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| --- | --- | --- |
| Assumption | Anticipated EFFECT ON CONCLUSIONS | Refs |
| Exponential DFE for drivers & passengers | ABC estimates effective selection coefficients | 81 |
| Cells are well-mixed (no spatial structure) | Reduced Hill-Robertson interference | 19,82,83 |
| Gompertzian growth dynamics in-between drivers | Decreased inferred strength of drivers relative to no growth constraints | 68 |
| Only 50% of tumors progress to cancer | Mutational burdens widen as progression probability declines | 68 |
| No (reciprocal) sign epistasis | Stronger fitness benefits of drivers in adaptive contexts | 84,85 |
| Constant mutation rate for each tumor | Hill-Robertson interference would increase | 86 |
| Simulated tumor is genotyped at transformation | Late (subclonal) mutations are ignored; incidence age reduced | 19 |
| Malignancy occurs at 1,000,000 (stem) cells | Reduced variation in cancer incidence times (as true detection times varies) | 68 |
| Subclonal mutations are undetected by genotyping | Lower estimated fitness effects of drivers & passengers (subclonal mutations experience less selection) | 87 |
| No dominance | Nearly-unbiased estimate of heterozygous passenger fitness cost; underestimation of driver benefit | 88 |

**Supplementary File 1. Assumptions of model of tumor evolution and anticipated effects.**