Hierarchical Bayesian Modeling of Antibody Kinetics: Extensions and Refinements

Kwan Ho Lee

UC Davis

2025-05-22

Overview

- Incorporates feedback from Dr. Morrison, Dr. Aiemjoy, and lab discussion
- Focus exclusively on (Teunis and Eijkeren 2016) two-phase within-host model
- Clarifies full hierarchical Bayesian modeling structure
- Explicitly distinguishes between priors, hyperpriors, transformations
- Reorders: **Start from observation model → build upward**

Big Picture: What Are We Modeling?

We are modeling **how antibody levels change over time** in response to infection, using multiple individuals and multiple biomarkers (antigen-isotype combinations, (j = 1, 2, ..., 10)).

Goals:

- Understand the **average pattern** for each biomarker
- Allow for **individual-level variation**
- **Share information** across individuals to improve inference

This motivates using a **hierarchical Bayesian model**.

Step 1: Observation Model (Data Level)

Observed (log-transformed) antibody levels:

$$\log(y_{\text{obs},ij}) \sim \mathcal{N}(\log(y_{\text{pred},ij}(\theta_{ij})), \tau_j^{-1}) \tag{1}$$

The expression above corresponds to line 54 of `model.jags`:

```
    logy[subj,obs,cur_antigen_iso] ~ dnorm(mu.logy[subj,obs,c
```

Measurement precision prior:

$$\tau_j \sim \text{Gamma}(a_j, b_j) \tag{2}$$

The expression above corresponds to line 75 of `model.jags`:

```
  prec.logy[cur_antigen_iso] ~ dgamma(prec.logy.hyp[cur_antige
```

Parameter Summary

Table 1: Parameter summary for antibody kinetics model.

Symbol	Description
μ_y	Antibody production rate (growth phase)
μ_b	Pathogen replication rate
γ	Clearance rate (by antibodies)
α	Antibody decay rate
ρ	Shape of antibody decay (power-law)
t_1	Time of peak response
y_1	Peak antibody concentration

Note: Only the first 6 are typically estimated. y_1 is derived from the ODE solution at t_1.

Step 2: Within-Host ODE System (Teunis and Eijkeren 2016)

$$\frac{dy}{dt} = \begin{cases} \mu_y y(t), & t \leq t_1 \\ -\alpha y(t)^\rho, & t > t_1 \end{cases} \quad \text{and} \quad \frac{db}{dt} = \mu_b b(t) - \gamma y(t) \tag{3}$$

- Initial conditions: $y(0) = y_0$, $b(0) = b_0$
- Transition at t_1: when $b(t_1) = 0$

Step 3: Closed-Form Solutions

Antibody concentration:

- For $t \leq t_1$:

$$y(t) = y_0 e^{\mu_y t} \tag{4}$$

- For $t\, t_1$:

$$y(t) = y_1 \left(1 + (\rho - 1)\alpha y_1^{\rho-1}(t - t_1)\right)^{-\frac{1}{\rho-1}} \tag{5}$$

The expression above corresponds to lines 18-50 of `model.jags`:

```
    mu.logy[subj, obs, cur_antigen_iso] <- ifelse(

        # `step(x)` returns 1 if x >= 0;
        # here we are determining which phase of infection we
        # active or recovery;
        # `smpl.t` is the time when the blood sample was colle
        # relative to estimated start of infection;
        # so we are determining whether the current observatio
        # the time when the active infection ended.
```

Step 4: Derived Quantities

- **Clearance Time** t_1:

$$t_1 = \frac{1}{\mu_y - \mu_b} \log\left(1 + \frac{(\mu_y - \mu_b)b_0}{\gamma y_0}\right) \tag{7}$$

The expression above is indirectly represented by lines 8-12 of `model.jags`:

```
    beta[subj, cur_antigen_iso] <-
      log(
        y1[subj,cur_antigen_iso] / y0[subj,cur_antigen_iso]
        ) /
      t1[subj,cur_antigen_iso]
```

- **Peak Antibody Level** y_1:

$$y_1 = y_0 e^{\mu_y t_1} \tag{8}$$

Full Parameter Model (7 Parameters)

Subject-level parameters for each subject$i$ and biomarker j:

$$\theta_{ij} \sim \mathcal{N}(\mu_j, \Sigma_j), \quad \theta_{ij} = \begin{bmatrix} y_{0,ij} \\ b_{0,ij} \\ \mu_{b,ij} \\ \mu_{y,ij} \\ \gamma_{ij} \\ \alpha_{ij} \\ \rho_{ij} \end{bmatrix} \tag{9}$$

- These 7 parameters represent the **full biological model** (antibody + pathogen dynamics)

From Full 7 Parameters to 5 Latent Parameters

- Although the model estimates 7 parameters, for modeling antibody kinetics $y(t)$, we focus on **5-parameter subset**:

$$y_0, \quad t_1(\text{derived}), \quad y_1(\text{derived}), \quad \alpha, \quad \rho$$

- These 5 parameters are **log-transformed** into the latent parameters θ_ij used for modeling.

Core Parameters Used for Curve Drawing

Although the full model estimates **7 parameters**, only **5 key parameters** required to draw antibody curves:

- y_0: initial antibody level
- t_1: time of peak antibody response (derived)
- y_1: peak antibody level (derived)
- α: decay rate
- ρ: shape of decay

Note: t_1 and y_1 are **derived from the full model** - These 5 are sufficient for prediction and plotting

Step 5: Subject-Level Parameters (Latent Version)

Each subject i and biomarker j has latent parameters:

$$\theta_{ij} = \begin{bmatrix} \log(y_{0,ij}) \\ \log(y_{1,ij} - y_{0,ij}) \\ \log(t_{1,ij}) \\ \log(\alpha_{ij}) \\ \log(\rho_{ij} - 1) \end{bmatrix} \tag{10}$$

Distribution:

$$\theta_{ij} \sim \mathcal{N}(\mu_j, \Sigma_j)$$

The expression above reflects the prior distribution specified on line 66 of `model.jags`:

```
par[subj, cur_antigen_iso, 1:n_params] ~ dmnorm(mu.par[cur_
```

Step 6: Parameter Transformations (log scale priors)

JAGS implements latent parameters (par) as:

Table 2: Log-Scale Transformations of Antibody Model Parameters in JAGS.

Model Parameter	Transformation in JAGS
y_0	$\exp(\text{par}_1)$
y_1	$y_0 + \exp(\text{par}_2)$
t_1	$\exp(\text{par}_3)$
α	$\exp(\text{par}_4)$
ρ	$\exp(\text{par}_5) + 1$

The table above corresponds to lines 58-62 of `model.jags`:

```
y0[subj,cur_antigen_iso]    <- exp(par[subj,cur_antigen_iso
y1[subj,cur_antigen_iso]    <- y0[subj,cur_antigen_iso] + e
t1[subj,cur_antigen_iso]    <- exp(par[subj,cur_antigen_iso
alpha[subj,cur_antigen_iso] <- exp(par[subj,cur_antigen_iso
```

Step 7: Population-Level Parameters (Priors)

The biomarker-specific mean vector μ_j has a **hyperprior** :

$$\mu_j \sim \mathcal{N}(\mu_{\text{hyp},j}, \Omega_{\text{hyp},j}) \tag{11}$$

Where:

- $\mu_{\text{hyp},j}$: **prior mean** for the population-level parameters
- $\Omega_{\text{hyp},j}$: **prior covariance** encoding uncertainty about μ_j (e.g., $100 \cdot I_7$ for weakly informative prior)

The expression above corresponds to line 73 of `model.jags`:

```
mu.par[cur_antigen_iso, 1:n_params] ~ dmnorm(mu.hyp[cur_anti
```

Clarification:

- $\mu_{\text{hyp},j}$ defines the **center of a distribution, not** a single point guess.
- In Bayesian modeling, **priors and hyperpriors are distributions** over unknown quantities, capturing full uncertainty

Step 8: Prior on Covariance Matrices

We also don't know how much individual parameters vary. So we assign a **Wishart prior** to the **inverse** covariance matrix:

$$\Sigma_j^{-1} \sim \mathcal{W}(\Omega_j, \nu_j) \tag{12}$$

- Ω_j : prior scale matrix (small variance across parameters, often $0.1 \cdot I_7$)
- ν_j : degrees of freedom

The expression above corresponds to line 74 of `model.jags`:

```
prec.par[cur_antigen_iso, 1:n_params, 1:n_params] ~ dwish(om
```

Higher $\nu_j \rightarrow$ more informative prior (stronger prior).

Lower $\nu_j \rightarrow$ more weakly informative (broader prior or weaker prior).

This tells the model how much we expect individuals to vary from the average for biomarker j.

Putting It All Together

The model is built hierarchically across five conceptual levels:

1. **Observed data:** noisy log antibody concentrations from serum samples
2. **Latent individual parameters:** hidden antibody dynamics θ_{ij} for each subject-biomarker pair
3. **Population-level means:** average antibody parameters for each biomarker
4. **Hyperpriors on means:** our belief about the likely range of biomarker-specific population means
5. **Priors on variability:** our belief about how much individual parameters vary around the population mean

This structure allows us to account for uncertainty at every level, while borrowing strength across subjects and biomarkers.

Summary of the Hierarchy

1. **Top Level**:
   - For each biomarker j, the true mean antibody trajectory parameters μ_j come from a prior:
     - $\mu_j \sim \mathcal{N}(\mu_{\text{hyp},j}, \Omega_{\text{hyp},j})$
2. **Middle Level**:
   - For each person i, their parameters:
     - $\theta_{ij} \sim \mathcal{N}(\mu_j, \Sigma_j)$
3. **Bottom Level**:
   - Their actual observed antibody levels are noisy measurements of predictions from θ_{ij}:
     - $\log(y_{\text{obs},ij}) \sim \mathcal{N}(\log(y_{\text{pred},ij}(\theta_{ij})), \tau_j^{-1})$

Where:

- $y_{\text{pred},ij}(\theta_{ij})$ is the predicted antibody trajectory based on θij.
- So predictions directly use θ_{ij} to compute $y_{\text{pred},ij}$, and then compare to observed data

Clarification: How Bottom Level Depends on Middle Level

We know the following facts:

1. θ_{ij} are the **subject-level latent parameters** (like $y_0, b_0, \mu\_b, \mu\_y, \gamma, \alpha, \rho$).
2. From θ_{ij}, we **calculate** the antibody trajectory $y_{\text{pred},ij}(t)$ using the ODE solution.
3. The **observed log-antibody** $\log(y_{\text{obs},ij})$ is modeled as a **noisy version** of $\log(y_{\text{pred},ij})$.
4. τ_j is the precision (measurement noise precision for biomarker j).

Thus, at the **Bottom Level**, we model:

$$\log(y_{\text{obs},ij}) \sim \mathcal{N}(\log(y_{\text{pred},ij}(\theta_{ij})), \tau_j^{-1})$$

Here:

- The **mean** is $\log(y_{\text{pred},ij}(\theta_{ij}))$ — depends on the **ODE solution** which itself depends on θ_{ij}.

Model Comparison (Teunis and Eijkeren 2016) vs. Our Presentation

Table 3: Comparison of Teunis (2016) model and this presentation's model assumptions.

Component	(Teunis and Eijkeren 2016)	This Presentation
Pathogen ODE	$\mu_0 b(t) - cy(t)$	$\mu_b b(t) - \gamma y(t)$
Antibody growth ODE	$\mu y(t)$	$\mu_y y(t)$
Antibody decay ODE	$-\alpha y(t)^r$	$-\alpha y(t)^\rho$
Growth mechanism	Pathogen-driven	Self-driven

Teunis, Peter F. M., and J. C. H. van Eijkeren. 2016. "Linking the Seroresponse to Infection to Within-Host Heterogeneity in Antibody Production." *Epidemics* 16: 33–39.