Abstract Submitted
for the MAR12 Meeting of
The American Physical Society

Drift, draft, waves, and ratcheting: evolutionary models of cancer progression CHRISTOPHER MCFARLAND[1], Harvard University, KIRILL KOROLEV[2], LEONID MIRNY[3], MIT — Recent evidence has found that many mutations are detrimental to tumor growth in cancer. These mutations, called *passenger mutations,* are distinguished from the better known cancer-causing *driver mutations*, which increase a tumor cell's proliferative capacity. How passenger mutations arise, despite selection against them, is not well understood nor fully explained by existing theory. Here, we extend several population genetics models to explain their accumulation in a precancerous population of cells and compare our findings against stochastic simulations. We find that passenger mutations alter and can avert progression to cancer. The probability of cancer depended heavily, and non-monotonically, on both the deleteriousness and rate of mutations. Counter-intuitively, high mutation rates decrease the likelihood of cancer—a finding recently corroborated by clinical data[1]. Our models suggest that therapies exploiting passenger mutations can avert cancer and may be more effective than targeting driver mutations.

1. Birkbak, N.J., et al., *Paradoxical relationship between chromosomal instability and survival outcome in cancer.* Cancer Res, 2011. **71**(10): p. 3447-52.

[1]PhD Candidate in Biophysics
[2]Pappalardo Fellow in Physics
[3]Professor of Health Sciences and Technology and Physics; Broad Institute Associate Member

Christopher McFarland
Harvard University

Date submitted: 20 Nov 2011 Electronic form version 1.4