Analysis of COVID-19 Models To Determine Key Factors in Treatment

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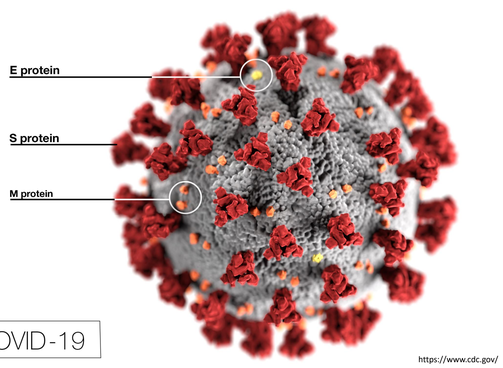
Abstract

- **Background:** The outbreak of COVID-19 became a pandemic in early 2020 and has caused over 2 million deaths worldwide.
- **Goal:** Increase understanding of COVID-19 viral dynamics on an intercellular level through mathematical modeling
- **Methods:** Use MATLAB ODE Toolbox to perform a sensitivity analysis on two different viral dynamic models
- **Comparison Factors:**
  - Peak Viral Load
  - Time of Peak Viral Load
  - Time Till Recovery
- **Impact:** Improve patient specific treatment and guide development of biosensors

Background



- The COVID-19 pandemic is caused by SARS-CoV-2
  - RNA virus that hijacks host cells to replicate
  - Spike proteins → receptor mediated entry
  - ACE2 receptors found in the lungs and small intestines

Treatment Considerations	Method for Reducing Viral Production	Method for Reducing Viral Infection	FDA Approved Treatment
Lopinavir/Ritonavir	✓		
Hydroxychloroquine (HCQ)	✓	✓	
Interferons (FN-β-1a)	✓		
Remdesivir	✓		✓

Methods

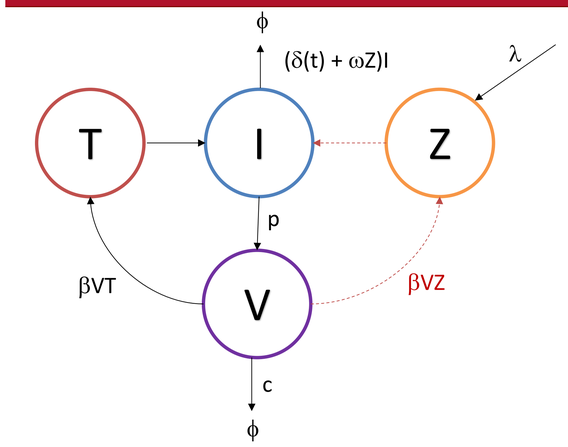


Fig. 1: Schematic Diagram of Model

Analysis:
1. Start with set parameters (Table 2 and 3)*
   1. T(0) = 6*10^4, Z(0) = 0, I(0) = 0
2. Simulate using equations 1 and 2 in MATLAB
3. Modify parameters individually by -50%, -25%, -10%, -1%, 1%, 10%, 25%, 50%, and 100%
4. Calculate peak viral load, day of peak viral load, and time till recovery (viral load below 10^2 after peak)
5. Calculate differentials with respect to original values: (change in output parameter)/(change in input parameter)
6. Determine patterns in the data

Parameter	Description
T	Target Cell: pneumocytes
Z	Immune Cell: T lymphocytes
I	Infected Cells
V	Viral Cells
β	Viral Infection Rate
δ_0	Base Death Rate of Infected Cells
d	Death Rate of Immune Cells
c	Clearance of Viral Particles
p	Production of Viral Particles
ω	Killing Rate by Innate Immune Response
λ	Recruitment of Lymphocytes to Infection Site
σ	Parameter of the Adaptive Immune Response
μ	Time Delay of Adaptive Immune Response

Table 1: Summary of Model Parameters

$$\dot{T} = -\beta VT,$$
$$\dot{Z} = \lambda - dVZ,$$
$$\dot{I} = \beta VT - [\delta(t) + \omega Z]I,$$
$$\dot{V} = pI - cV,$$

Eq. 1: Modified Model

$$\dot{T}_1 = -\beta VT_1,$$
$$\dot{T}_2 = \lambda - \beta VT_2,$$
$$\dot{I} = \beta V(T_1 + T_2) - [\delta(t) + \omega T_2]I,$$
$$\dot{V} = pI - cV,$$

Eq. 2: Original Model

Parameter	Patient 1	2	3	4	7	8	10	14	Avg
β, d	$4.8*10^{-8}$	$5.9*10^{-8}$	$3.6*10^{-6}$	$7.3*10^{-7}$	10^{-6}	$9.1*10^{-8}$	$4.6*10^{-7}$	$4*10^{-5}$	$5.7485*10^{-6}$
c	17	39	4.40	4.4	209	108	0.89	20	50.3362
p	$7.9*10^5$	$1.3*10^5$	$1.2*10^3$	$5.7*10^3$	$1.1*10^5$	$1.2*10^5$	$1.66*10^2$	$6.5*10^3$	$1.4545*10^5$
ω	$2.1*10^{-4}$	$1.6*10^{-4}$	10^{-3}	$1.1*10^{-3}$	$4.5*10^{-4}$	$4*10^{-5}$	10^{-9}	$1.4*10^{-2}$	0.0021
σ	0.001	0.1	0.1	0.5	0.11	0.1	0.93	1.8	0.4551
μ	10	8	9	6	9	6	15	6	8
$V(0)$	10^{-3}	10^{-4}	10^{-3}	10^{-4}	10^{-3}	10^{-4}	10^{-4}	10^{-5}	$4.2625*10^{-4}$

Table 2: Model Parameters Values

*Results are based on data from Patients 1,2,3, 7 and 8

Constants	Value
λ	10^4 cells/mL/day
δ_0	2 cells/day
T_{final}	30 days

Table 3: Initial Parameters

Results

+++/--- = strong positive/negative correlation, ++/-- = mostly positive/negative correlation, +/- some positive/negative correlation, ? = mix of positive and negative correlation, 00 = all zeros, 0 = most zero, p = depends on patient

	λ	β	ω	p	c	δ_0	μ	σ	T_0	V_0	d
Max Viral Load	---	+++	---	++	---	---	0,+	0,-	++	p	+++
Day of Max Viral Load	?	?	0,?	-	?	0	0,+	0	-	0,-	0
Days Till Recover	?	?	p	?	?	0,-	0,p+	0,p-	?	0,p+	0

Table 4: Results for Modified Model

	λ	β	ω	p	c	δ_0	μ	σ	T_0	V_0
Max Viral Load	++	?	--	++	--	---	0	0,p+	+	p
Day of Max Viral Load	0	--	0,+	0,-	+	0, +	00	00	0,-	00
Days Till Recover	++	++	--,p0	+	--	--	++	--	0,+	0

Table 5: Results for Two Target Model

Discussion

- Lambda has opposite effects on max viral load in the two models
- Decreasing viral production (by using medicines) reduces magnitude and delays peak viral load
- Reducing infection by viral particles (β) decreases peak viral load in the modified model
- Develop treatments by targeting mechanisms that act on parameters other than β and p

Future Direction

- Perform more simulations
  - Chose other parameter regions
  - Include other models
  - Change more than one variable at a time

Acknowledgements

I would like to thank my research advisor professor Wade Trappe for his guidance on this research project. Furthermore, I would like to thank Dean Antoine and the JJ Slade Research program for the advice and opportunity to present my work.

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