

Modelling Host-Pathogen Dynamics of *Salmonella*

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The dynamics of invasion of cells by pathogenic bacteria is a multiscale stochastic process consisting of several stages including attachment of bacteria, entry, vacuolar escape, replication and transmission to other cells. The pathogen *Salmonella enterica* is particularly interesting, as it has been shown to hyper-replicate (HR) within the cytoplasm of some epithelial cells but remain slow-growing within the vacuole of others. To better understand the causes of HR, we have developed a stochastic model of invasion using rates and probabilities from previously published experiments. In addition, we have used the CellProfiler image segmentation software to analyze time-lapse fluorescence microscopy images, taken by our collaborators, of *Salmonella* invading HeLa cells over a wide range of multiplicities of infection (MOI). To identify the HR phenotype cell-by-cell, we have developed a set of criteria based on bacterial growth measurements of individually tracked infected cells. We found that the estimated HR fractions (the fraction of infected cells which hyper-replicate) do not vary strongly versus MOI, but stay in the 5-15% range. In contrast, our simplest model predicted the HR fraction to quickly rise to 100% at high MOI. This indicates that we cannot treat all bacteria as independent and identical when it comes to the “decision” to remain vacuolar, or to escape into the cytoplasm and hyper-replicate.