Within-host Model of Poliovirus Control by Defective Interfering Particles and Interferon

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Abstract

We use a system of ordinary differential equations to model a therapeutic strategy for polio through the usage of defective interfering particles (DIPs). DIP is a defective variant of wild-type (WT) virus lacking a protein capsid essential for viral replication. We also introduce interferon as a representative of the immune system.

Introduction

Poliovirus is a single-stranded RNA virus which causes poliomyelitis. Interferon is a group of signal-proteins induced by the presence of microbial or viral infection. Interferon is able to trigger the antiviral defense of neighboring cells. In mathematical models, the effects of IFN are usually represented in the following ways:

- Protection of some susceptible cells from infection through transforming them into refractory state.
- Directly killing some infected cells.

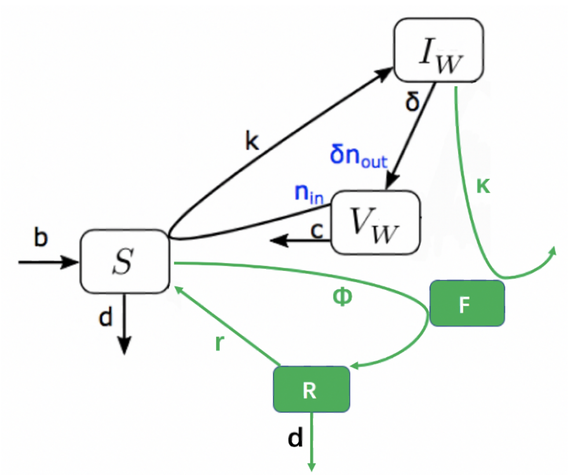


Figure 1:WT in human body with only IFN as the natural defensive mechanism

Therapeutic Strategy: DIP

Although vaccines exist, poliovirus is still not fully eradicated in areas with limited health resources. In addition, in recent years there are increasing cases of vaccination-derived strains of poliovirus. We model an alternative strategy, which is adding Defective Interfering Particles (DIPs) of poliovirus [1].

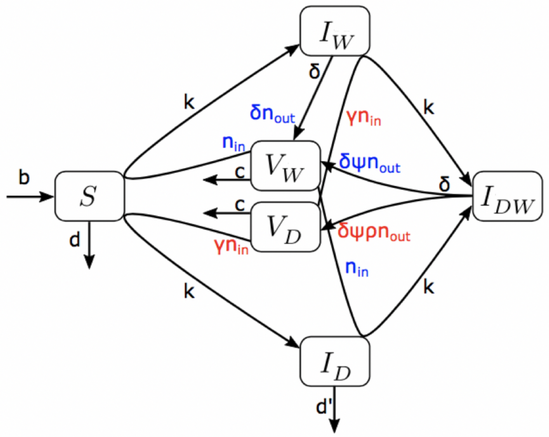


Figure 2:Using DIPs as to control the replication of WT

Defective Interfering Particles

DIPs are non-viable variants of WTs that are unable to complete the replication cycles by themselves. During co-infection with WTs, DIPs act as parasites and can be used to control the WTs throught the following procedures:

- During co-infection with WT, DIP steals capsid protein from WT, thereby reducing the overall WT viral load.
- With smaller genome, DIPs are able to outcompete the WT due to greater replication rate.
- Once the WT population has been depleted, DIPs are incapable of reproducing further.

Analysis of R_0

The disease free equilibrium (DFE) is the equilibrium point of the model in the absence of disease.The range of R_0 determines if a disease is able to invade a population.

- $R_0 < 1$: DFE is locally asymptotically stable. Disease is unable to spread in the population
- $R_0 > 1$: DFE is unstable. Disease is able to spread.

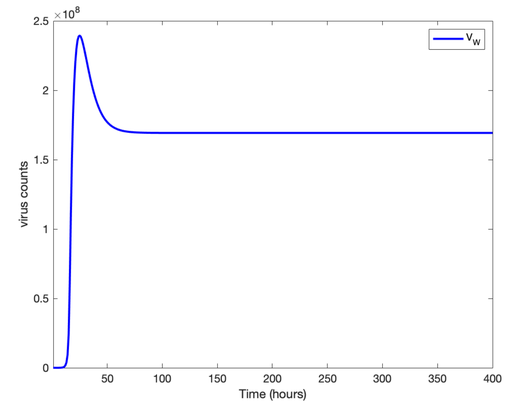
For compartmental epidemic models under certain constraints, we are able to calculate the R_0 through the following procedures [2]:

- Sort the compartments so that the first m compartments correspond to infected individuals. All disease free states are defined as
$$X_s = \{x \geq 0 | x_i = 0, i = 1, 2, ..., m\}$$
- Distinguish the new infections from all other changes in population through expressing systems of equation as
$$\dot{x}_i = f_i(x) = \mathcal{N}_i(x) - \mathcal{P}_i(x), i = 1, 2, ..., n \quad (1)$$
where $\mathcal{N}$ indicate the new infections, $\mathcal{P}$ are other population changes.
- If x_0 is a DFE of (1), then the derivatives $D\mathcal{N}(x_0)$ and $D\mathcal{P}(x_0)$ are partitioned as
$$D\mathcal{N}(x_0) = \begin{pmatrix} N & 0 \\ 0 & 0 \end{pmatrix}, D\mathcal{P}(x_0) = \begin{pmatrix} P & 0 \\ J_3 & J_4 \end{pmatrix}$$
where N and P are defined by
$$N = \left[\frac{\partial \mathcal{N}_i}{\partial x_j}(x_0)\right], P = \left[\frac{\partial \mathcal{P}_i}{\partial x_j}(x_0)\right], 1 \leq i, j \leq m$$
- $R_0 =$ largest eigenvalue of NP^{-1}

For system with only IFN and for system with both IFN and DIPs, R_0 are the same as
$$(S_{DFE}\delta k n_{out})^{\frac{1}{2}}(c + S_{DFE}k n_{in})^{-\frac{1}{2}}(\delta + \kappa)^{-\frac{1}{2}}$$
where $S_{DFE} = \frac{b(d+r)}{d(d+r+\phi)}$, indicating the number of susceptible cells when there is no viral infection. The result indicates that R_0 is independent of DIP.

Other Criteria to Assess DIP

Although DIPs make no difference in terms of the ability of WT to invade a population, simulation results suggest the possibility to assess the effectiveness of DIP in the other aspect. This part is still in progress. We are planning to look at steady state of WT, peak viral load, time taken to reach peak, etc.



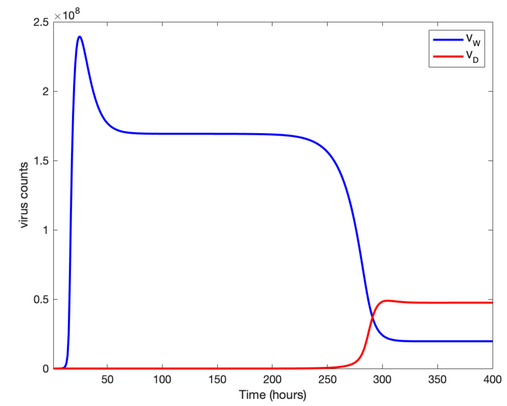


Figure 3:System with IFN only (top), and with both IFN and DIP added at t=100(bottom).

[1] Bingham A, Rousseau E, Shaw L, Andino R, Bianco S. Two-Patch Organ Model for Competition Between Defective Interfering Particles and Wild-Type Poliovirus. preprint. 2019.

[2] van den Driessche P, Watmough J, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Mathematical Biosciences*,Volume 180, Issues 1–2, 2002.