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A STOCHASTIC INTRACELLULAR MODEL OF ANTHRAX INFECTION WITH SPORE GERMINATION HETEROGENEITY

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During inhalational anthrax infection, *Bacillus anthracis* spores are ingested by phagocytes such as alveolar macrophages and dendritic cells. The spores begin to germinate and then proliferate inside the phagocytes, which may eventually lead to death of the host cell and the release of bacteria into the extracellular environment. Alternatively, some phagocytes may be successful in eliminating the intracellular bacteria and will recover. As a generalisation of modelling work previously developed for *Francisella tularensis* [1], we consider a stochastic, Markov chain model for the intracellular infection dynamics of *B. anthracis* in a single phagocyte, incorporating spore germination and maturation, bacterial proliferation and death, and the possible release of bacteria due to cell rupture [4]. The model accounts for potential heterogeneity in the spore germination rate, with the consideration of two extreme cases for the rate distribution: continuous Gaussian and discrete Bernoulli. Through Bayesian inference, the model is parameterised using *in vitro* measurements of intracellular spore and bacterial counts for the Sterne 34F2 strain of *B. anthracis* [2, 3]. By extending and adapting the methodologies used for *F. tularensis*, we can estimate the rupture size distribution for infected phagocytes, as well as the mean time until phagocyte rupture and bacterial release. Our results support the existence of significant heterogeneity in the germination rate across different spores, with a subset of spores expected to germinate much later than the majority. Furthermore, in agreement with experimental evidence, our results suggest that the majority of spores taken up by macrophages are likely to be eliminated by the host cell, but a few germinated spores may survive phagocytosis and lead to the death of the infected cell. Finally, we discuss how this stochastic modelling approach, together with dose-response data, can allow us to quantify and predict individual infection risk following exposure.

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1 Introduction

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