Executable Storytelling with Rule-Based Models

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The **C**entre for the **M**athematical **M**odelling of **I**nfectious **D**iseases (**CMMID**)
London School of Hygiene and Tropical Medicine

Language

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With a good language for writing down computational models, models in that language are like stories, describing and explaining what happens next. . .

Rule-Based Models

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$$\mathcal{L} \xrightarrow{k} \mathcal{R}$$

- $\mathcal{L}$ and $\mathcal{R}$ are pattern graphs, k is a rate
- κ-calculus (Danos and Laneve 2004 – similar spirit to π-calculus)
- In the κ-calculus graphs are site- or port-graphs
- *Stochastic Graph Rewriting System* (Behr et al. 2016 – algebraic approach)
- Graph rewriting as structured cospans (Cicala 2019)
- For a certain class of rule, Stochastic GRS $\cong$ Stochastic Petri

Rules and Mixtures

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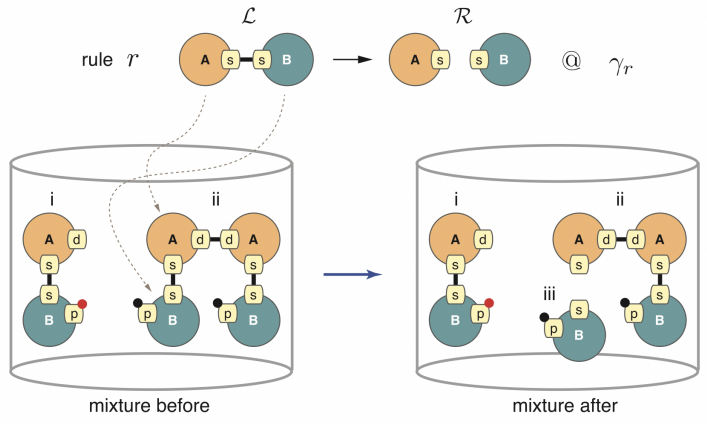
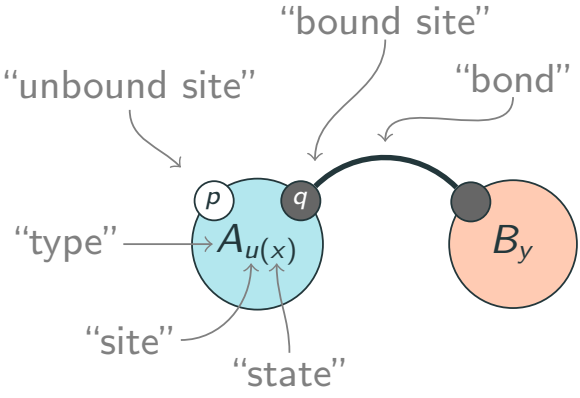



```
A(s[1]), B(s[1]) -> A(s[.]), B(s[.]) @ gamma_r
```


Pierre Boutillier et al. "The Kappa platform for rule-based modeling". In: *Bioinformatics* 34.13 (July 2018), pp. i583–i592.
ISSN: 1367-4803. DOI: 10.1093/bioinformatics/bty272

Anatomy of a Pattern Graph




```
A(p[.], q[1], u{x}), B(r[1], v{y})
```

Rules > Reactions

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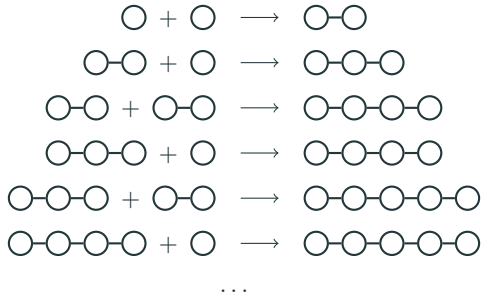
```
A(u[.]), A(d[.]) -> A(u[1]), A(d[1])
```



Estimated PCR response

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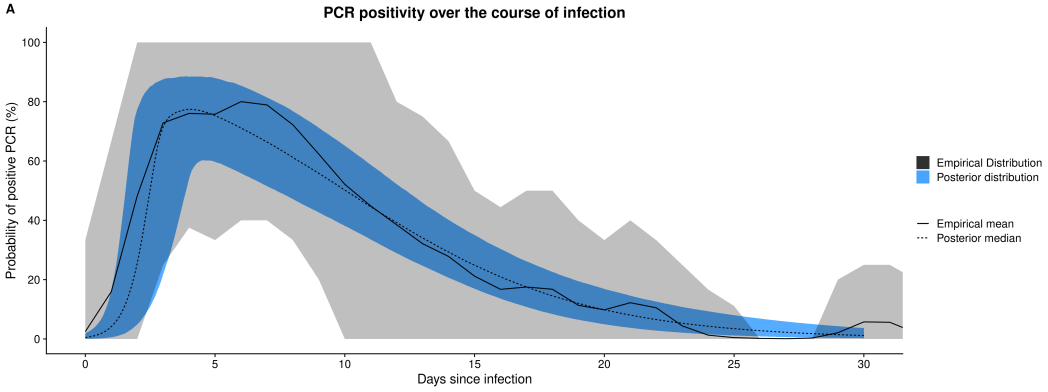
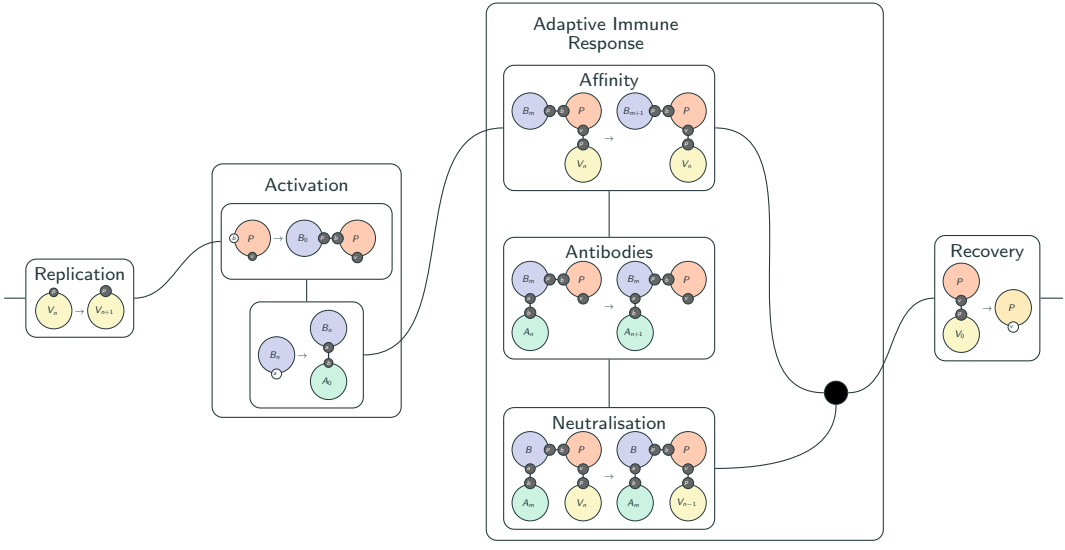


Joel Hellewell et al. "Estimating the effectiveness of routine asymptomatic PCR testing at different frequencies for the detection of SARS-CoV-2 infections". In: *BMC medicine* 19.1 (2021), pp. 1–10. DOI: 10.1186/s12916-021-01982-x

Assumptions...

- adaptive immune response is the relevant mechanism
- innate immune response can be neglected
- probability of positive PCR $\propto$ cycle threshold
- log(size of virus population) $\propto$ cycle threshold
- transmission rate $\propto$ log(size of virus population)
- no changes in behaviour

A “Simple” Immune Model

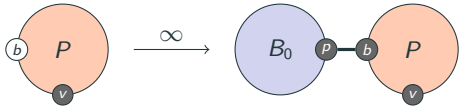


Virus Replication

$n > 0$

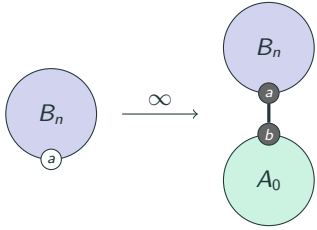
- V represents a virus population in an individual
- The counter n represents log(viral load)
- Better would be to have a carrying capacity
- In principle unbounded
- In practice truncated

Adaptive Response Activation (I)



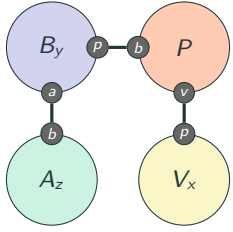
- B_n represents a population of B-cells with affinity n
- Really, adaptive response needs innate response first
- That takes non-zero time (days) not represented here

Adaptive Response Activation (II)

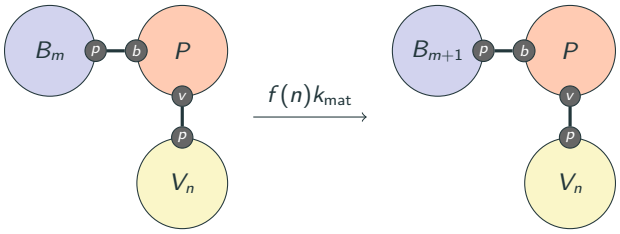


- A_n represents log(number of antibodies)

Activation Complete

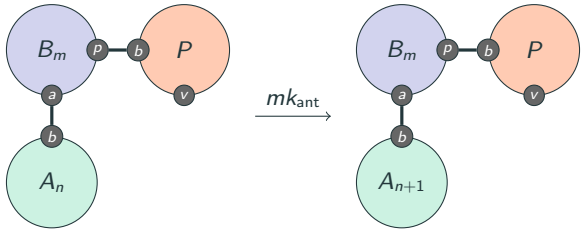


Affinity Maturation



- Simple idea, $f(n) = n$.

Antibody Production



Virus Neutralisation

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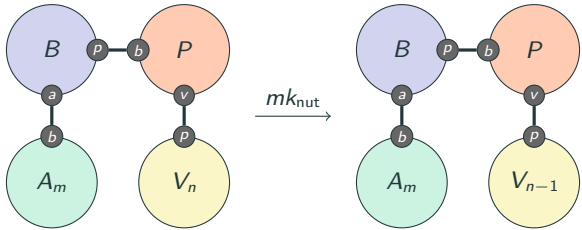

Recovery

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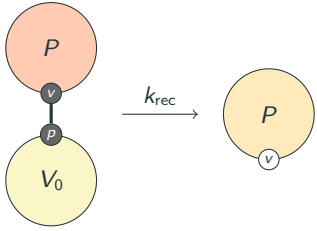
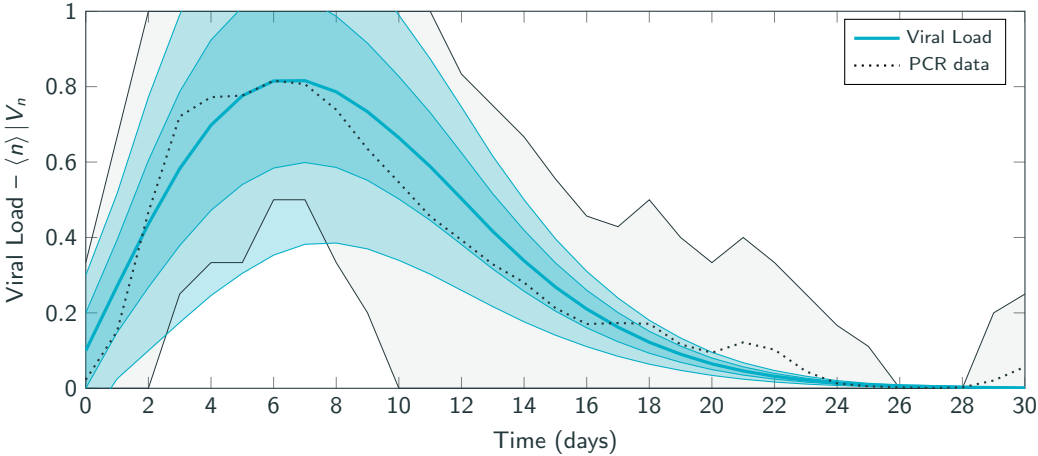
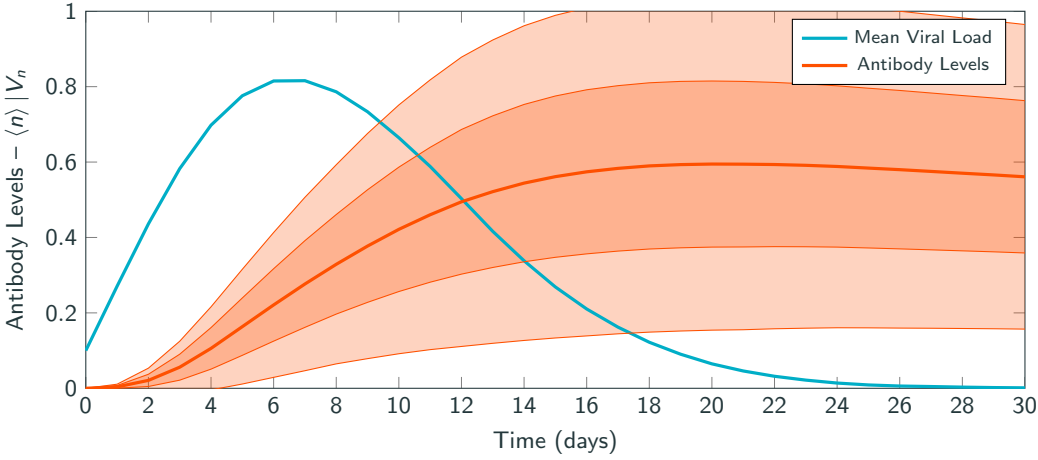


Simulated Viral Load



Simulated Antibody Levels



Viral Load Distribution Time Series – $\Pr(n)|V_n$

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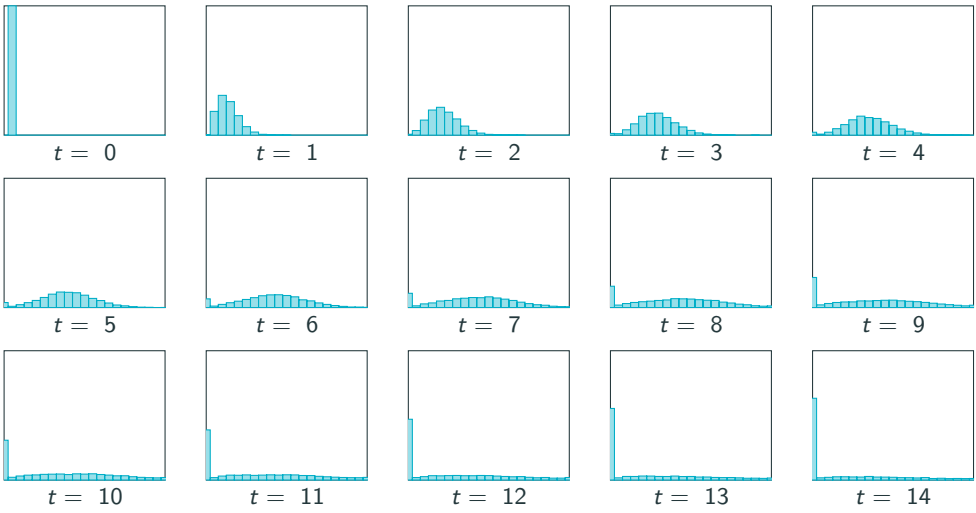
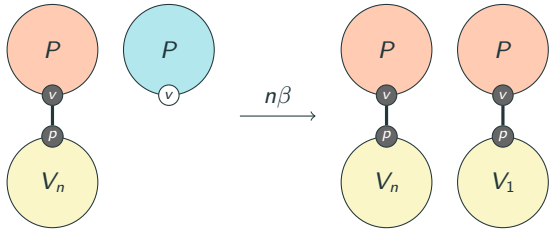
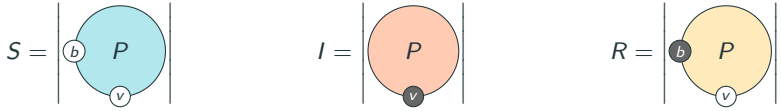


Transmission



Observables:



Epidemic Curve

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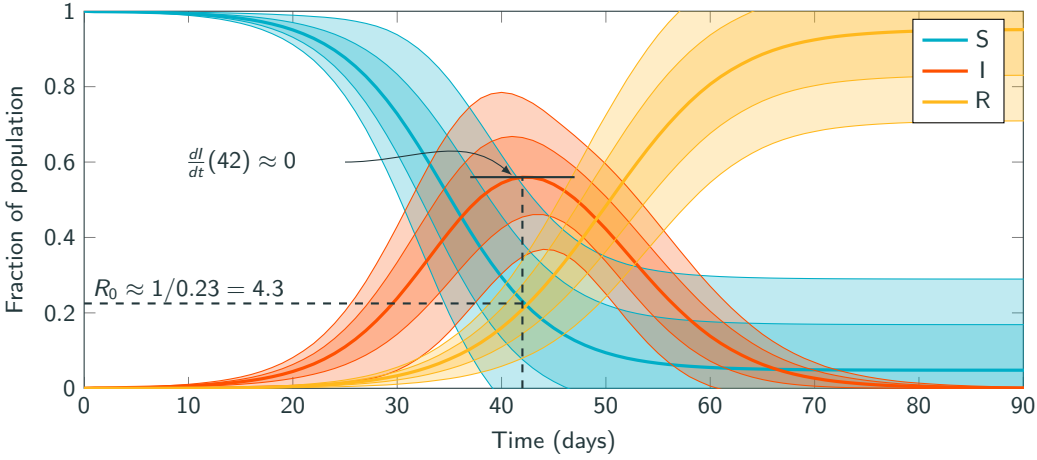

Epidemic Curve

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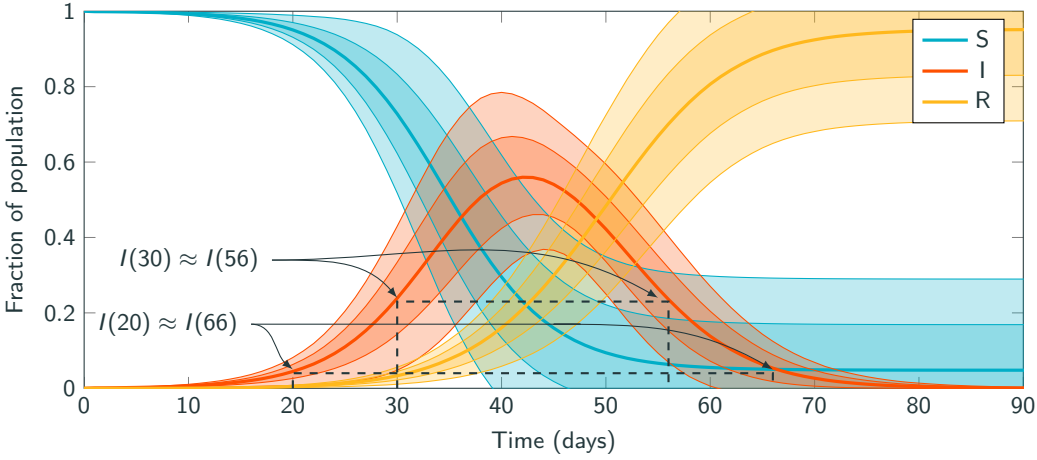
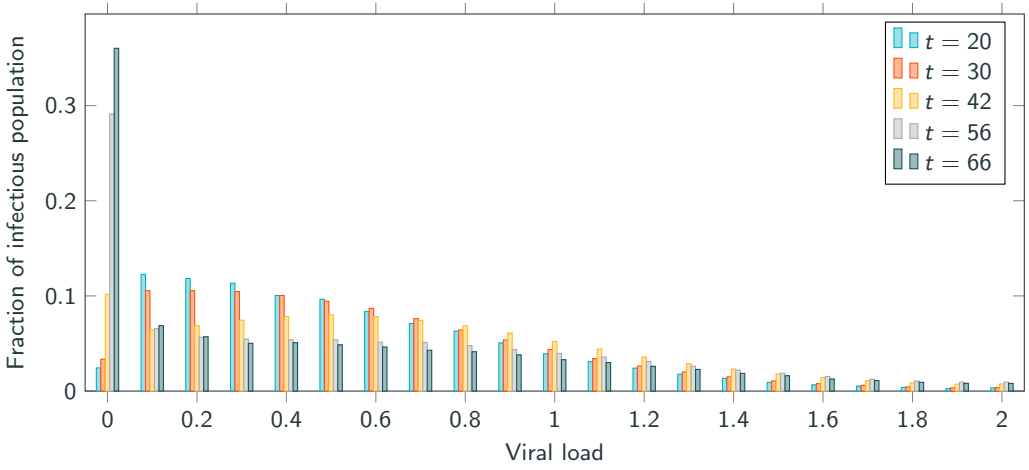


Dynamic Viral Load



Sequels

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- Innate immune response
- Affinity maturation
- Valence > 1 sites
- Hierarchical rules
- Other open systems
- Crazy idea

References

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Thank you – Questions?

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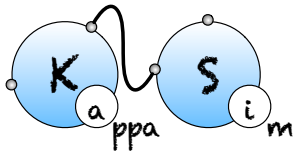

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