Supplemental Material: Model and Derivations

Bayesian Hierarchical Model for Immune Responses to Leishmania-tick borne Co-Infection Study

Felix Pabon-Rodriguez, Grant Brown, Breanna M. Scorza

1 Qualitative Categories for Disease Status

To assess CVL disease progression of subjects over time, we took into account LeishVet stage, pathogen load, and level of anti-*Leishmania* antibodies as explained in the paper. Each dog was classified based on the scoring proposed by Solano-Gallego et al. [1]. We further aggregate this scoring into the qualitative categories described below. For ith dog at time $t+1$, we define disease state $D_{i,t+1}$ as follows,

$$D_{i,t+1} = \begin{cases} 1\,(\text{Healthy}), & \text{if } LeishVet = 0 \,\text{or}\, 1 \\ 2\,(\text{Asymptomatic}), & \text{if } LeishVet = 2 \\ 3\,(\text{Symptomatic}), & \text{if } LeishVet = 3 \,\text{or}\, 4 \\ 4\,(\text{Removed}), & \text{if removed due to severe case of Leishmaniasis,} \end{cases} \tag{1}$$

2 Bayesian Hierarchical Model

For $N = 50$ dogs, and $T = 7$ time points, the proposed model is structures as follows

$$\begin{aligned} P_{i,t+1} &\sim Normal(M^{P}_{i,t}\boldsymbol{\beta}_P + X_i\boldsymbol{\alpha}_P,\, \sigma^2_P) \\ A_{i,t+1} &\sim Normal(M^{A}_{i,t}\boldsymbol{\beta}_A + X_i\boldsymbol{\alpha}_A,\, \sigma^2_A) \\ D_{i,t+1} &\sim Multinomial(1;\, \pi^{(1)}_{i,t},\, \pi^{(2)}_{i,t},\, \pi^{(3)}_{i,t},\, \pi^{(4)}_{i,t}) \\ \pi^{(k)}_{i,t} &= \frac{exp\Big[M^{D(k)}_{i,t}\boldsymbol{\beta}^{(k)}_D + X_i\boldsymbol{\alpha}_D\Big]}{1 + \sum_{g=1,2,3} exp\Big[M^{D(g)}_{i,t}\boldsymbol{\beta}^{(g)}_D + X_i\boldsymbol{\alpha}_D\Big]} \end{aligned} \tag{2}$$

for $i = 1, \ldots, N$ and $t = 1, \ldots, T$; and where

$$
\begin{aligned}
d^P_{i,t} &= P_{i,t} - P_{i,t-1} \\
d^A_{i,t} &= A_{i,t} - A_{i,t-1} \\
M^P_{i,t} &= [P_{i,t} \quad D^{(1)}_{i,t}P_{i,t} \quad D^{(2)}_{i,t}P_{i,t} \quad D^{(3)}_{i,t}P_{i,t} \quad D^{(1)}_{i,t}d^P_{i,t} \quad D^{(2)}_{i,t}d^P_{i,t} \\
&\qquad D^{(3)}_{i,t}d^P_{i,t} \quad D^{(1)}_{i,t}d^A_{i,t} \quad D^{(2)}_{i,t}d^A_{i,t} \quad D^{(3)}_{i,t}d^A_{i,t}] \\
M^A_{i,t} &= [P_{i,t} \quad A_{i,t} \quad D^{(1)}_{i,t}d^P_{i,t} \quad D^{(2)}_{i,t}d^P_{i,t} \quad D^{(3)}_{i,t}d^P_{i,t} \quad D^{(1)}_{i,t}d^A_{i,t} \\
&\qquad D^{(2)}_{i,t}d^A_{i,t} \quad D^{(3)}_{i,t}d^A_{i,t}] \\
M^{D(k)}_{i,t} &= [D^{(k)}_{i,t} \quad D^{(k)}_{i,t}P_{i,t} \quad D^{(k)}_{i,t}A_{i,t}] \\
M^{D(g)}_{i,t} &= [D^{(g)}_{i,t} \quad D^{(g)}_{i,t}P_{i,t} \quad D^{(g)}_{i,t}A_{i,t}] \\
X_i &= [1 \quad age_i \quad snap_i \quad dpp_i \quad trt_i]
\end{aligned}
\tag{3}
$$

3 Derivations

3.1 Complete Data Likelihood

Let θ_P, θ_A, and θ_D be the vectors of parameters associated with pathogen load, anti-Leishmania antibodies and disease status, respectively. Then, the complete data likelihood could be written as

$$
\begin{aligned}
f(P, A, D|\theta_P, \theta_A, \theta_D) &= \prod_{i=1}^{N} \Big[f(P_{i,1})f(A_{i,1})f(D_{i,1}) \prod_{t=2}^{T} \Big\{ f(P_{i,t}|P_{i,t-1}, \theta_P) f(A_{i,t}|A_{i,t-1}, \theta_A) f(D_{i,t}|D_{i,t-1}, \theta_D) \Big\} \Big] \\
&\propto \prod_{i=1}^{N} \Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1}) \prod_{t=2}^{T} \Bigg\{ \Big(\frac{1}{\sigma_P} exp\Big\{ -\frac{1}{2\sigma_P^2}(P_{i,t} - \eta^P_{i,t-1})^2 \Big\} \Big) \\
&\qquad \cdot \Big(\frac{1}{\sigma_A} exp\Big\{ -\frac{1}{2\sigma_A^2}(A_{i,t} - \eta^A_{i,t-1})^2 \Big\} \Big) \\
&\qquad \cdot \Big({\pi^{(1)}_{i,t-1}}^{D^{(1)}_{i,t-1}} \cdot {\pi^{(2)}_{i,t-1}}^{D^{(2)}_{i,t-1}} \cdot {\pi^{(3)}_{i,t-1}}^{D^{(3)}_{i,t-1}} \cdot {\pi^{(4)}_{i,t-1}}^{1-D^{(1)}_{i,t-1}-D^{(2)}_{i,t-1}-D^{(3)}_{i,t-1}} \Big) \Bigg\} \Bigg]
\end{aligned}
\tag{4}
$$

3.2 Full Conditionals (Model Components)

Since pathogen load, antibodies level, and disease status were not observed for some of the time points, which is known as latent variables, then we estimated the corresponding components of the model for those time points. Therefore, the full conditional for the three main components of the model are given below.

3.2.1 Disease Status

$$f_c(D|P,A,\theta_P,\theta_A,\theta_D) \propto \prod_{i=1}^{N}\Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1})\prod_{t=2}^{T}\Bigg\{exp\Big\{-\frac{1}{2\sigma_P^2}(P_{i,t}-\eta_{i,t-1}^{P})^2\Big\} \cdot \Big({\pi_{i,t-1}^{(1)}}^{D_{i,t-1}^{(1)}} \cdot {\pi_{i,t-1}^{(2)}}^{D_{i,t-1}^{(2)}} \cdot {\pi_{i,t-1}^{(3)}}^{D_{i,t-1}^{(3)}} \cdot {\pi_{i,t-1}^{(4)}}^{1-D_{i,t-1}^{(1)}-D_{i,t-1}^{(2)}-D_{i,t-1}^{(3)}}\Big)\Bigg\}\Bigg] \tag{5}$$

3.2.2 Pathogen Load

$$f_c(P|A,D,\theta_P,\theta_A,\theta_D) \propto \prod_{i=1}^{N}\Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1})\prod_{t=2}^{T}\Bigg\{exp\Big\{-\frac{1}{2\sigma_P^2}(P_{i,t}-\eta_{i,t-1}^{P})^2\Big\}\Bigg] \tag{6}$$

3.2.3 Antibodies Level

$$f_c(A|P,D,\theta_P,\theta_A,\theta_D) \propto \prod_{i=1}^{N}\Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1})\prod_{t=2}^{T}\Bigg\{exp\Big\{-\frac{1}{2\sigma_A^2}(A_{i,t}-\eta_{i,t-1}^{A})^2\Big\}\Bigg] \tag{7}$$

3.3 Full Conditionals (Parameters)

If ω_1 is equal to one of the parameters in $\{\beta_P, \alpha_P, \sigma_P^2\}$, then the full conditional is given by

$$f_c(\omega_1|.) \propto \prod_{i=1}^{N}\Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1})\prod_{t=2}^{T}\Bigg\{exp\Big\{-\frac{1}{2\sigma_P^2}(P_{i,t}-\eta_{i,t-1}^{P})^2\Big\}\Bigg\}\Bigg] \cdot \pi(\omega_1) \tag{8}$$

If ω_2 is equals to one of the parameters in $\{\beta_A, \alpha_A, \sigma_A^2\}$, then the full conditional is given by

$$f_c(\omega_2|.) \propto \prod_{i=1}^{N}\Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1})\prod_{t=2}^{T}\Bigg\{exp\Big\{-\frac{1}{2\sigma_A^2}(A_{i,t}-\eta_{i,t-1}^{A})^2\Big\}\Bigg\}\Bigg] \cdot \pi(\omega_2) \tag{9}$$

Finally, if ω_3 is equals to one of the parameters in $\{\beta_D^{(k)}, \alpha_D\}$ for $k = 1, 2, 3$, then the full conditional is given by

$$f_c(\omega_3|.) \propto \prod_{i=1}^{N}\Bigg[f(P_{i,1})f(A_{i,1})f(D_{i,1})\Bigg\{\prod_{t=2}^{T}\Big({\pi_{i,t-1}^{(1)}}^{D_{i,t-1}^{(1)}} \cdot {\pi_{i,t-1}^{(2)}}^{D_{i,t-1}^{(2)}} \cdot {\pi_{i,t-1}^{(3)}}^{D_{i,t-1}^{(3)}} \cdot {\pi_{i,t-1}^{(4)}}^{1-D_{i,t-1}^{(1)}-D_{i,t-1}^{(2)}-D_{i,t-1}^{(3)}}\Big)\Bigg\}\Bigg] \cdot \pi(\omega_3) \tag{10}$$

References

[1] Solano-Gallego L, Miró G, Koutinas A, et al. LeishVet guidelines for the practical management of canine leishmaniosis. Parasites & Vectors. 2011;4(86). doi:https://doi.org/10.1186/1756-3305-4-86.