

Building a theoretical model of viral dynamics for SARS-CoV-2 and IAV co-infection



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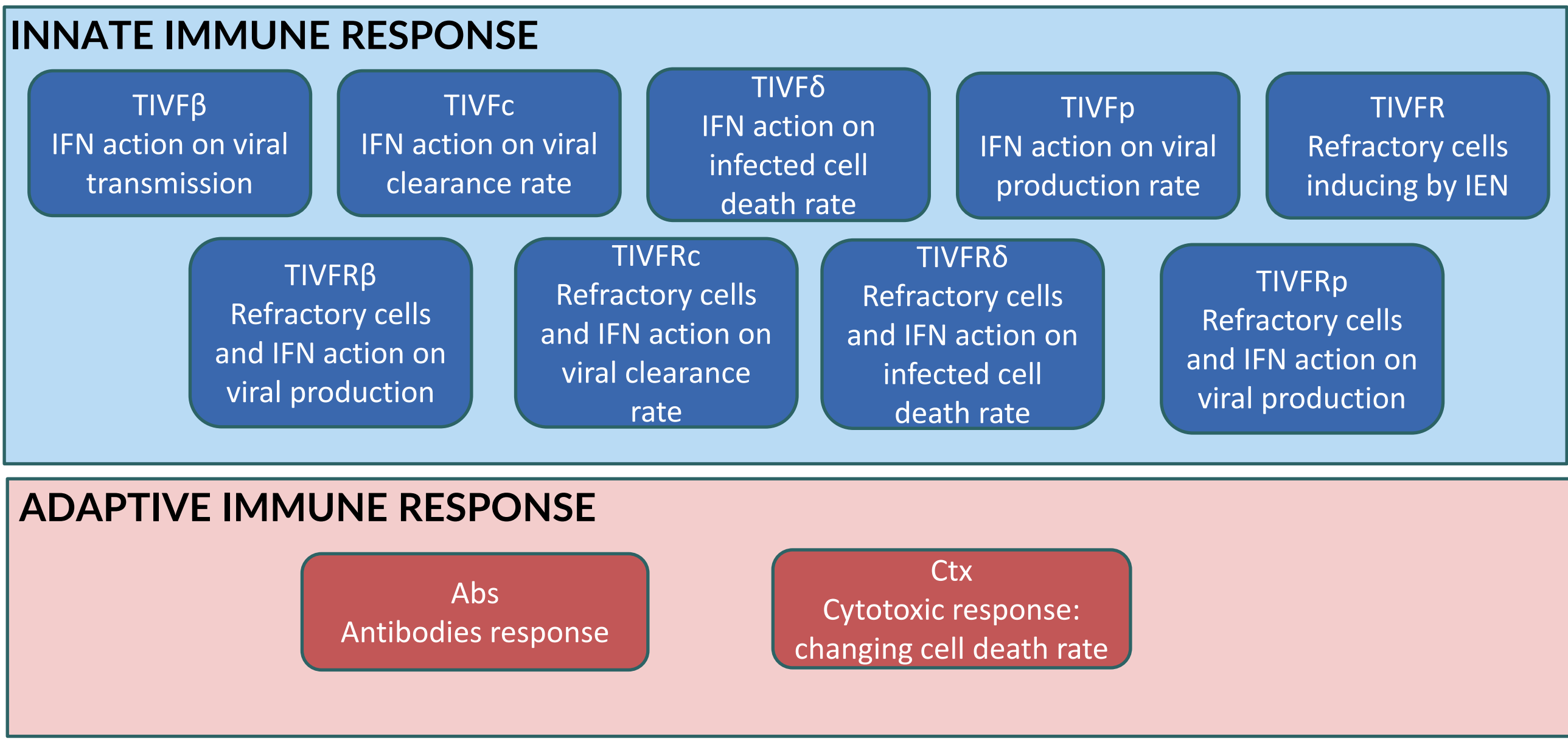


Context

- Acute respiratory infections are a leading cause of acute illness
- Annually 3 to 5 million of cases of Influenza A virus (IAV) infections worldwide [1]
- 700 million SARS-CoV-2 infections since the first case [2]
- Co-circulation increases the risk of co-infection which could lead to more severe disease [3]
- Still unclear how these viruses interact within patient and potentially modulate virulence and disease progression
- Immune system seems to have a major role on co-infections ([4],[5])
- Need to address fundamental questions regarding intra-host spread, viral clearance and role of immunity in case of IAV and SARS-CoV-2 co-infection.

Methods

Selection of mechanistic models for mono-infection



Objective: Build a theoretical mathematical model of viral dynamics for SARS-CoV-2 and IAV co-infection

- Building a model of mono-infection for IAV and RSV
Use viral load from humans
Test different models that incorporate immune response
Select the best model
- Building a model of co-infection
Use model of mono-infection
Simulate the model in different scenarios

Model of co-infection

- Use best model selected in mono-infection estimation
- Simulation using population parameters and random effects

Scenarios of investigation

- Order of infection
- Delay between infections
- Susceptibility of cells

Metrics

- Area under the curve (AUC)
- Viral peak
- Time until viral clearance

Susceptibility of cells in upper respiratory tract (URT)

- IAV infects all cells of URT [6]
- Use of ACE2 and TMPRSS2 receptors by SARS-CoV-2 [7]
- 1-20% of cells of URT have ACE2 and TMPRSS2 receptors [7]

Data

- 607 SARS-CoV-2 infected individuals from National Basketball Association's (NBA) testing program data [8]
- 287 IAV infected individual from clinical trial [9]

Results

Selected model of mono-infections

- Reduction of viral production by IFNs
- Refractory cells induced by IFNs
- Cytotoxic response

Viral tropism of IAV and SARS-CoV-2

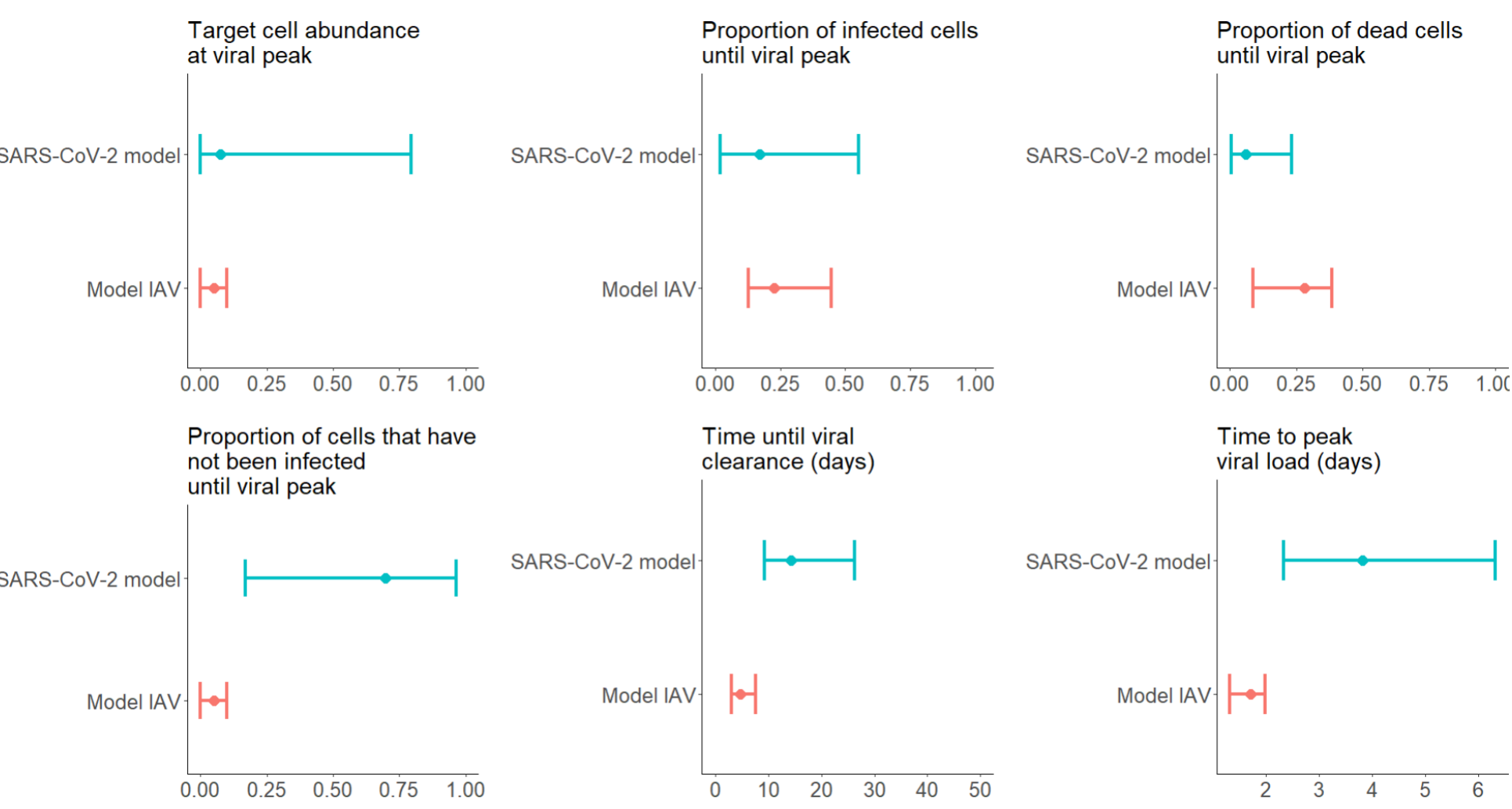


Figure 1. Metrics obtained for mono-infection

Simulation of viral kinetics

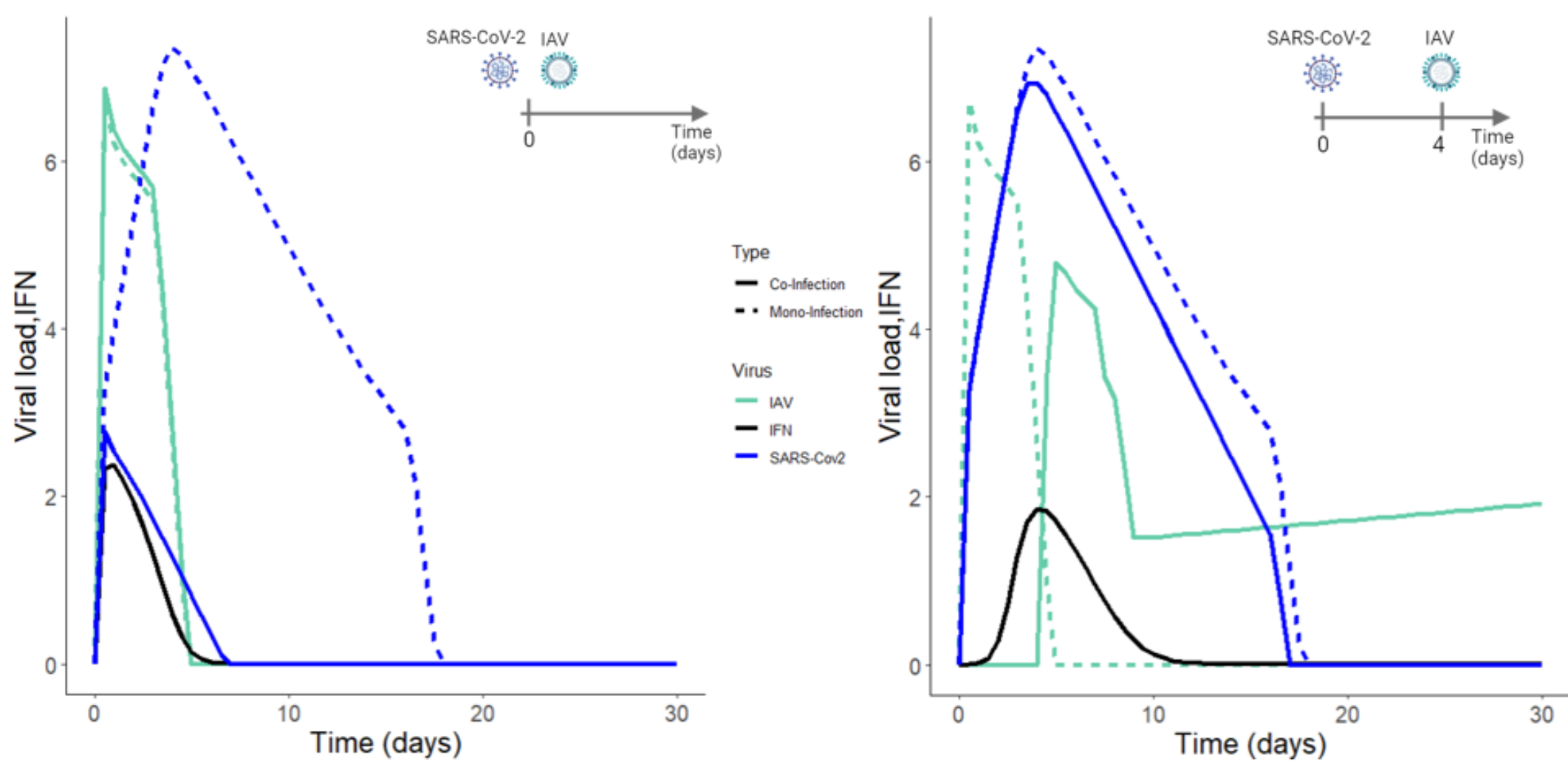


Figure 2. Viral load and IFN simulated for mono- and co-infection

- When SARS-CoV-2 and IAV co-infect simultaneously, SARS-CoV-2 load is reduced by 3 fold and reaches its peak 3 days earlier, while IAV load is unchanged
- If there is at least 2 day of delay between infections, IFN-induced protection reduces the viral peak by 3-fold for SARS-CoV-2 and by 1.2 fold for IAV
- The antiviral state induced by SARS-CoV-2 increases by 4-fold the AUC of IAV
- When IAV infection precedes by at least 1 day, the AUC of SARS-CoV-2 decreases by 10-fold

Effect of delay and susceptibility of cells

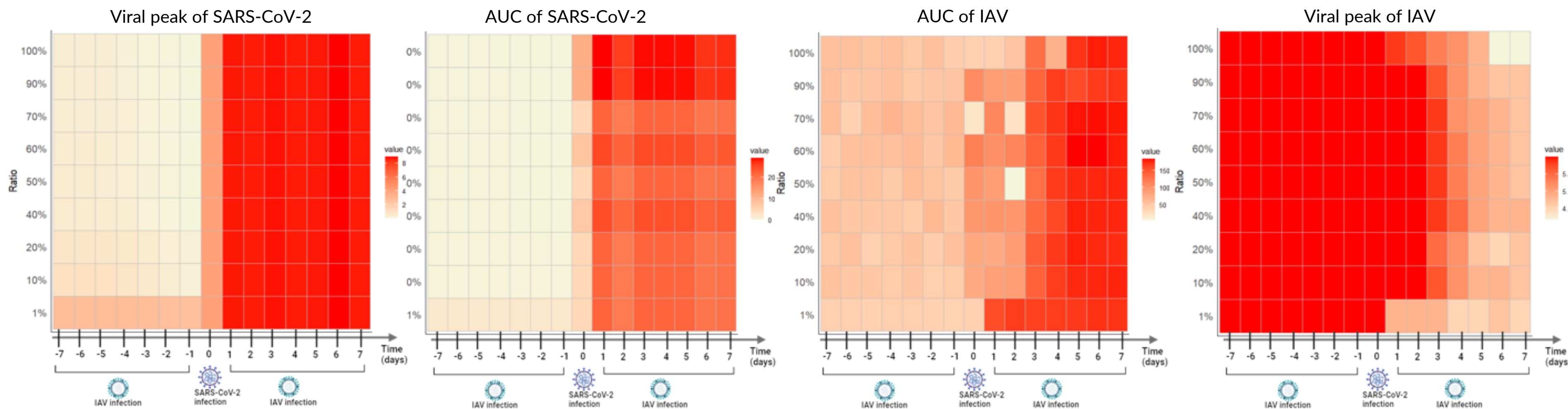
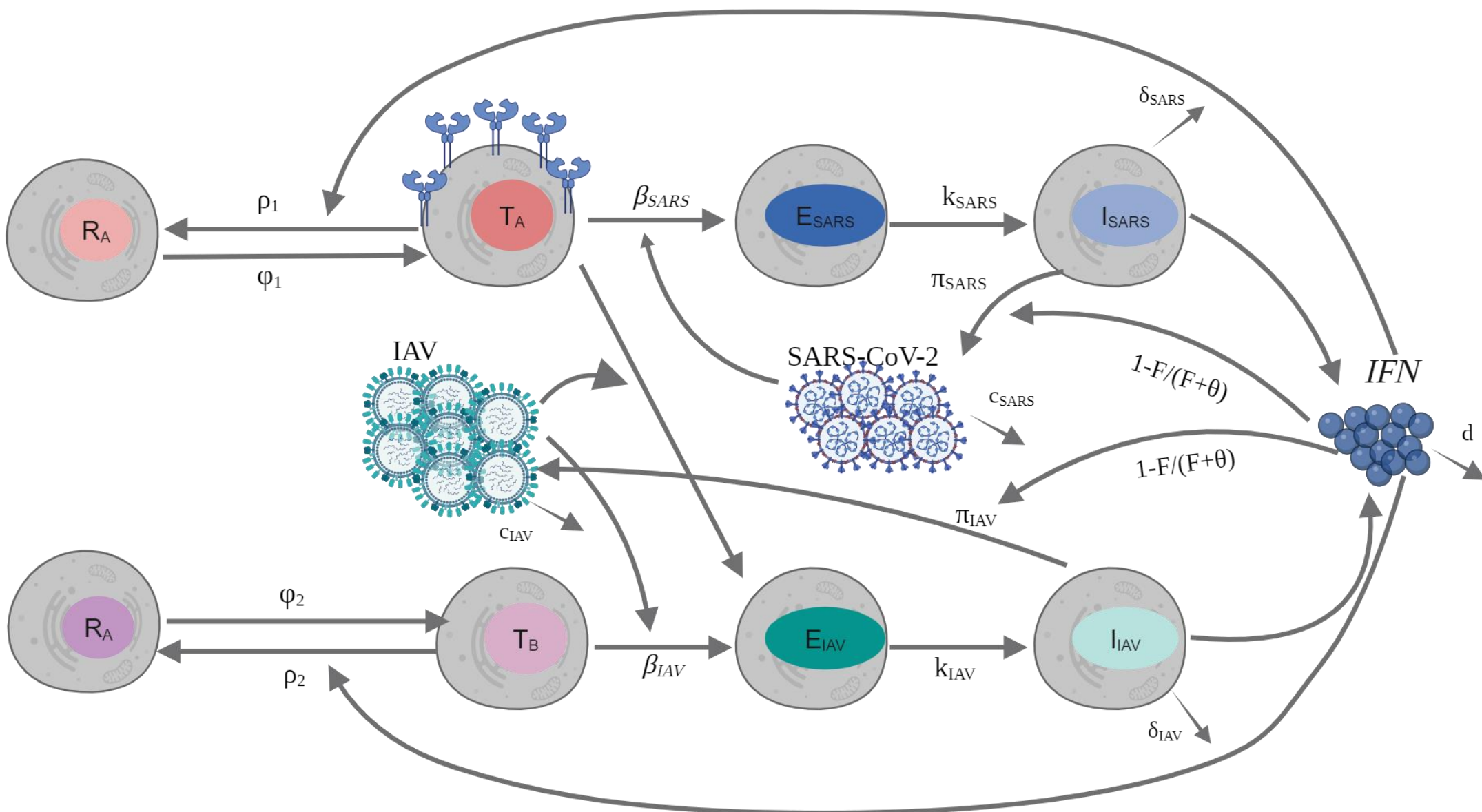


Figure 3. Heatmap of AUC and viral peak of IAV and SARS-CoV-2

Co-Infection model



References

[1] World Health Organization Influenza (Seasonal) Fact Sheet-2018; [2] World Health Organization COVID-19 dashboard-2024;[3] Petat et al., Viruses, 2021;[4] Fonzelez, Journal of Virology, 2018; [5] Pizzorno et al., Journal of Infectious Disease, 2022; [6] Lakadamyali et al., Microbes Infect, 2004; [7] Hou et al., Cell, 2020;[8] Kissler et al., PLoS Biol, 2021; [9] Asher et al., PLoS Comput Biol, 2023

Conclusion

- IFN plays a pivotal role in modulating viral load kinetic by reducing viral production and inducing cells to become refractory to the virus
- IAV highly reduces SARS-CoV-2 kinetics
- SARS-CoV-2 does not reduce IAV kinetic unless the delay is at least 2 days between infections
- Viral interactions between IAV and SARS-CoV-2 could be studied in the context of antiviral strategies

