Bayesian Generalized Mixed Modeling of Relative Breadth of Mosaic and CON-M HIV-1 Vaccines

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***Short Abstract* — Genetic diversity is a challenge that the scientific community must overcome before the development of a global HIV-1 vaccine is realized. Two vaccine strategies addressing genetic diversity, namely HIV-1 global consensus envelope sequence (CON-M) and polyvalent vaccine antigens (Mosaic), have been shown to increase the number of positive immune responses in vaccinated monkeys exposed to HIV-1. We investigate the relative breadth of of the CON-M and Mosaic vaccine immune responses in an animal study using a Bayesian generalized linear mixed model for Poisson counts. We compare the conclusions to those resulting from the analogous frequentist case and address missing data considerations.**

***Keywords* — HIV-1 vaccines, Bayesian generalized linear mixed model, missing data.**

I. Purpose

GENETIC diversity is a challenge that the scientific community must overcome before the development of a global HIV-1 vaccine is realized. Two vaccine strategies addressing genetic diversity are of interest: HIV-1 global consensus envelope sequence (CON-M) and polyvalent vaccine antigens (Mosaics). Each vaccine has been shown to increase the number of positive immune responses in vaccinated monkeys exposed to HIV-1. Two recent studies were designed to determine if animals given the mosaic vaccine have an advantage over those given the consensus vaccine. The data in [1] and [2] were analyzed using generalized linear mixed models for Poisson counts, controlling for vaccine type (Mosaic or Consensus), protein type (Gag, Env, Pol in [1] and Gag, Nef in [2]) T-cell type (CD4 or CD8), and random animal effect.

Preliminary results in both studies suggest that vaccine effect is confounded by T-cell type. However, classification of T-cell responses as CD4 or CD8 was not possible for some of the subjects in [2], resulting in a reduction in the number of animals whose T-cell effect could be assessed in the model. To fit the desired generalized linear mixed model including T-cell effect, we use a restricted dataset consisting of the 14 complete cases from the sample of 21 animals. This simple approach to analyzing a dataset with missing values does not take advantage of all of the available data.

A Bayesian hierarchical model incorporating the uncertainty in the missing data is proposed as a suitable alternative. Our approach is to (1) assess model stability using a Bayesian model for the complete cases, (2) analyze the missing data pattern, and (3) apply a method which is appropriate for the missing data pattern observed.

II. Preliminary Results

The frequentist model is a log-linear fit of the mean parameter of the Poisson distribution with random animal effect. The analogous Bayesian model fits a similar log-linear model with very diffuse normal priors on the regression parameters (assumed independent *a priori*). We model the standard deviation of the normal random effect with a Uniform(.01, 1) prior.

As expected, the posterior means and medians closely resemble the maximum likelihood estimates. The 95% confidence intervals and credible sets from the two models tend to agree in width and location, suggesting that the model is stable. Because both models indicate a significant interaction among vaccine, protein, and T-cell effects, isolating the magnitude of the Vaccine effect is not possible. Future work will include consideration of more informative priors using the results in [1], investigation of the missing data pattern, and incorporation the missing data into the model.

References

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