

Toward an in silico viral kinetic model for Covid-19 with pharmacodynamic effects

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Background

- The aim of this work is to adopt the rationale for the viral kinetics of SARS-CoV-2
- Viral load data has been collected at hospitals in Singapore, Germany, Korea and France
- Limited data is available
- Remdesivir is an antiviral drug developed for Ebola
- Acts by reducing the replication of the virus

$$\begin{aligned}\frac{dT}{dt} &= -\beta TV \\ \frac{dI}{dt} &= \beta TV - \delta I \\ \frac{dV}{dt} &= pI - cV\end{aligned}$$

Eq 1. ODE for target cells (T), infected cells (I), viral load (V)

Methods

- A system of ordinary differential equations (ODE) is used to model the target cells (T), infected cells (I) and viral load (V) of a patient.
- Adopt a target cell limited model created for Influenza [1]
- The MATLAB solver ode45 is used
- To estimate the parameters the MATLAB Genetic Algorithm function was used

$$\sum_{i=1}^N (\log_{10} data_i - \log_{10} output_i)^2$$

- Due to identifiability issues it is not possible to estimate all four parameters, so the viral clearance rate was set to 2.4 [2]

$$\frac{dV}{dt} = (1 - \varepsilon)pI - cV$$

- To model the impact of Remdesivir on a patient, an efficacy term was used. It was assumed that the efficacy is constant, and the effects start on day 0

Results

- Large range of parameters
- Does not always reflect what is currently known about the progression of the virus.
- To make any significant difference to the time which the viral load is detectable, the efficacy needs to be very high.
- 99% efficacy reduces detectable time by 3 days

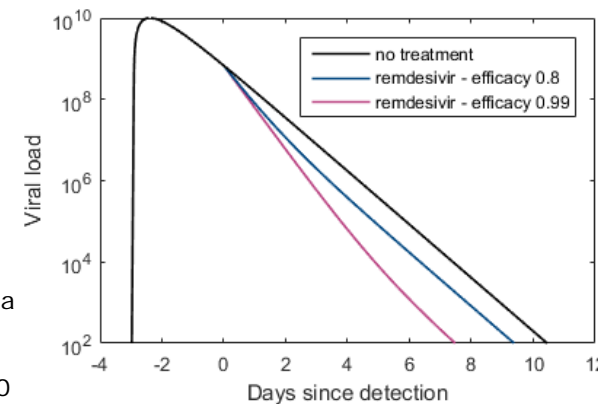


Fig 2. Effect of Remdesivir on viral load

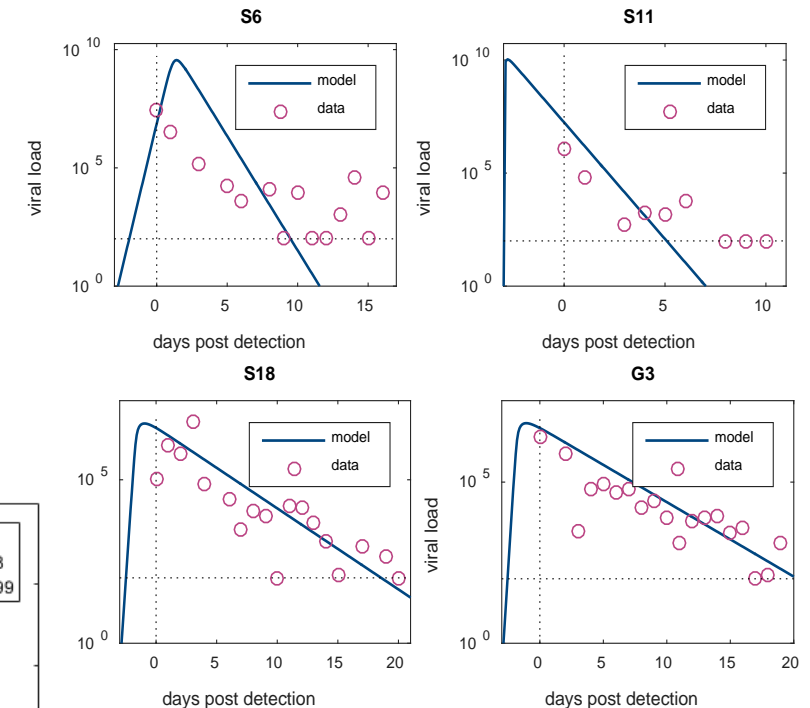
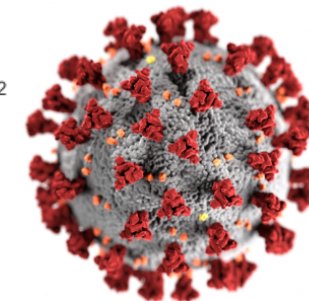


Fig 1. Fitted viral kinetic model for four patients using genetic algorithm



References

- Baccam P, Beauchemin C, Macken C, Hayden F, Perelson A. Kinetics of Influenza A Virus Infection in Humans. *Journal of Virology* 2006; 80(15): 7590-7599. <https://doi.org/10.1128/jvi.01623-05>
- Esteban A, Hernandez-Vargas, Jorge X, Velasco-Hernandez. In-host Mathematical Modelling of COVID-19 in Humans. *Annual Reviews in Control* 2020; 50: 448-456. <https://doi.org/10.1016/j.arcontrol.2020.09.006>