**Detecting periods of increased growth and driver effects from multiple or single tumors using bulk**

Real-time [[too wordy]] 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, while affecting genes involved in different biological processes. With the current advances of sequencing technology, we have thousands of sequenced bulk tumors, expected to soon increase by a log-scale. This data explosion has led to the development of many computational methods that aim to detect drivers, either through statistical recurrence, or deviation from background metrics (e.g. genomic mutation rates). However, these methods might underperform when recurrence is low, or the genomic metrics are unaffected. [[need cohort]] At the same time, to our knowledge, none of these approaches aims to model the effect of the driver mutation and variations in tumor growth. [[what is the prob. ? ID drivers w/o recurr.? just from freq.?]] In this environment we have developed a framework that considers different growth models based on mutational frequencies from sequenced cancer samples to i) identify periods of positive growth, ii) suggest driver presence and iii) estimate the driver’s potential effect, from single tumors[[MG:reword - but this is our pt. ]]. [[MG: need to def]] [[MG :more about model]]. To evaluate our framework, we first tested our model using tumor simulations. Then, we implemented our model on 993 linear tumors from the Pancancer Analysis of Whole Genomes consortium (PCAWG). As expected, predicted drivers and driver genes are significantly enriched during periods of positive growth. Overall, our results shed light to the dynamics of tumor progression indicating cell development, cell differentiation and multicellular processes as significantly affected. Interestingly, different types of mutations appear to have adverse effects on tumor growth. Promoter mutations seem to play an important [[MG: wd]] role in cancer progression, while nonsense mutations seem to positively affect only tumor suppressor genes. Finally, we implemented our framework on a deep-sequenced acute myeloid leukemia tumor (AML). [[can compare w cohort?]] Our main growth and effect peaks aligned very closely with missense mutations from known cancer genes. Moreover, by testing for positive growth enrichment in our 993 PCAWG dataset, our analysis suggested the potential presence of additional driver candidates [[MG : validating our driver disc? should we move up?]] which map with some previously unexplained growth peaks. Granted current and future advances in sequence depth, number of genomes and sampling techniques, our framework aims to depict variations in cancer growth, identify driver effects and reveal important genomic regions, even in the absence of recurrence or genomic background violation. At the same time, our results indicate the significance of whole genome sequencing in order to better model tumor progression which can, in turn, unravel new roles for non-coding regions.