims to depict cancer growth, driver effects and reveal important genomic regions, even in the absence of recurrence.