Abstract Submitted
for the OSF15 Meeting of
The American Physical Society

**Collateral Sensitivity Networks Limit the Emergence of Drug Resistance via Clonal Interference** JEFF MALTAS, VICTORIA WOBSTER, ZANDER GALLUPPI, KEVIN WOOD, University of Michigan — Bacterial populations are often comprised of heterogeneous mixtures. Mutants within these populations may confer collateral resistance, or resistance to antibiotics the population has yet to encounter. Interestingly, recent work has focused on the existence of *collateral sensitivity,* or increased susceptibility to antibiotics. These studies demonstrate that the evolutionary dynamics of isogenic populations can be controlled via drug-cycling according to collateral sensitivity networks. This raises a complimentary question – can heterogeneous populations comprised of multiple resistant mutants be controlled by sequential drug administration? Here, we evolved a collateral sensitivity and resistance network for the gram-positive bacteria *Enterococcus faecalis*. Using these networks we were able to demonstrate judicious drug scheduling can significantly reduce overall growth in heterogeneous populations with complimentary drug-susceptibility profiles. While population heterogeneity is often viewed as a bet hedging strategy beneficial to survival, our results indicate collateral sensitivity can be used to limit the emergence of drug resistance by enhancing heterogeneity and facilitating clonal interference between coexisting resistant phenotypes.

Jeff Maltas
University of Michigan

Date submitted: 25 Sep 2015 Electronic form version 1.4