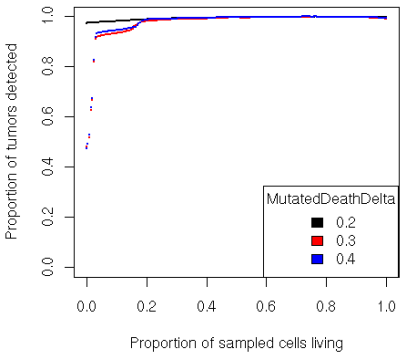
SI Appendix

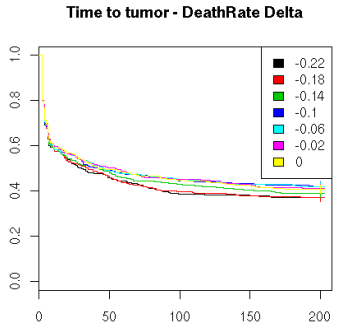
We simulated the importance of the proportion of dead vs. alive cells in the samples of biological fluids analyzed. A plot of the effects of differences where the proportion of sampled cells is varied is provided here. The effect on tumor detection of varying the sampling proportions of living vs. dying cells depends on the difference in the risk of dying for mutated phenotype compared with wild type phenotype ("mutated death delta") with almost no effect when this difference is <0.2, which is the range used in the simulations. Even at higher values of delta, there is very little effect, as long as at least 10–20% of the sample is from the entire population mixed with the dying cells.

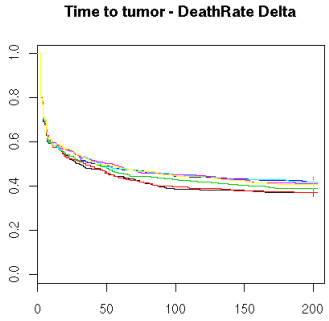
The importance of the sampling and its proportion is related to the difference between the survival ("low susceptibility to disturbance or high death avoidance") advantage of the mutant compared to the wild type.

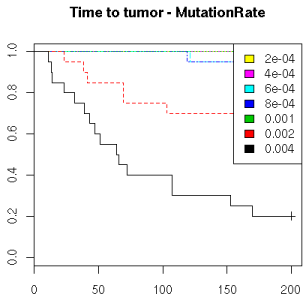


The effect on tumor detection of varying the sampling proportions of living vs. dying cells depends on the difference in the risk of dying for mutated phenotype compared with wild-type phenotype ("mutated death delta") with almost no effect in when this difference is <0.2, which is the range used in the simulations. Even at higher values of delta, there is very little effect as long as there are at least 10% samples from the entire population mixed with the dying cells.

We have provided several figures below showing Kaplan-Meier plots for time to tumor development across various ranges of parameters, including the “mutated Death Delta” (i.e., the decrease in the death rate for a mutated clone); the “mutated Growth Delta” (the increase in growth/colonization rate for a mutated clone), and the mutation rate. These plots give a general idea of the sensitivity to different parameters on the emergence of tumors. The observed behavior of tumor formation under the effects of disturbances is relatively stable for various ranges of growth and death rates. It is clear that the rate is sensitive to increasing the mutation rate to unrealistic levels.







Kaplan-Meier plots for time to tumor development across various ranges of parameters are presented to generally indicate the sensitivity of the model to specific parameters. Including here are the “mutated Death Delta” (i.e., the decrease in the death rate for a mutated clone); the “mutated Growth Delta” (the increase in growth/colonization rate for a mutated clone), and the mutation rate.