

# Foot-and-Mouth Disease Virus, Epithelial Cell Death and PDE Models

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Foot-and-mouth disease virus (FMDV) is a highly infectious animal virus that affects cloven-hoofed animals (including cattle, sheep and pigs). Because FMDV is a serious global socio-economic threat, it has been studied extensively for many decades. However, there are still several significant knowledge gaps in the pathogenesis of the disease. In particular, the predilection for certain epithelial tissues to develop vesicular lesions is currently unexplained. For example, epithelial cell lysis is extensive in the epithelial tissue of the bovine tongue, which results in the development of vesicular lesions. Nevertheless, the epithelium of the dorsal soft palate (DSP) does not show similar signs, even though it is a primary infection site of FMDV. The factors which influence epithelial cell death and the development of lesions are the focus of this work, which is one of the few modelling studies on the within-host dynamics of FMDV.

With the aim of identifying potential determinants of FMDV-induced epithelial cell lysis in cattle, a spatially explicit 1D PDE model was developed to investigate the roles played by bovine epithelial thickness and cell layer structure. Numerical investigations demonstrated that these two factors alone do not explain the formation of lesions and, consequently, additional biological complexity is essential to explain the bifurcation in epithelial cell behaviour. Detailed exploration of parameter space offered an insight on the importance of potential differences in viral replication and receptor distribution between epithelia and between epithelial cell layers. The 1D epithelial tissue model has been subsequently expanded to a 3D structure, to facilitate the study of the size, as well as the occurrence of lesions, while greater biological realism has been added to the model by incorporating the antiviral activity of interferon to allow its effects on the FMDV dynamics in epithelium to be explored.