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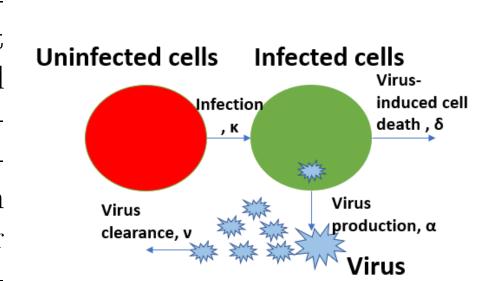
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Background

Understanding the mechanisms of within-host kinetics of the humoral (and cellular) immune response to a viral, parasite, or bacterial infection is crucial to foresee better surveillance and intervention strategies in the con- Figure 1: Flow describing the text of infectious diseases.



dynamics of uninfected cells, infected cells, and infectious virus

Objectives

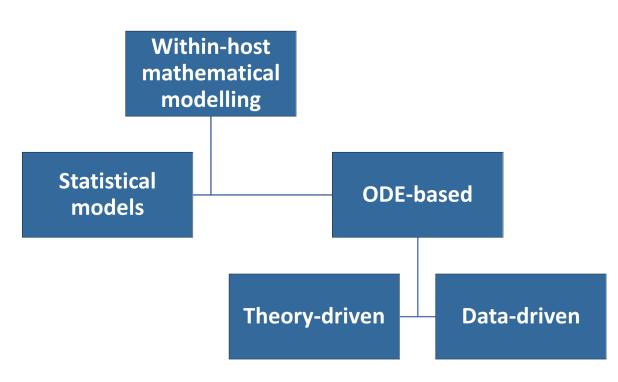
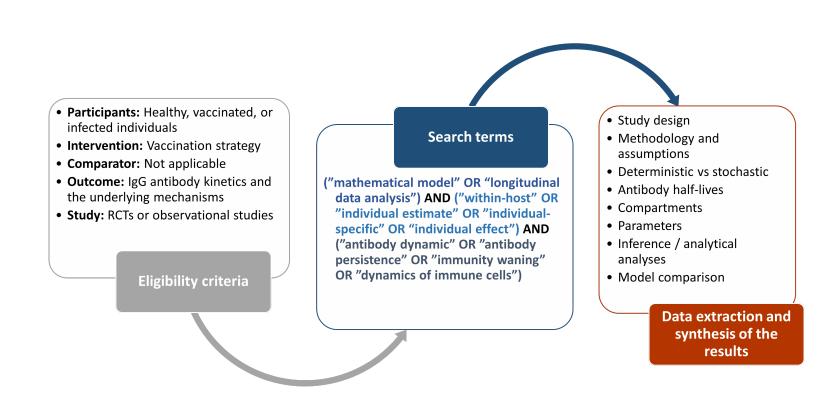


Fig. 2: Classification of the within-host mathematical models

- To find within-host mechanistic modeling to study humoral immunity processes after vaccination or natural infection. This is crucial to unravel the specific components of the immune system and their dynamics. In particular, we focus on data-driven and theory-driven mechanistic approaches.
- Describe the within-host models and the underlying dynamics of immune cells when encountering a pathogen, and how these processes can lead to an individual-specific response.

Methodology



References

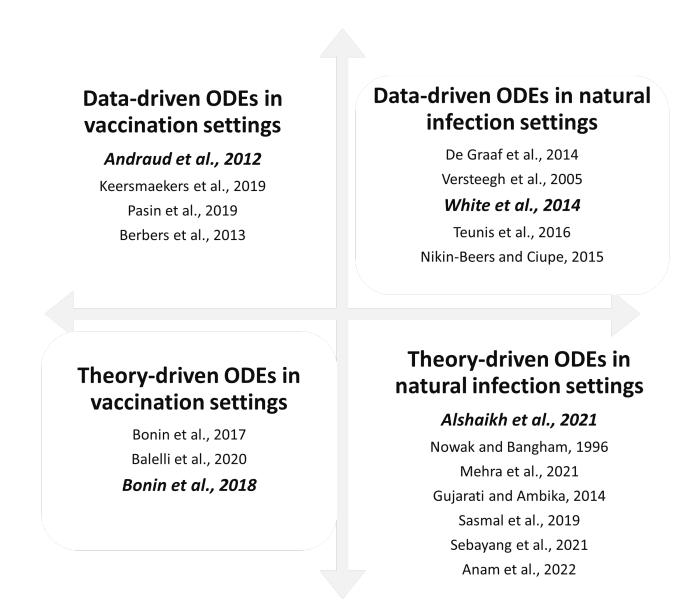
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Results

To date, only 20 publications out of 77 have relied on mechanistic models to study the dynamics of humoral immunity.

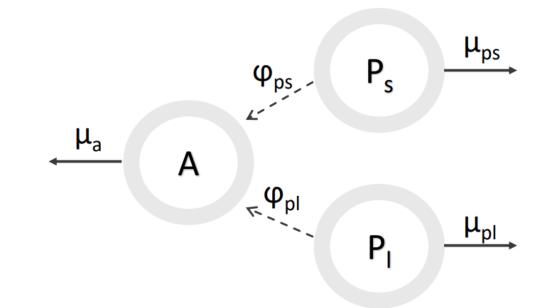


A. Data-driven in vaccination

Andraud et al., [1] assumed no renewal of plasma cells. P_s decline first, and P_l decline last since the latter reside in the bone marrow. Moreover, different models were studied:

• Full model

- Asymptotic model: $\mu_l = 0$
- Plasma cell driven **kinetic:** $\frac{\mu_s,\mu_l}{\mu_a} << 1$



B. Theory-driven in vaccination

Bonin et al. [4] accounted for a **pre-existing innate immune response**, defined as the homeostasis term. On top of that, there were different subpopulations of individuals, e.g., those having autoimmune diseases, or receiving immunomodulatory therapy.

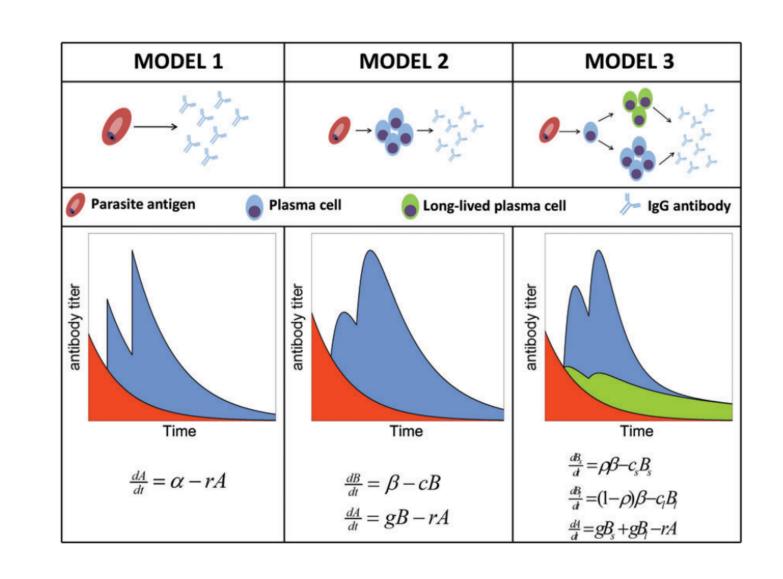
> Virus inoculation Antigen presenting cells Naive and effector CD8+ T cells Populations Short- and long-living cells Memory B cells Antibodies

Simulation scenarios:

- a) First Yellow Fever vaccine
- b) Booster dose ten years after the first dose
- c) Different levels of CD8+ T cells
 - d) Distinct doses of Yellow Fever vaccine

C. Data-driven in natural infection

White et al., [2] studied the impact of maternal immunity on Malaria infections in children.



D. Theory-driven in natural infection

Alshaikh et al., [5] modeled the co-infection between HIV/HTLV accounting for pre-existing HIV antibodies.

Susceptible CD4+ T cells HIV-infected cells Populations {HTLV-infected cells Free-HIV particles from infected cells HIV-specific antibodies Both HIV and HTLV have the same target of susceptible CD4+ T cells

Findings

1. COMPARTMENTS

• Data-driven approaches: Tend to be more simplistic and have more similarities between them.

• Theory-driven approaches: Typically study more complicated dynamics into various interconnections between these.

2. PARAMETERS

- Data-driven approaches: Linear, nonlinear mixed approaches. Exponential decay, bi-exponential, power functions. Smoothing functions and binary functions represent normally the time of vaccination. On the other hand, natural infection studies assumed a boost of antibody titer after exposure.
- Theory-driven approaches: Simulation approaches to generate the parameters (e.g., Poisson or Binomial distributions).

3. INFERENCE/ANALYTICAL ANALYSES

- Data-driven approaches: Use of Maximum likelihood estimation (MLE) Bayesian hierarchical approaches with Monte Carlo Markov Chain (MCMC).
- Theory-driven approaches: Model's equilibria and stability.

4. COVARIATES

Study groups are widely studied. However, there is a lack of information on geographical **background**, surveillance systems, and age [3].

5. MODEL COMPARISON

- Data-driven approaches: Difficulties in Bayesian approaches due to the number of parameters and complexity issues. WAIC (Watanabe-Akaike information criteria) for future modelling work AIC (Akaike information criteria) within MLE [6].
- Theory-driven approaches: Comparison to simulated data.

Conclusion

• More research is needed on the **methods of in**ference in data-driven mechanistic models, such as semi-parametric to full parametric tools, as well as incorporating more data and measurements to feed the model.

• We emphasize that some of the biological mechanisms must be distinguished in vaccination or natural infection settings.

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