Compositional Cyber Physical Epidemiology for Covid-19 Modelling

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Overview:

1. Current Covid-19 situation around the world
2. Types of epidemiological Modelling
3. Need for comparing models
4. Difficulties in Comparing models
5. CCPE Modelling Techniques
    a. Controller Analysis
    b. Simple economic modelling

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Current Covid-19 situation

- 177.8 million cases, 3.84 million deaths
- Many countries recovering from the 2nd wave of infections
- Multiple variants: Alpha, Beta, Gamma, Delta
- Unequal vaccination rates around the world
- Fungus Infections
- Questions on how and when to lift the lockdowns?
- Ramping up the healthcare infrastructures around the world

Vaccination Rates

Single Dose, Fully vaccinated

In India:

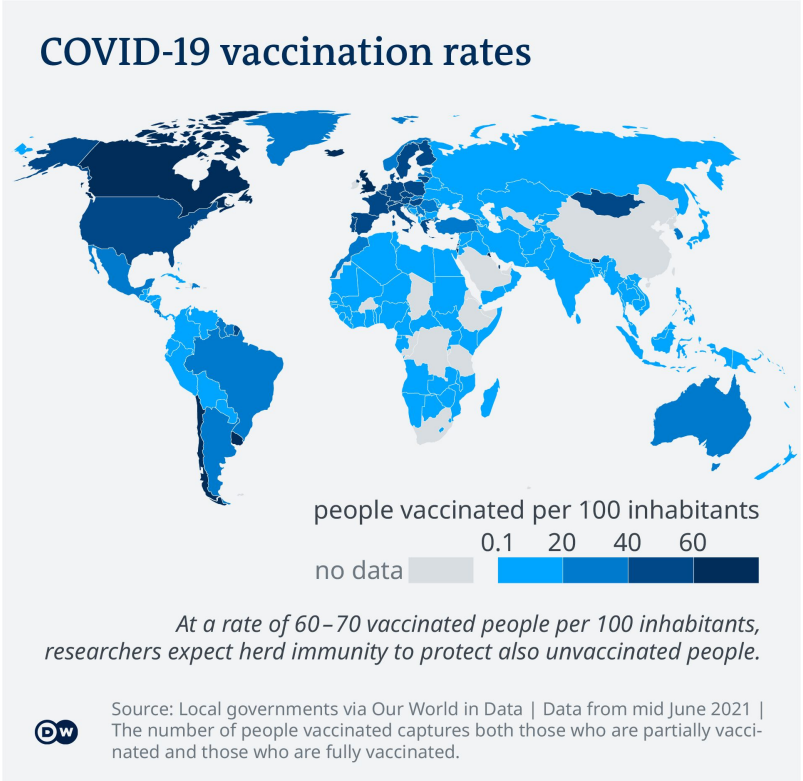
15.2%, 3.5%

In USA:

53.1%, 44.4%

In New Zealand:

11.5%, 6.6%



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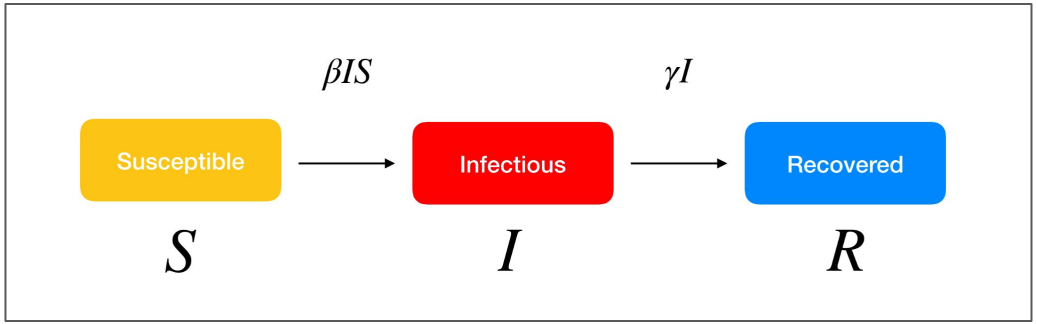
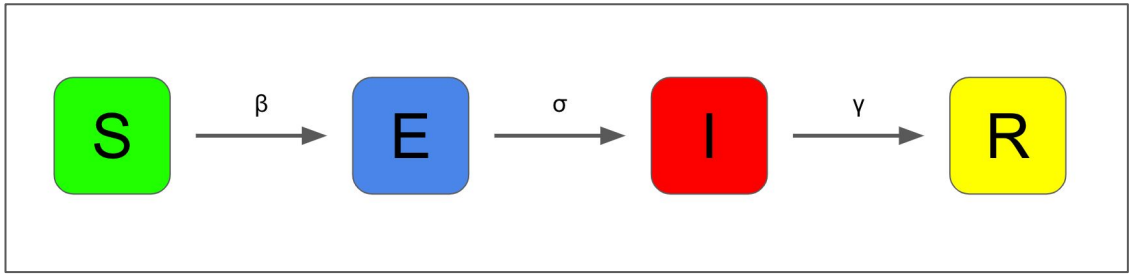
A. Deterministic Models (Macro Modelling)

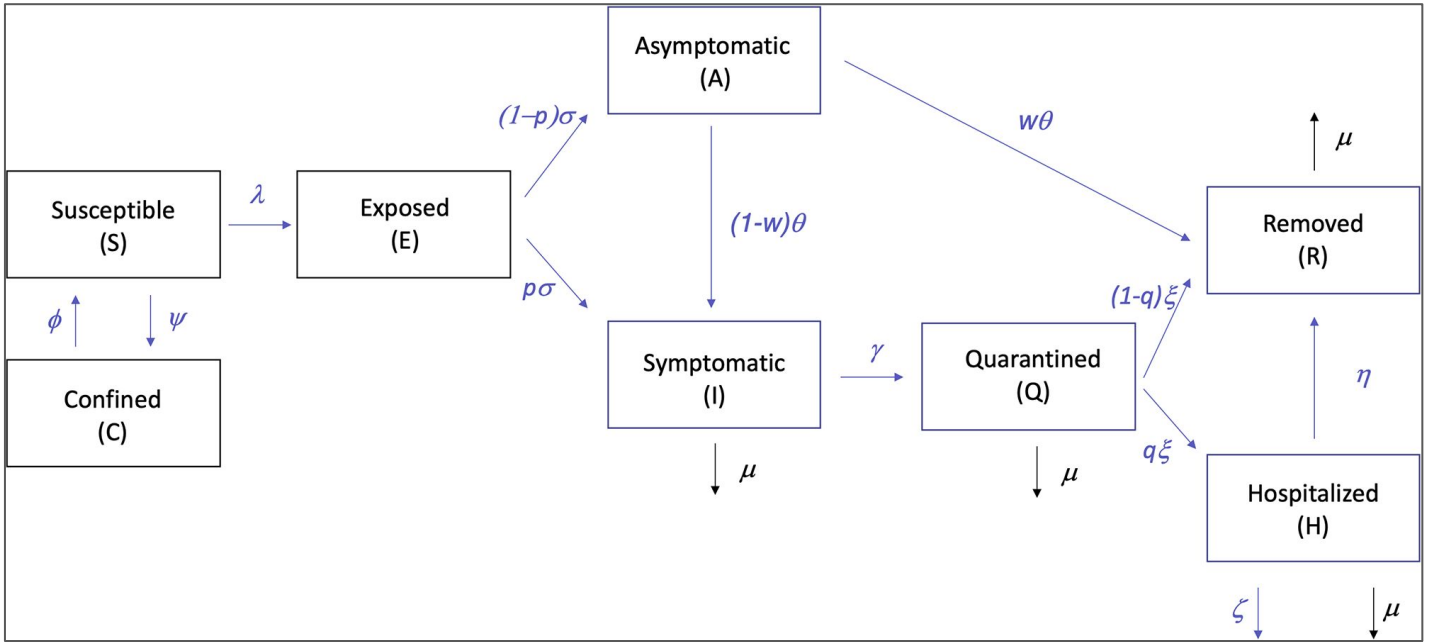
- In a deterministic model, individuals in the population are assigned to different subgroups or compartments, each representing a specific stage of the epidemic.
- The transition rates from one class to another are mathematically expressed as derivatives, hence the model is formulated using differential equations.

Examples of Deterministic Models





Examples of Deterministic Models



Models used in this research work

1. Modified SEIR Model:

a. Introduces new states to capture the infected-untested and infected-confirmed.

b. Infected-untested ----> Recovered (Some people might get cured on their own without any medical assistance)

c. Most of the infected-untested can be considered as asymptomatic cases.

$$\frac{dS}{dt} = -\beta S(\epsilon P + I_u + I_c)$$

$$\frac{dE}{dt} = \beta S(\epsilon P + I_u + I_c) - \alpha E$$

$$\frac{dP}{dt} = \alpha E - \delta P$$

$$\frac{dI_u}{dt} = \delta P - (\gamma + c) I_u$$

$$\frac{dI_c}{dt} = c I_u - \gamma I_c$$

$$\frac{dR_u}{dt} = \gamma(1 - CFR) I_u$$

$$\frac{dR_c}{dt} = \gamma(1 - CFR) I_c$$

$$D = 1 - S - E - P - I_u - I_c - R_u - R_c$$

Models used in this research work

2. CovidSim 2.0:

a. Introduces multiple sub-stages for each stage of the infection.

b. Considers isolation at hospital and isolation at home with different transmission capabilities.

Number of susceptible individuals

$$\frac{dS}{dt} = -\frac{S}{N}\left(\beta_P(t)\sum_{k=1}^{n_P} P_k(t) + \beta_I(t)\left(\sum_{k=1}^{n_I} I_k(t) - I_{Iso}(t) - I_{Home}(t)c_{Home}\right) + \psi\right)(1 - c_{Cont}(t))$$

Number of individuals in the latent period

$$\frac{dE_1}{dt} = \frac{S}{N}\left(\beta_P(t)\sum_{k=1}^{n_P} P_k(t) + \beta_I(t)\left(\sum_{k=1}^{n_I} I_k(t) - I_{Iso}(t) - I_{Home}(t)c_{Home}\right) + \psi\right)(1 - c_{Cont}(t)) - \varepsilon E_1$$

$$\frac{dE_k}{dt} = \varepsilon E_{k-1} - \varepsilon E_k \qquad (1 < k \le n_E)$$

Number of individuals in the prodromal period

$$\frac{dP_1}{dt} = \varepsilon E_{n_E} - \varphi P_1$$

$$\frac{dP_k}{dt} = \varphi P_{k-1} - \varphi P_k \qquad (1 < k \le n_P)$$

Number of individuals in the symptomatic period

$$\frac{dI_1}{dt} = \pi P_{n_P} - \gamma I_1$$

$$\frac{dI_k}{dt} = \gamma I_{k-1} - \gamma I_k \qquad (1 < k \le n_I)$$

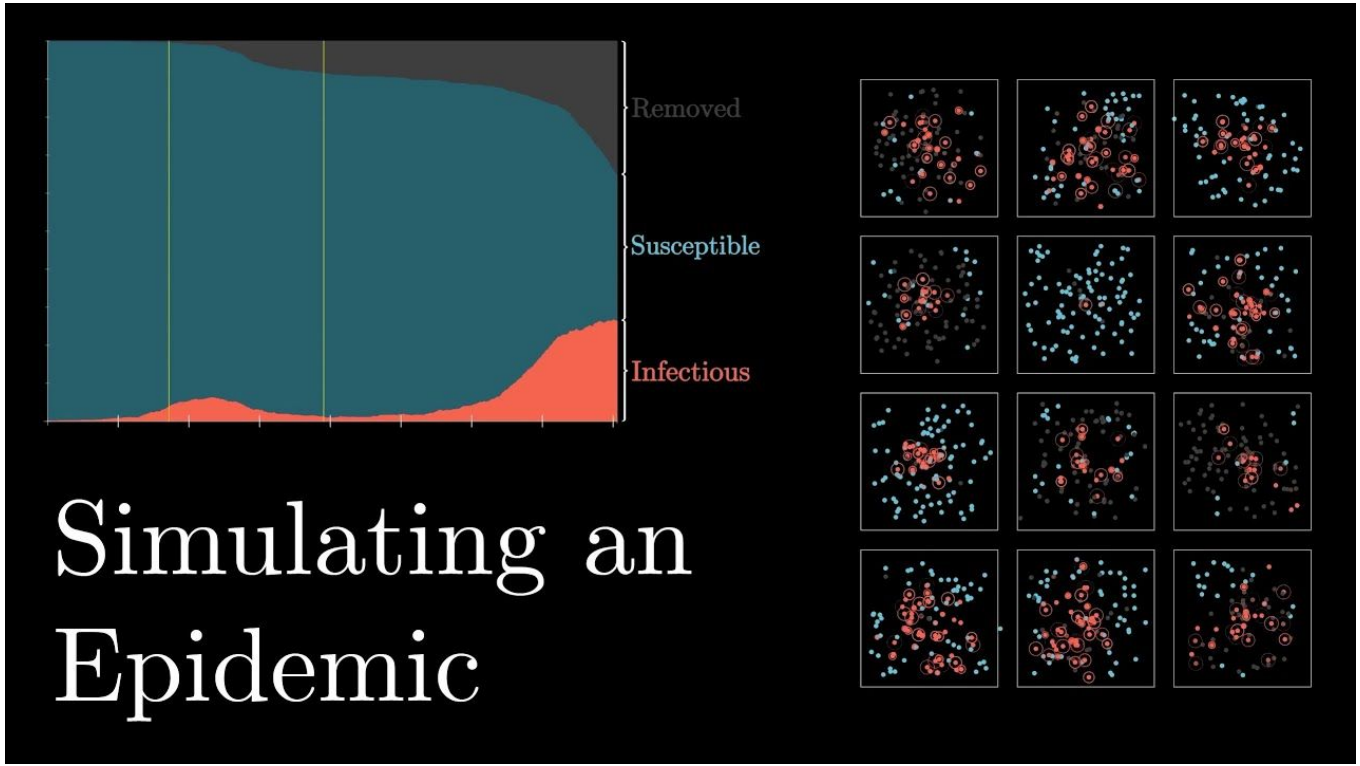
Number of removed individuals

$$\frac{dR}{dt} = \gamma(1 - p_{Sick}p_{Death})I_{n_I}$$

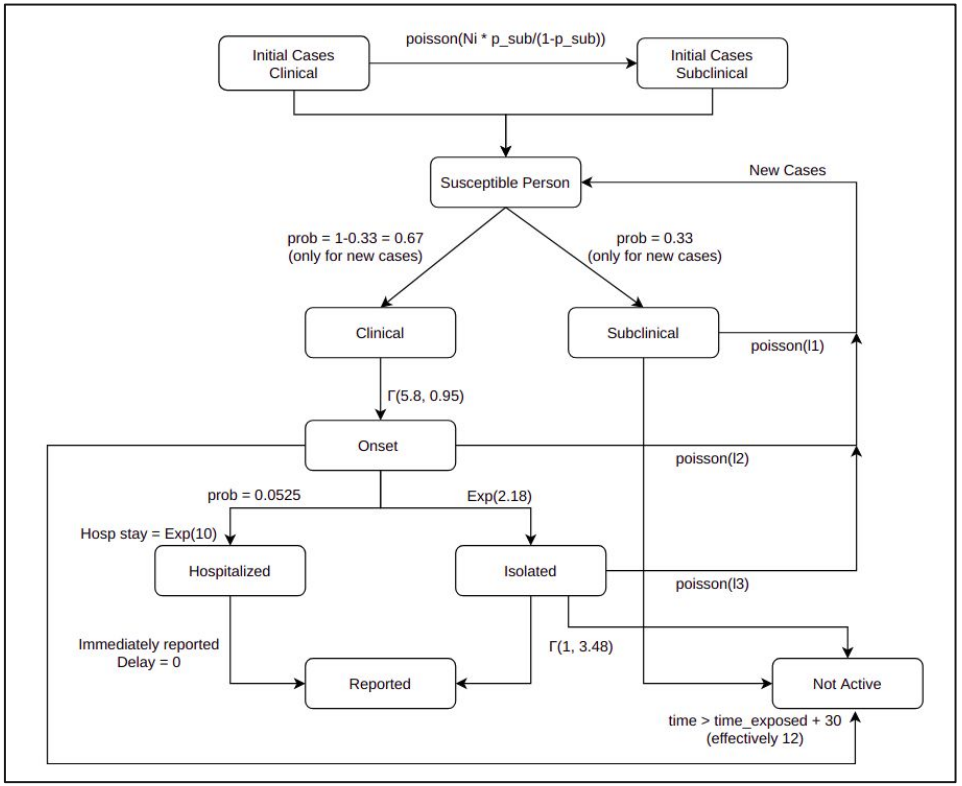
B. Stochastic Models (Micro Modelling)

- A stochastic model is a tool for estimating probability distributions of potential outcomes by allowing for random variation in one or more inputs over time.
- Generate different possible trajectories using multiple iterations to realize the various potential outcomes.
- Each individual is handled separately unlike the deterministic models where they are grouped in certain classes and subclasses.

Stochastic Modelling of a epidemic



Examples of Stochastic Models



Parameter	Value	Source
Distribution of generation times	$Weibull(5.67, 2.83)$	Feretti et al
Distribution of exposure to onset (days)	$T_1 \sim \Gamma(5.8, 0.95)$	Lauer et al
Distribution of onset to isolation (days) (from data)	$T_2 \sim Exp(2.18)$	Davies et al
Distribution from isolation to reporting	$\Gamma(1, 3.48)$	Fitted to data
Relative infectiousness of subclinical cases	$R_{sub}/R_{clin} = 50\%$	Davies et al
Proportion of subclinical infections	$p_{sub} = 33\%$	Davies et al
Relative infectiousness after isolation	$c_{iso} = 65\%$	Davies et al
Reproduction number for clinical infections (no case isolation or control)	$R_{clin} = 3$	Estimated
Basic reproduction number (no case isolation or control)	$R_0 = p_{sub}R_{sub} + (1 - p_{sub})R_{clin}$ =2.5	
Proportion of infections needing hospitalisation	$p_h = 5.25\%$	Verity et al
Length of hospital stay	$T_H \sim Exp(10)$	Zhou et al
Population size	$N_{pop} = 5$ million	

Creating cases in stochastic Model

- The model is simulated using a time step of $\delta t = 1$ day. At each step, infectious individual i produces a Poisson distributed number of secondary infections with mean

$$\lambda_i = R_i \left(1 - \frac{N(t)}{N_{pop}}\right) C(t) F(t - T_{I,i} - T_{iso,i}) \int_t^{t+\delta t} W(\tau - T_{I,i})\, d\tau \quad (1)$$

where $R_i \in \{R_{clin}, R_{sub}\}$ is the individual's mean number of secondary infections, $T_{I,i}$ is time individual i became infected, $T_{iso,i}$ is the delay from becoming infected to being isolated, $C(t)$ is the control effectivity at time t (see below), and $F(t)$ is a function describing the reduction in infectiousness due to isolation:

$$F(s) = \begin{cases} 1 & s < 0 \\ c_{iso} & s > 0 \end{cases} \quad (2)$$

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Why do we need multiple models?

"All models are wrong but some are useful" - George E.P Box

- All the models have certain assumptions, regarding the various stages of the infection, the transmission rate, efficacy of a NPI measure, parameter estimations etc.
- Therefore no single model is an accurate representation of the situation.
- Hence there is a need to compare various models to understand the possible outcomes. Ensemble of models can reduce variance and increase the prediction confidence.

Difference between the models

Parameters	CCPE SEIR	CovidSim 1.0	Stochastic
Symptomatic/Asymptomatic	No	Yes	Yes
Testing rates	Yes	No	No
beta	R0 / (eps / delta + 1 / gamma)	(Ro/(ip * dp + di)) * (1 + amp * cos(2*3.1415*(t-tmax)/365)	R0/2.5
Control Policy	Multiple levels of restrictions	Lockdown and no lockdown	Multiple levels of restrictions
Delay in reporting cases	No	No	Yes
Infectiousness	No	No	Yes

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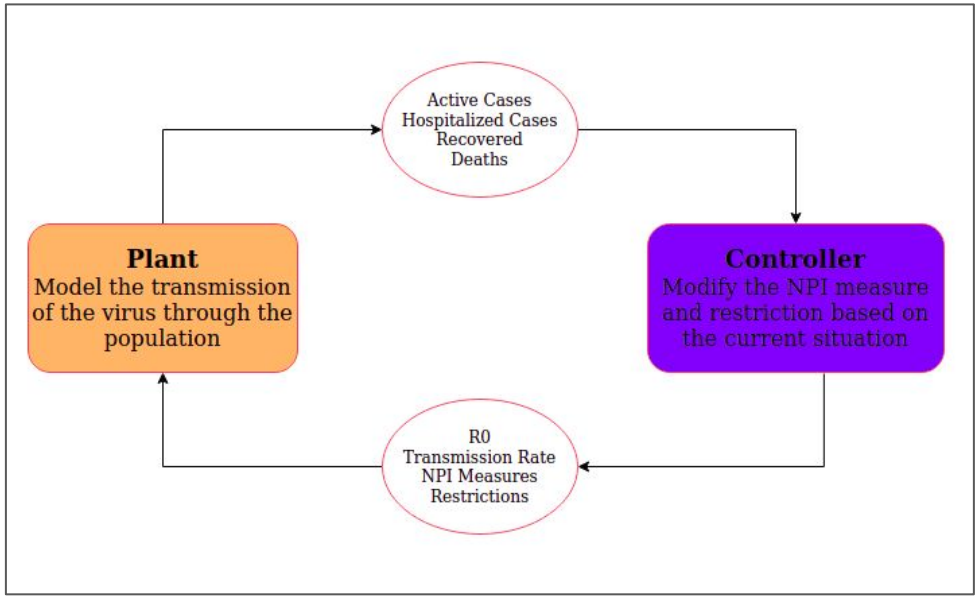
So why can’t we compare various models directly?

- Different models take in various different parameter values:
  - The SEIR Model only need the R0 and the testing rate value, whereas the Stochastic Model needs the R0 and the p_sick parameters.
- Levels of restrictions:
  - The Covidsim Model only has 2 states, lockdown and no lockdown where as the Stochastic/SEIR model have multiple states of restrictions.
  - Transition between these restrictions can either be predetermined or can be dynamic based on evolving case numbers.

Solving the problem



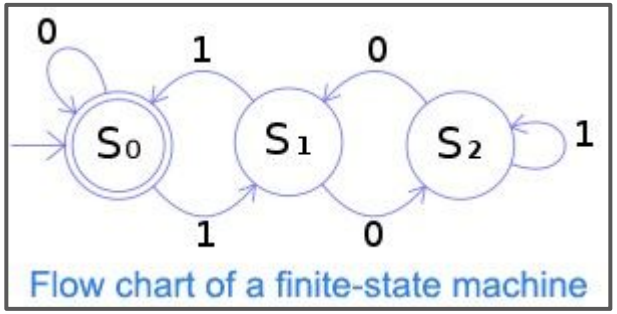
- Separate the disease dynamics (Plant) from the decision making process (Controller).
- Both the plant and controller are individual entities.
- They interact using a standardised interface where the set of required parameters are already available.

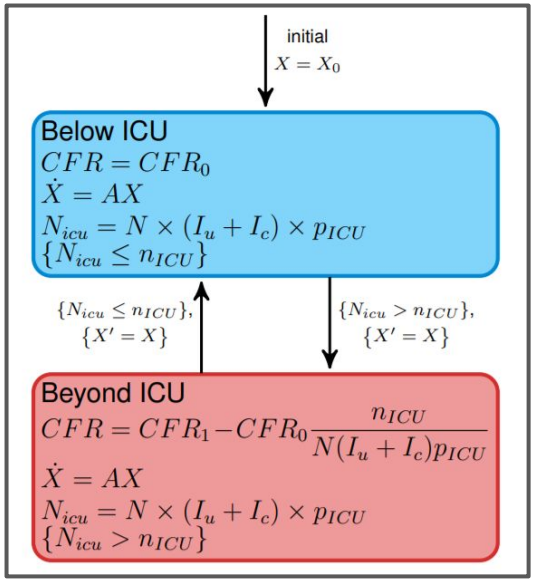
Compositional Cyber Physical Epidemiology

Why is CCPE useful?

- Consider the CovidSim model which only has 2 levels of restrictions: Lockdown and No Lockdown.
- By decoupling the plant and the controller and remodelling them as individually meaningful units, we can use a more complex controller on the CovidSim Plant.
- Initially the plants and controllers were developed together, but by using the CCPE framework they can be easily separated. Once separated we can interface any controller with any plant for generating their predictions.

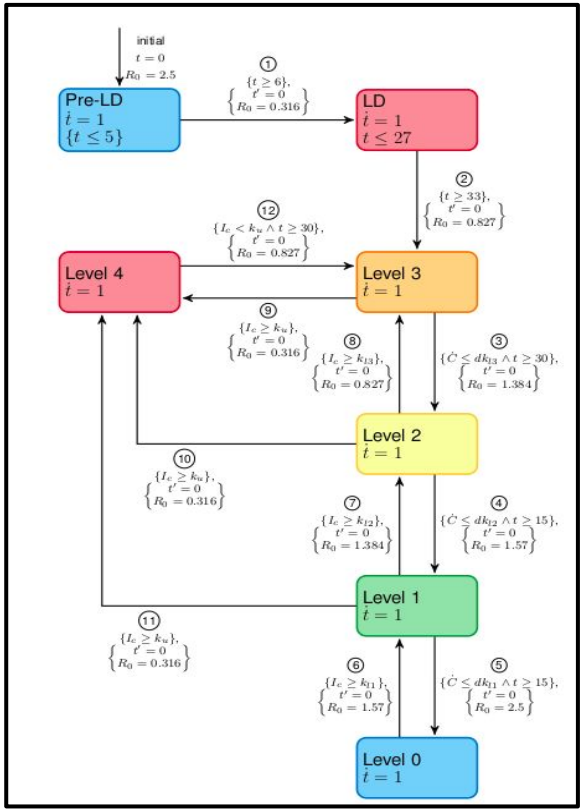
How are the plants and controllers developed?





- Transitions: Conditions + variable assignments
- States: Conditions to transition to other states + Variable updates/assignments (Direct or Differential)

Example of a controller in timed automata



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Models considered

What models were used in this research work?

- Modified SEIR
- CovidSim
- Stochastic Model

Why were these models used?

- Combination of macro and micro modeling techniques
- mixture of simple and complex models
- availability of good literature.

Which countries were analysed?

- All the modeling work is done on the data obtained from the Ministry of Health NZ.
- The cases, vaccination rates, testing rates etc. well documented and are publically available in NZ.
- Also they follow a 5 stage system to impose restrictions for various Covid situations (Level-0 to Level-4) which makes it easier to model the controller.

Levels and its restrictions

Intervention	Weight	Level 4	Level 3	Level 2	Level 1	Level 0
Widespread testing	0.186	✓	✓	✓	✓	✗
Temperature checkpoints	0.093	✓	✓	✓	✓	✗
Contact tracing	0.186	✓	✓	✓	✓	✗
Close contacts of confirmed cases ordered to self-isolate	0.093	✓	✓	✓	✓	✗
Large scale disinfection efforts	0.046	✓	✓	✓	✗	✗
Distribution of PPE to at-risk workers	0.093	✓	✓	✓	✓	✗
Hygiene public awareness efforts	0.186	✓	✓	✓	✓	✗
International travel ban	0.186	✓	✓	△	✗	✗
Domestic travel restrictions	0.093	✓	✓	△	✗	✗
People forced to remain home	0.186	✓	✗	✗	✗	✗
Bans on outdoor gatherings over 500 people	0.093	✓	✓	✓	✓	✗
Bans on indoor gatherings over 100 people	0.093	✓	✓	✗	✗	✗
Bans on recreational sports	0.046	✓	✓	✗	✗	✗
Bars and restaurants close	0.186	✓	△	✗	✗	✗
Schools close	0.186	✓	△	✗	✗	✗
Tertiary education facilities close	0.093	✓	△	✗	✗	✗
Small food retailers close	0.093	✓	✗	✗	✗	✗
Non-essential retail business close	0.093	✓	△	✗	✗	✗
Summation	2.184	2.184	1.673	1.116	0.930	0
Base reproduction number (R_0)		2.5	2.5	2.5	2.5	2.5
Final R value		0.316	0.827	1.384	1.570	2.5

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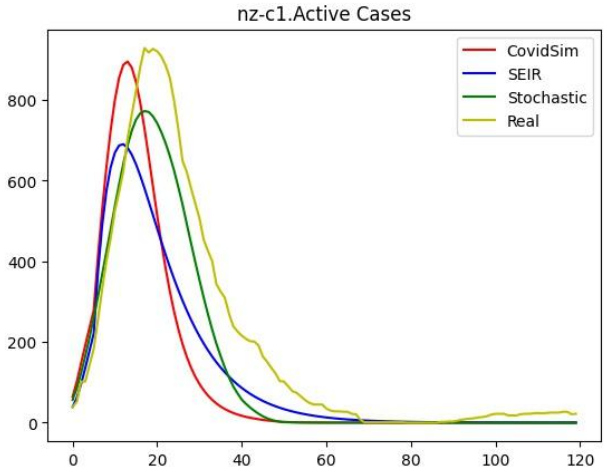
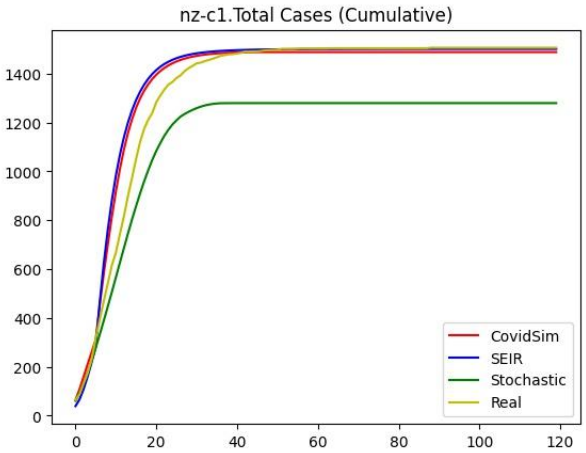
Controller Analysis

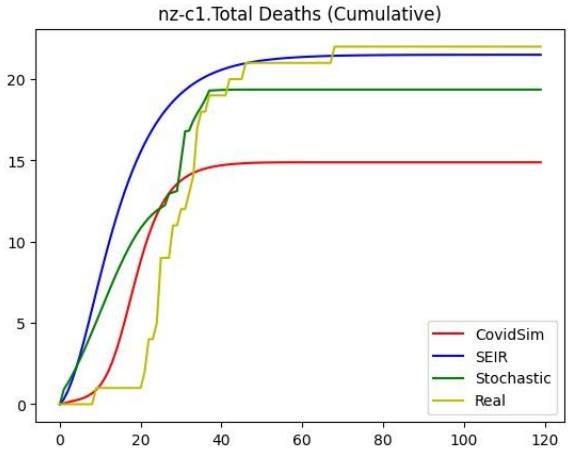
We can design and use multiple controllers with ease due to the decoupled nature of the model. There is no need to modify the plants once they are created.

In this research work we consider multiple different controllers and analyse the possible effects on the transmission of the virus. We also study the impact of specific parameters such as time and restriction levels on the final results.

NZ-C1 Controller



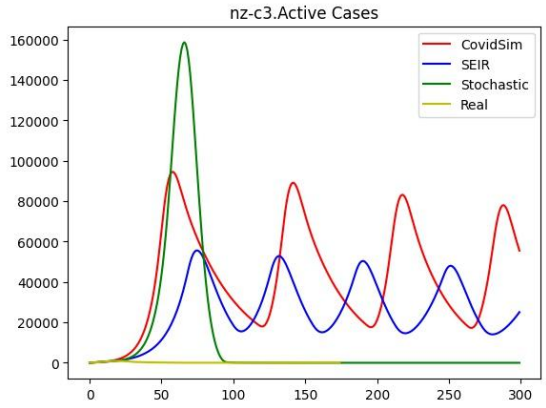


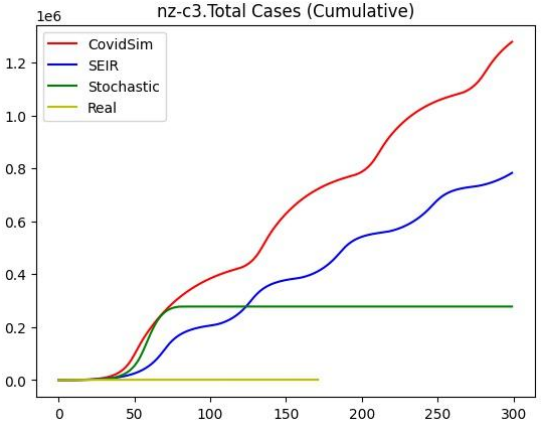


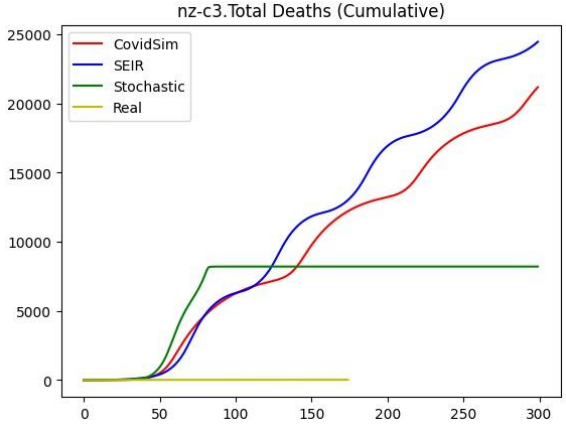
Very Strict control measure: 5 days at Level 0 initially and then permanently at Level 4.

Very high economic impact and people might not be able to sustain a living.

NZ-C3 Controller

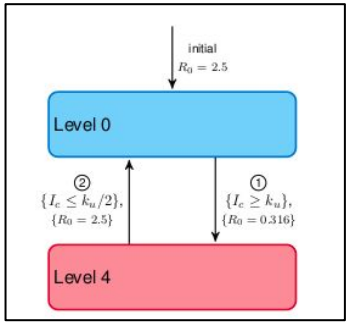






Very Lenient control measure: Switch between Level 0 and Level 4 based on active cases.
Long term effects and the virus will never exit the population.

Note that here the Stochastic Model dies down after 100 days this is due to the definition of active cases and the infectiousness parameter which reduces the capacity to spread the infection as time passes.



NZ-C2 Controller

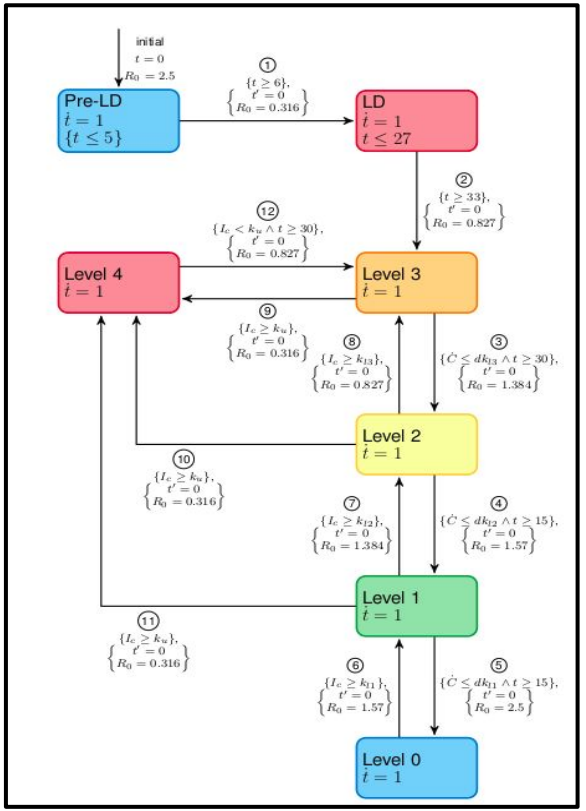
Very carefully designed controller. The transition between various states happens dynamically based on daily evolving situations.

For example:

We can reduce the restrictions from Level 3 to Level 2 if the daily cases fall below 10. Also we need to spend at least 14 days at each level before downgrading the restrictions to avoid continuous switching between levels.

Also we switch from Level 3 to Level 4 if the active cases are more than 100. Upgrading the restriction levels don't have any time constraints.

Each levels are closely examined and such criterias are created.



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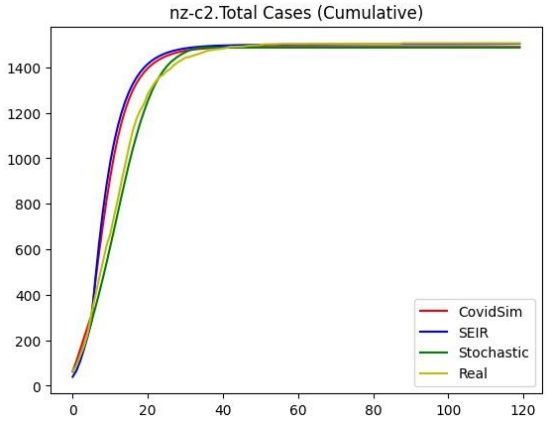
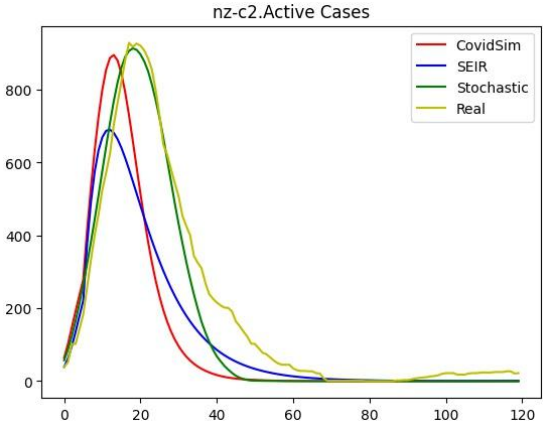
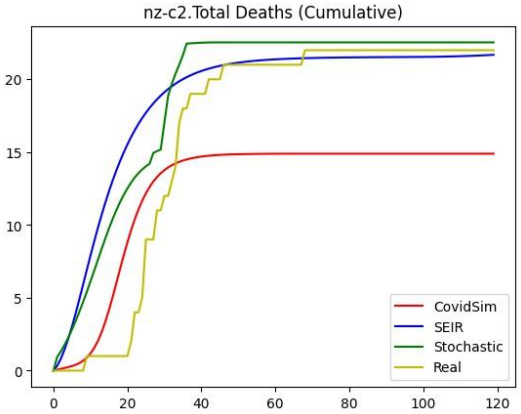
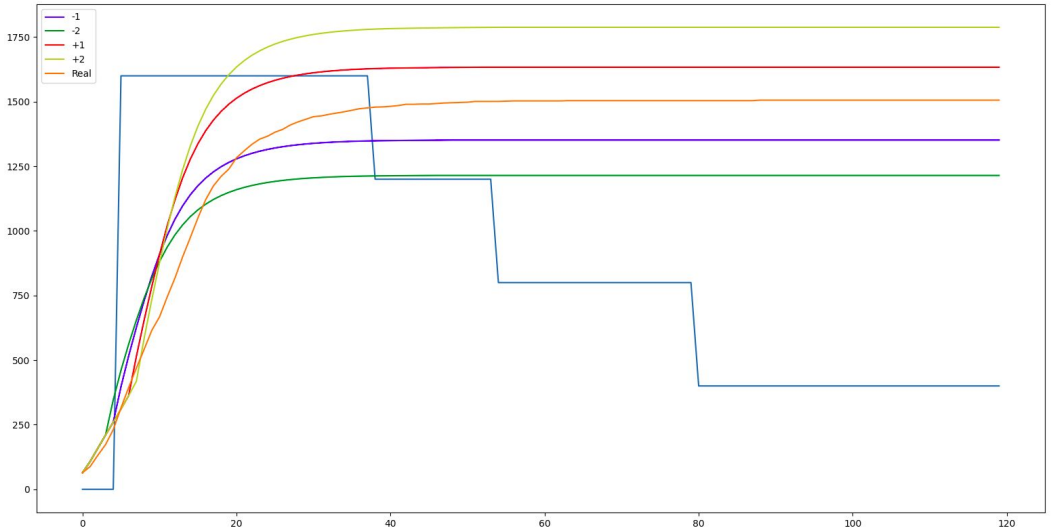




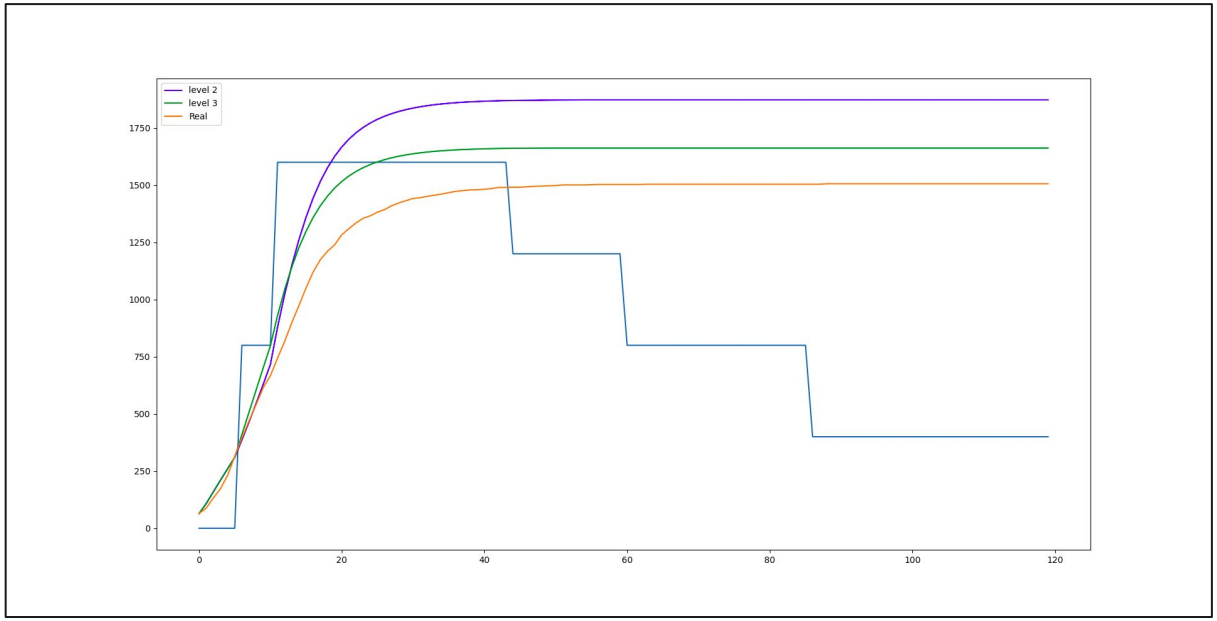


From our observations, the stochastic model is more powerful than the deterministic macro models but also requires more computational capacity. It's ability to generate various possible scenarios will be useful to generate a upper bound and lower bound for various metrics.

Starting Time of Restrictions



Intensity of early Restrictions

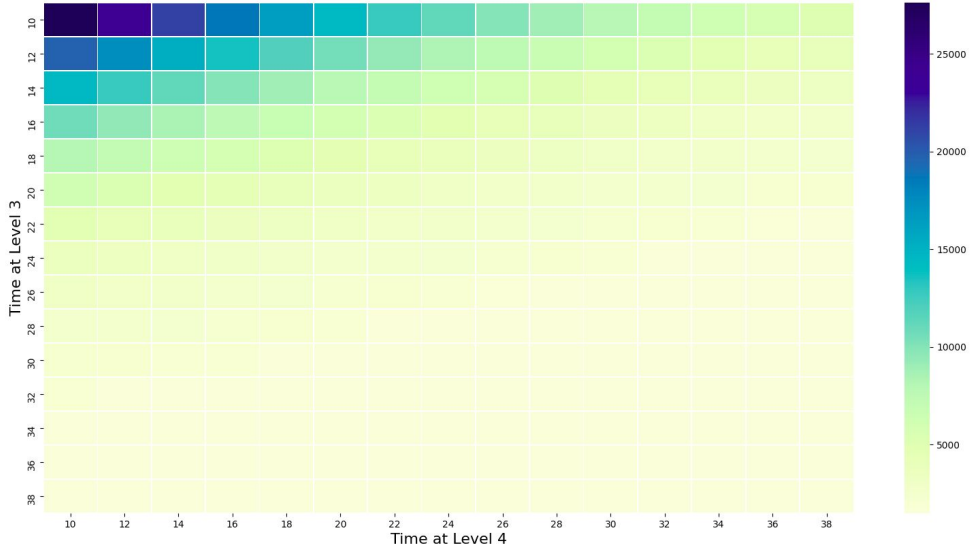


Level 2: 1873
5(0) -> 5(2) -> 33(4)

Level 3: 1662
5(0) -> 5(3) -> 33(4)

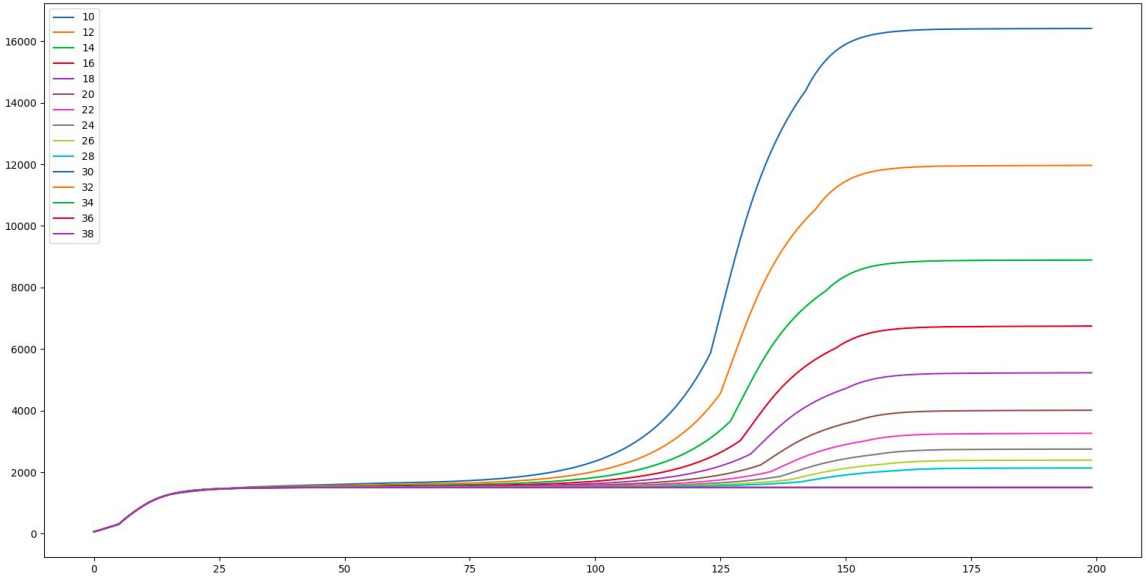
Level 4: 1506
5(0) -> 33(4)

How long is required?



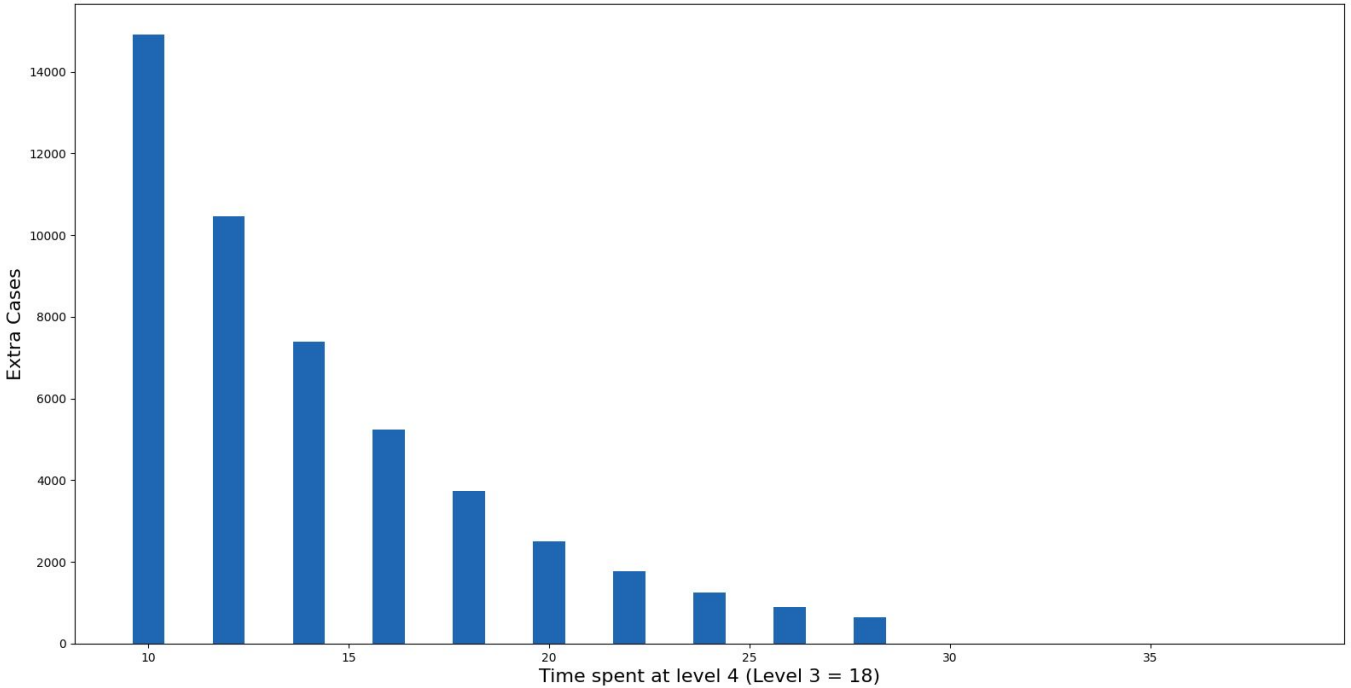
Initially 5 days at Level 0
Followed by **X days at Level 4**
And then **Y days at Level 3**

Time at Level 4

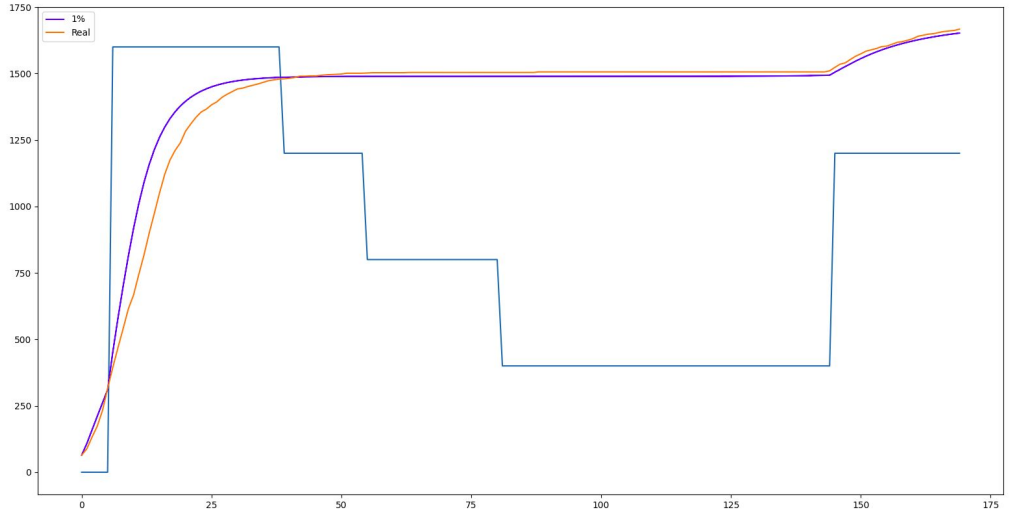


Level 0: 5 days
Level 4: 10-38 days
Level 3: 18 days
Level 2: 26

Impact of longer Restrictions



Second Wave Modeling by manual initialization



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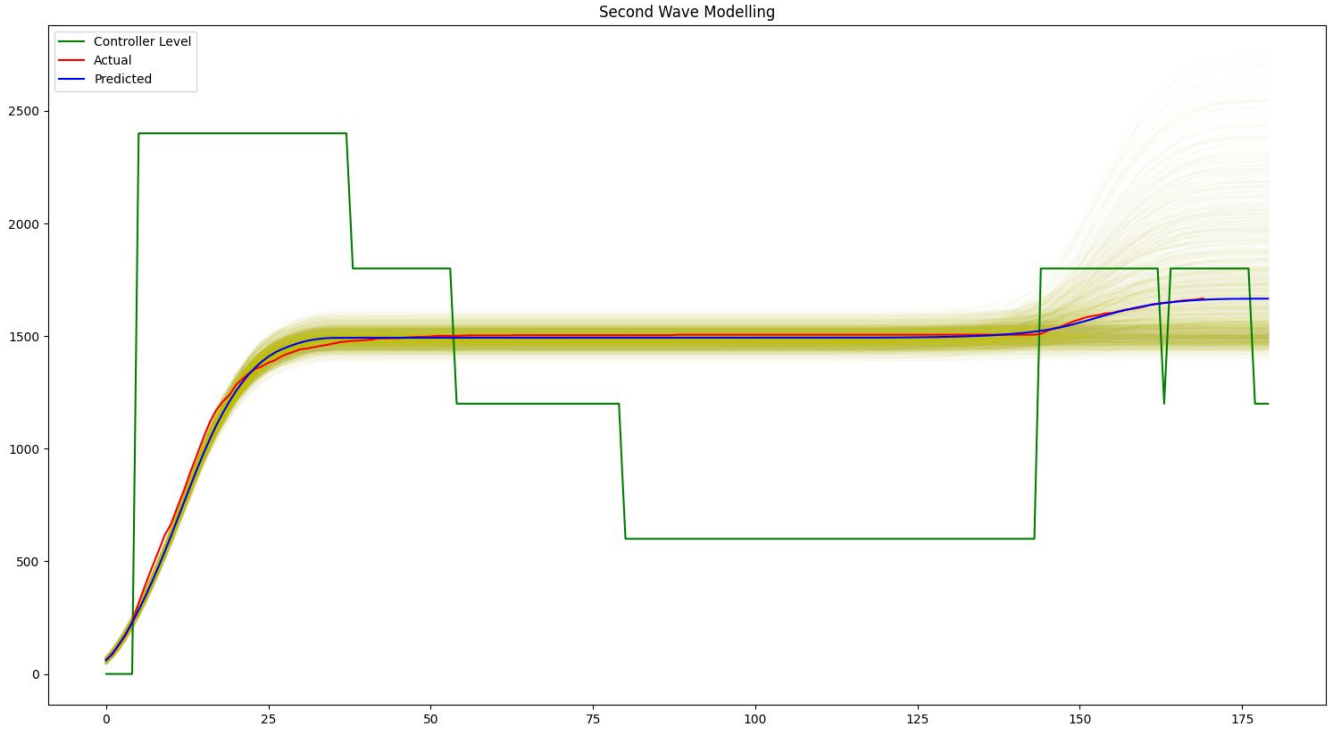
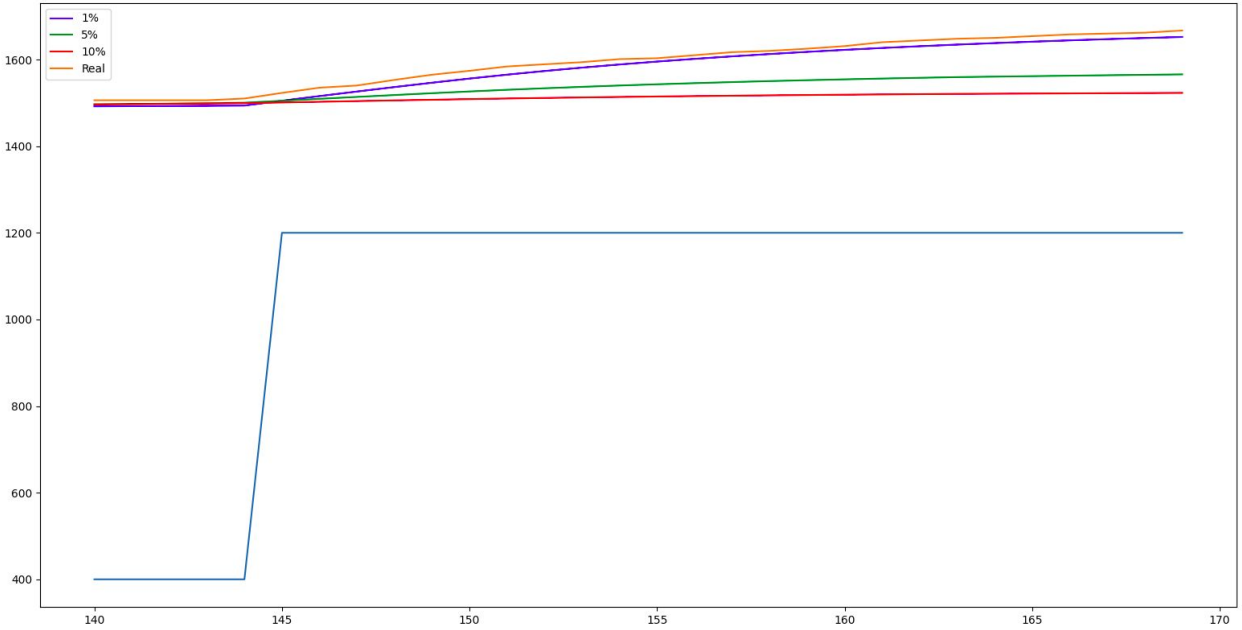


Effect of Testing Rates on Second Wave



Real: 1669
1%: 1654
5%: 1566
10%: 1523

Overview:

1. Current Covid-19 situation around the world
2. Types of epidemiological Modelling
3. Need for comparing models
4. Difficulties in Comparing models
5. CCPE Modelling Techniques
    a. Models worked with
    b. Controller Analysis
    c. Simple economic modelling

Economic Impact of Restriction

Developed using a simple economic indicator by using the metrics provided by the Reserve Bank of NZ. (Quarterly projections)

Alert level	GDP reduction (%)
1	3.8
2	8.8
3	19
4	37

Estimating the economic metrics

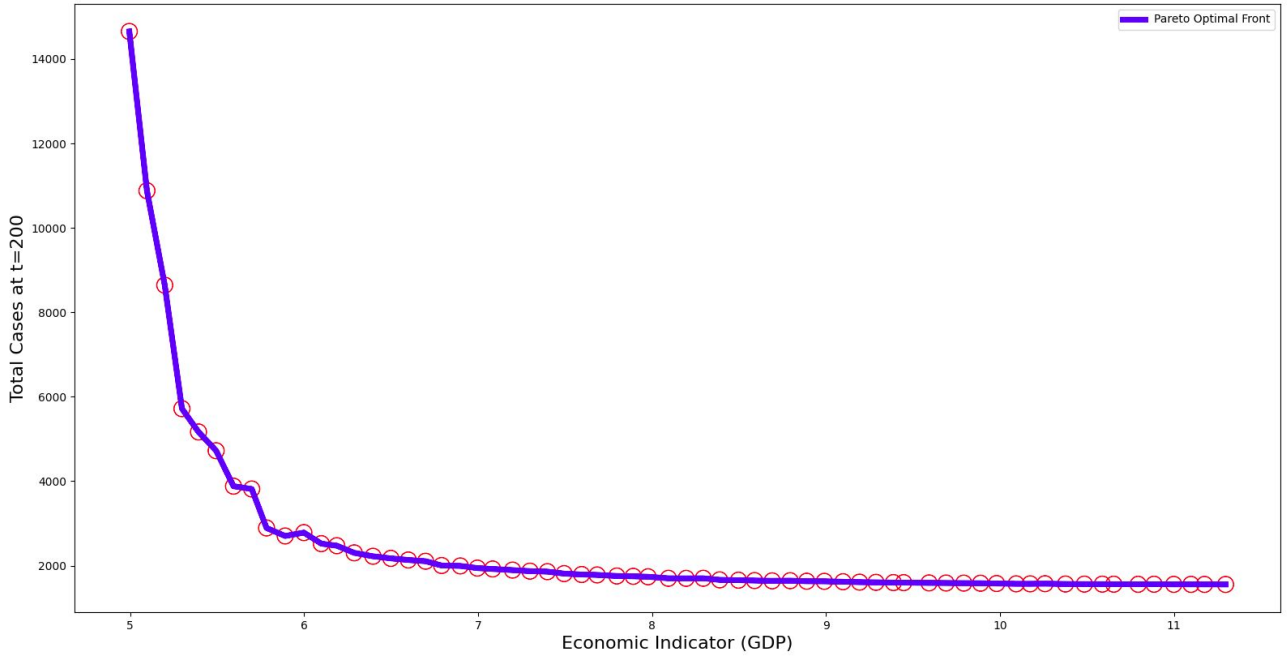
For convenience we refer to it as GDP. But this is not an accurate calculation but nevertheless can be used to help us determine the effects.

Equation 1: GDP = $\sum$ (Days at level i) * (GDP loss at level i)

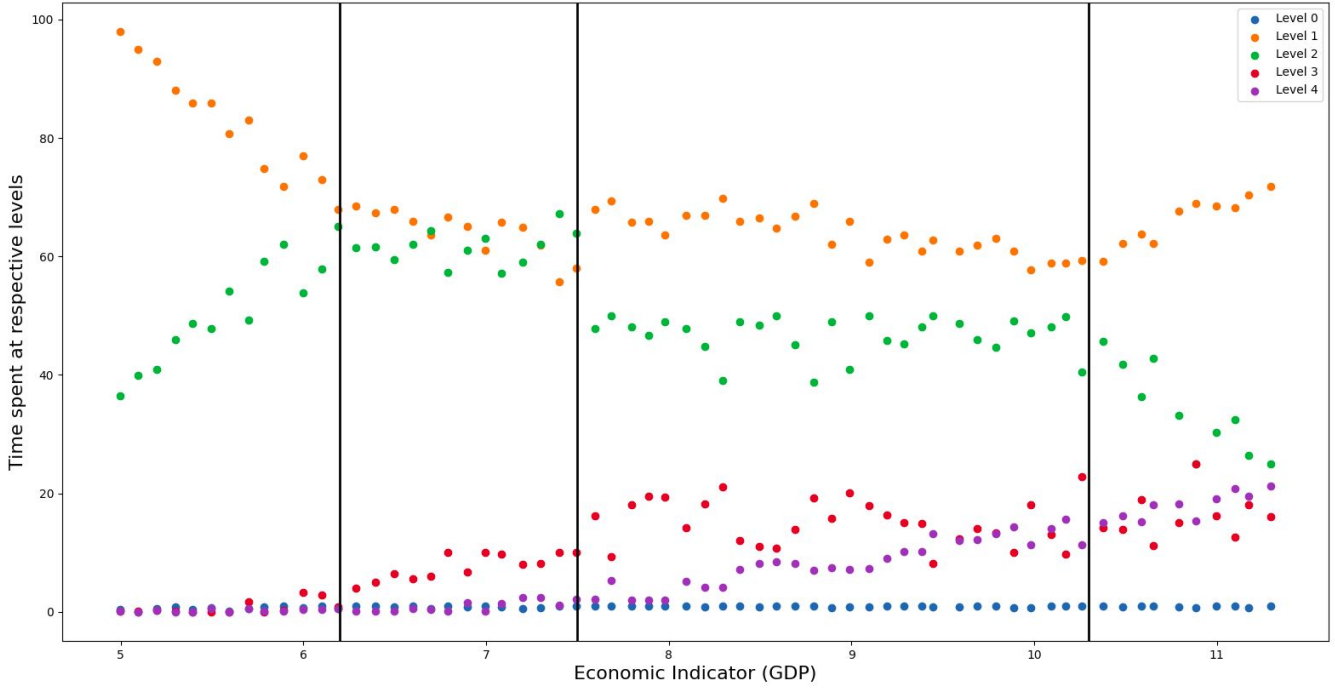
Equation 2: Total Cases (Directly obtained from the model)

We generate a pareto optimal front using the particle swarm optimizer by minimizing both the GDP and the total cases.

Pareto Optimal Front



Optimized days at each Level




Thank You
for
Listening...
any
questions?