Chapter 3

The Effect of Killer Virus on Competition in S. cerevisiae

3.1 Introduction

Saccaromyces cerevisiae (yeast), like all cellular species, is susceptible to predation, competition, and parasitism. Naturally-occurring yeasts frequently harbor so-called Killer viruses [1], double-stranded RNA (dsRNA) molecules that encode proteins that are toxic to non-killer strains, as well as proteins that confer toxin immunity [23]. In the simplest case, encounters between Killers and non-Killers have only two results: mating or death. Like other fungal viruses, yeast Killer viruses can only be transmitted by mating, and propagated only via replication of an infected and immune population [3,23]. Killer viruses have been isolated from yeast that occupy a wide range of habitats across the Earth, including hosts *S. cerevisiae, S. pombe, C. glabrata*, and *P. pastoris*, found in clinical, fermentation, and food isolates.[3, 12, 25, 30]. The wide, but not universal, occurrence of this phenomenon suggests there are a restricted set of ecological conditions that select for the killer phenotype.

The mechanisms of killing and immunity are best understood in *S. cerevisiae* and killer viruses K-1,

K-2, and K-28 [3]. Infection among killer yeast is caused by a member of the cytoplasmic-persisting family Totiviridae. In *Saccharomyces cerevisiae* there are three major killer viruses (ScV-M1, ScV-M2, and ScV-M28) [4], each of which encodes for a specific killer protein (K1, K2 and K28 respectively). Killer virus infection requires the presence of two elements: K-dsRNA and L-dsRNA [39]. K-dsRNA encodes for the killer protein and for cell immunity, while L-dsRNA encodes for the export of the killer protein to the extracellular space [20]. Both must be present for a yeast to be a ”killer” [4]. Once the killer protein enters the extra-cellular space, it can not bind to a killer yeast cell, due to the immunity conferred. If, however, the killer protein binds to a non-killer cell, the protein disrupts the cell wall potential (ion leakage) which results in cell death [2].

The killer virus is only transmitted sexually in yeast [5]. When diploid yeast is starved for nitrogen in the absence of a fermentable carbon source, they typically undergo meiosis and produce 4 haploid spores, 2 of each mating type. When infected haploid cells encounter uninfected cells of opposite mating type, transmission of the killer trait follows syngamy and restoration of the diploid states. Diploids may then reproduce mitotically (asexually) or, if poor growth conditions ensue, undergo another round of sporulation and meiosis. The benefits for being a killer are straightforward: in any interaction between killer yeast and sensitive yeast, the killer yeast can outcompete the sensitive yeast in a batch culture by production of killer pre-protoxin. However, if a killer yeast competes with a non-killer resistant yeast, the competitive outcome is not immediately clear [18]. Because the killer yeast expending nutrients and energy towards maintaining the killer virus and killer protein, a resistant yeast may be able to out compete the killer yeast. This chapter studies models of infection in chemostat conditions and dependence of possible biologically meaningful steady states of these models on system parameters. Growth rate is a quantitative measure of yeast cell fitness. We will use the growth rate data of infected and uninfected yeast strains to determine and compare numerical values of quantitative measures of fitness. Our hypothesis is that the fitness of the yeast cell harboring the both K and L dsRNA viruses is less than that of a partially uninfected yeast cell harboring only the L ds-RNA virus. Travisano [18] demonstrates that invasion of the killer yeast is not possible under certain conditions. Analysis of models performed in this paper allows one to specify the conditions on

the system parameters for which washout of the killer yeast is possible.

Below, the following models will be discussed:

- First we analyze the resistant yeast and killer yeast system with no spread of infection.
- Then we study a killer system with susceptible yeast, with no spread of infection.
- Lastly, we address the model with a nonresistant yeast in which infection can occur through sporulation.

3.1.1 Resistant Yeast and Killer Yeast System

Another model to consider is case where uninfected yeast is resistant to ”killer” toxin. We arrive at a ”pure competition model”: the interaction between two types of yeast only occurs through competition for the nutrients. We consider ethanol production conditions in a chemostat where there will be no sporulation, and no transmission of the virus. Model assumptions are listed below:

(a) strains interactions may be described using the law of mass action;
(b) the constant inflow rate equals the outflow rate;
(c) no killing of uninfected yeast by killer toxin and no transmission of virus.
(d) growth rates of the infected and uninfected strains are different.

Under these assumptions, the model has the following form:

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