Uncovering Genotoxic Effects Through Differential Equation Models: Investigating Bacteria, Drugs and Hidden Interactions

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We investigate the genotoxic effects that bacterial infections and antibiotics exert on human cells. Bacteria may induce mutations either by invading cells or by generating extracellular stress, and drugs can also have mutagenic effects. Moreover, complex interactions between the bacteria and the drug take place in the background. We modified the usual in-host pathogen models for chronic infections to create a new model by including self-replication for the bacteria, as well as a pathogen-loss term. We obtained a system of nonlinear differential equations which describes the interactions between healthy and infected human cells, the external bacteria, and possibly drug treatment. We carried out a detailed analysis of the model and discovered surprisingly complex dynamical phenomena, including bistability and different types of bifurcations (saddle-node, transcritical, pitchfork and backward). We determined the optimal infection rate from the bacteria's perspective, and noted that for certain parameter combinations, there is evolutionary risk when striving for this value. Realistic model extensions, such as drug-dependent infection rate and infection-based compartment structuring, were also examined. Finally, we looked into the cumulative genotoxic effect of different therapies and compared the results of the model with experimental data measuring DNA damage in cells. Our model provides insight and helps to understand how the aforementioned interactions influence the total mutagenic effects on cells.