Forecasting and Nowcasting Variant Proportions with Genomic Data at the Regional Level

University of Massachusetts, Amherst

Isaac MacArthur, **Maryclare Griffin**, Evan Ray, Nicholas Reich, Thomas Robacker, and Benjamin Rogers

June 16, 2025

Forecasting and Nowcasting Variant Proportions with Genomic Data at the Regional Level

University of Massachusetts, Amherst

Isaac MacArthur, **Maryclare Griffin**, Evan Ray, Nicholas Reich, *Thomas Robacker*, and Benjamin Rogers

June 16, 2025

Genomic Data and Variant Proportions

For COVID and other viral illnesses, viral samples are

- Collected from infected individuals

→ Sent to a lab

→ Processed

→ Classified into clades using an estimated phylogenetic tree

Proportion of samples across clades (variant proportions) informs:

- Mitigation efforts
- Treatment strategies

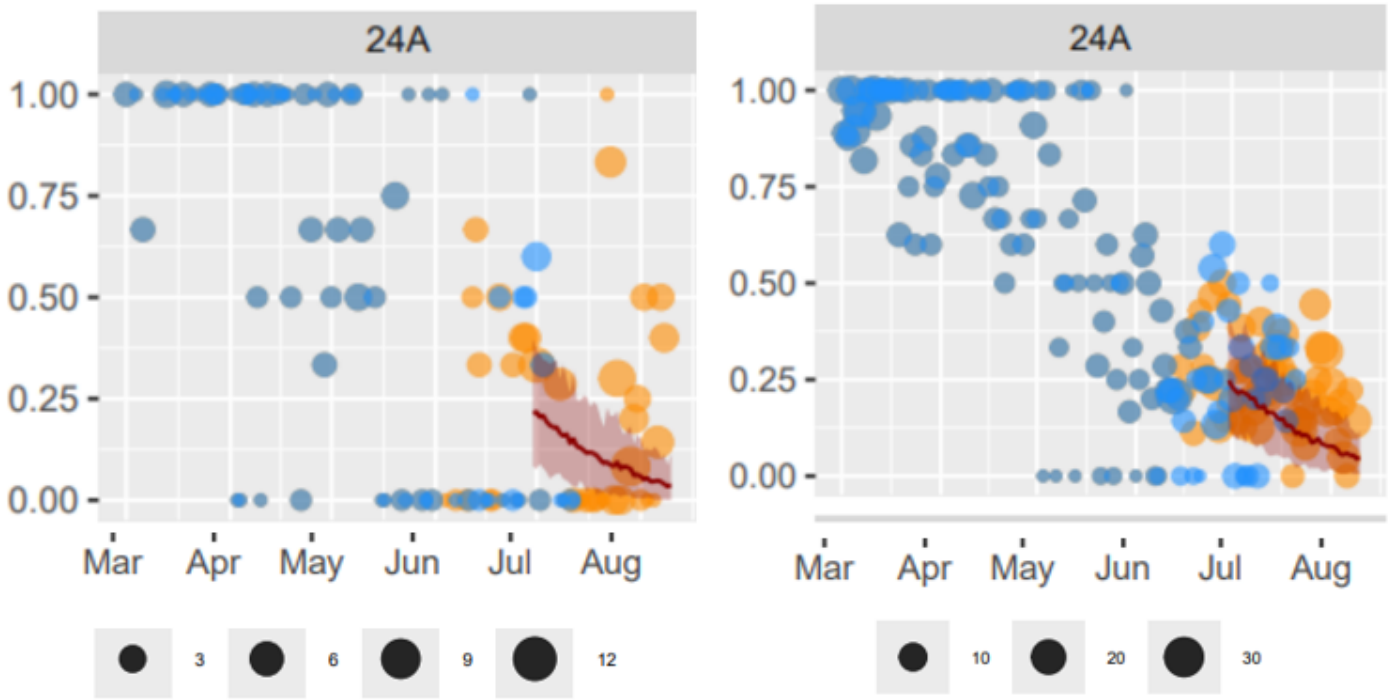
There is a need for local (state-level):

- Forecasts of variant proportions in the near future
- Nowcasts of variant proportions as samples during processing

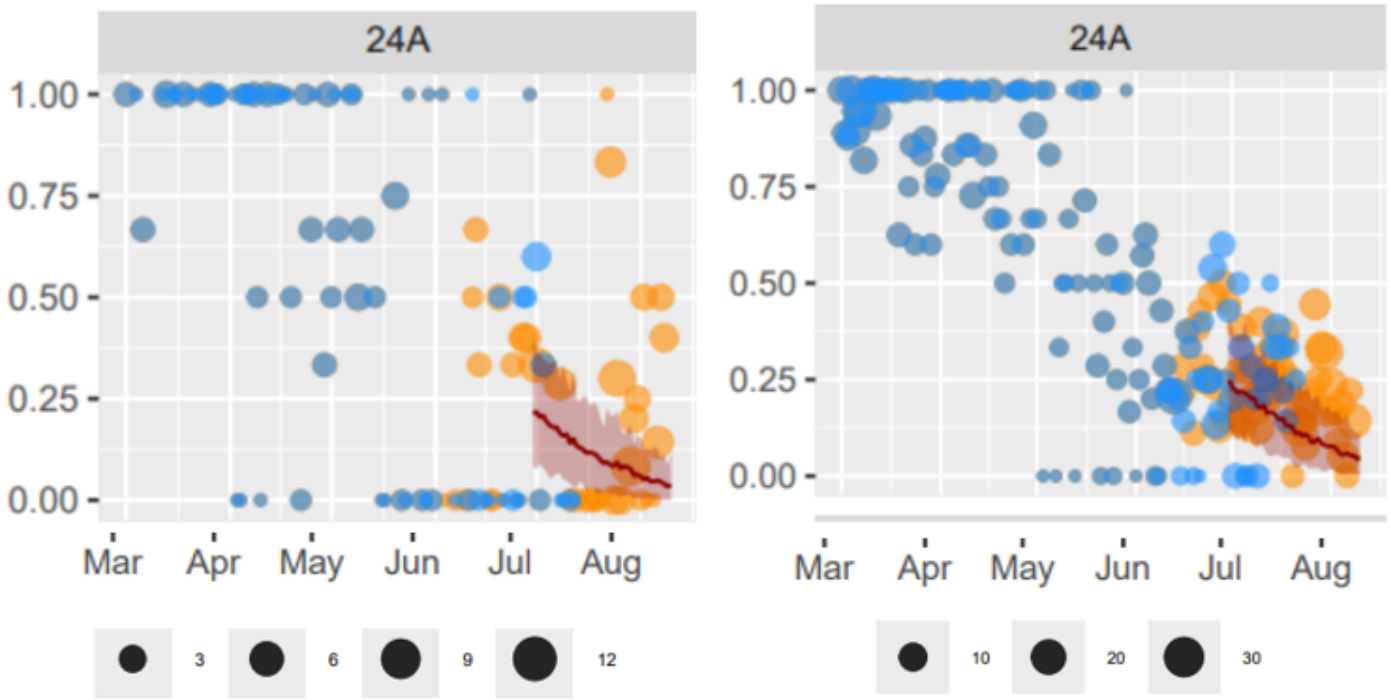
---

Bedford Lab provides sample data and estimated phylogenetic trees.

MA and MN Proportion 24A for July 31, 2024



MA and MN Proportion 24A for July 31, 2024



- Lags in data collection
- Low counts per state
- Poor evaluation data
- New clades can arise, clade assignments can change*

Previous Approaches to the Problem

Previous approaches support the use of simple models.

Abousamra, Figgins, and Bedford (2024):

- Consider country level data
- Use local Multinomial Logistic Regression (MLR) models
- Measure performance with median absolute error (MAE) relative to retrospective seven day averages
- Find MLR models outperforms alternatives
- Find a hierarchical MLR models bring benefits

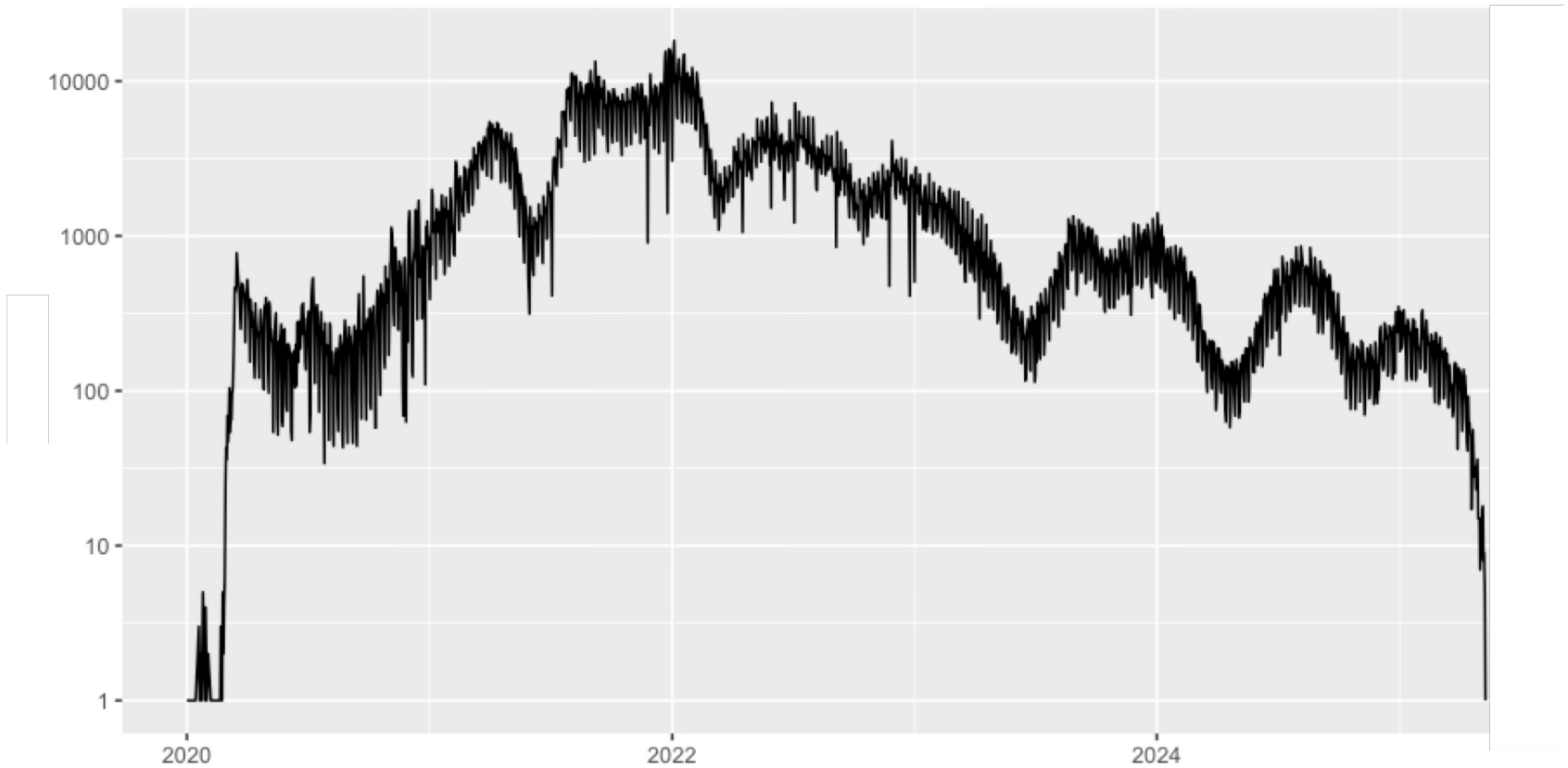
Multinomial Logistic Regression

Let C_{ltv} be the observed count of the v variant at the l location, on the t day, then for $v = 1, \ldots V$ and $l = 1 \ldots L$ and $t = 1 \ldots T$

$$C_{lt1}, \ldots C_{ltV} \mid \alpha_l, \beta_l, n_{lt} \sim$$
$$\text{Multinomial}\left(\frac{\exp\left(\alpha_{lv} + \beta_{lv} t\right)}{\sum_v \exp\left(\alpha_{lv} + \beta_{lv} t\right)}, n_{lt}\right)$$

Need for Sharing Across States

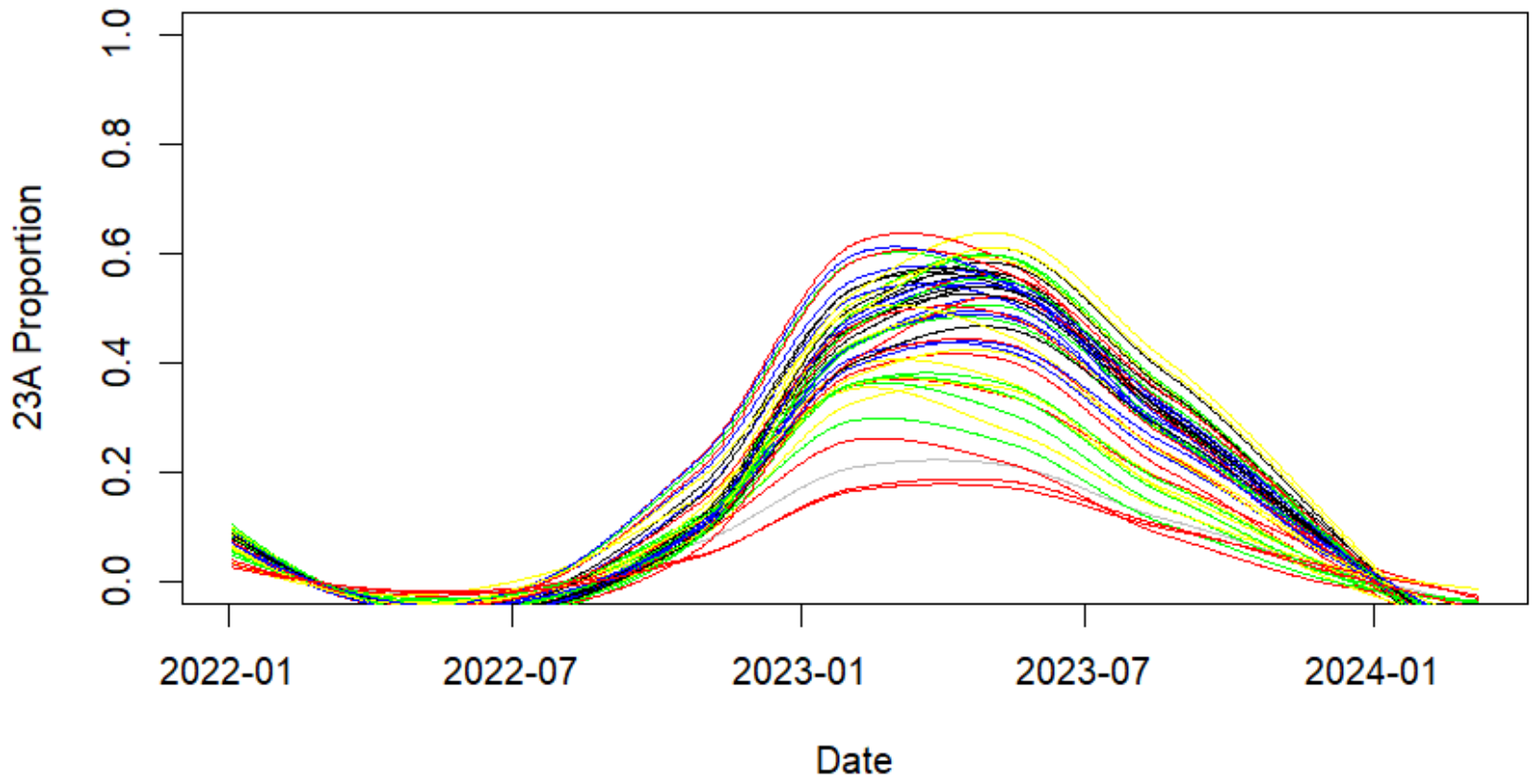
We do not observe many samples!



Some states do not submit viral samples at all.

Support for Sharing Across States

Variant proportions are similar across states!



Defining the Hierarchical Structure

As we saw, the MLR model has the form

$$C_{lt1}, \ldots C_{ltV} \mid \alpha_l, \beta_l, n_{lt} \sim \text{Multinomial}\left(\frac{\exp\left(\alpha_{lv} + \beta_{lv} t\right)}{\sum_v \exp\left(\alpha_{lv} + \beta_{lv} t\right)}, n_{lt}\right)$$

To extend the model we created a hierarchical structure of priors over the α and β. We assumed that for each $v = 1, \ldots, V$

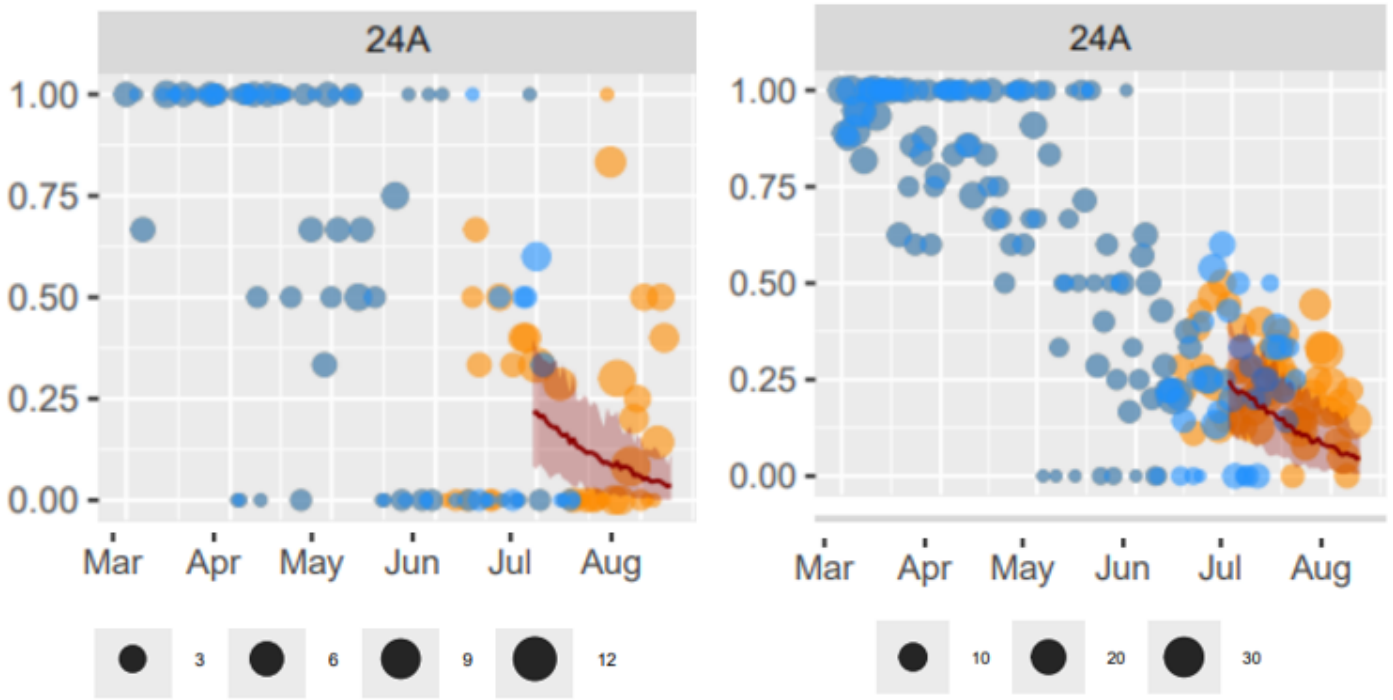
$$\beta_{1v}, \ldots \beta_{Lv} \mid \mu_{\beta v}, \tau^2_{\beta v} \overset{\text{iid}}{\sim} \text{normal}(\mu_{\beta v}, \tau^2_{\beta v}),$$

$$\alpha_{1v}, \ldots \alpha_{Lv} \mid \mu_{\alpha v}, \tau^2_{\alpha v} \overset{\text{iid}}{\sim} \text{normal}(\mu_{\alpha v}, \tau^2_{\alpha v}).$$

We then put non-informative priors on the $\mu_\beta, \mu_\alpha, \tau_\beta, \tau_\alpha$.

We also consider a Dirichlet-Multinomial generalization.

MA and MN Proportion 24A for July 31, 2024

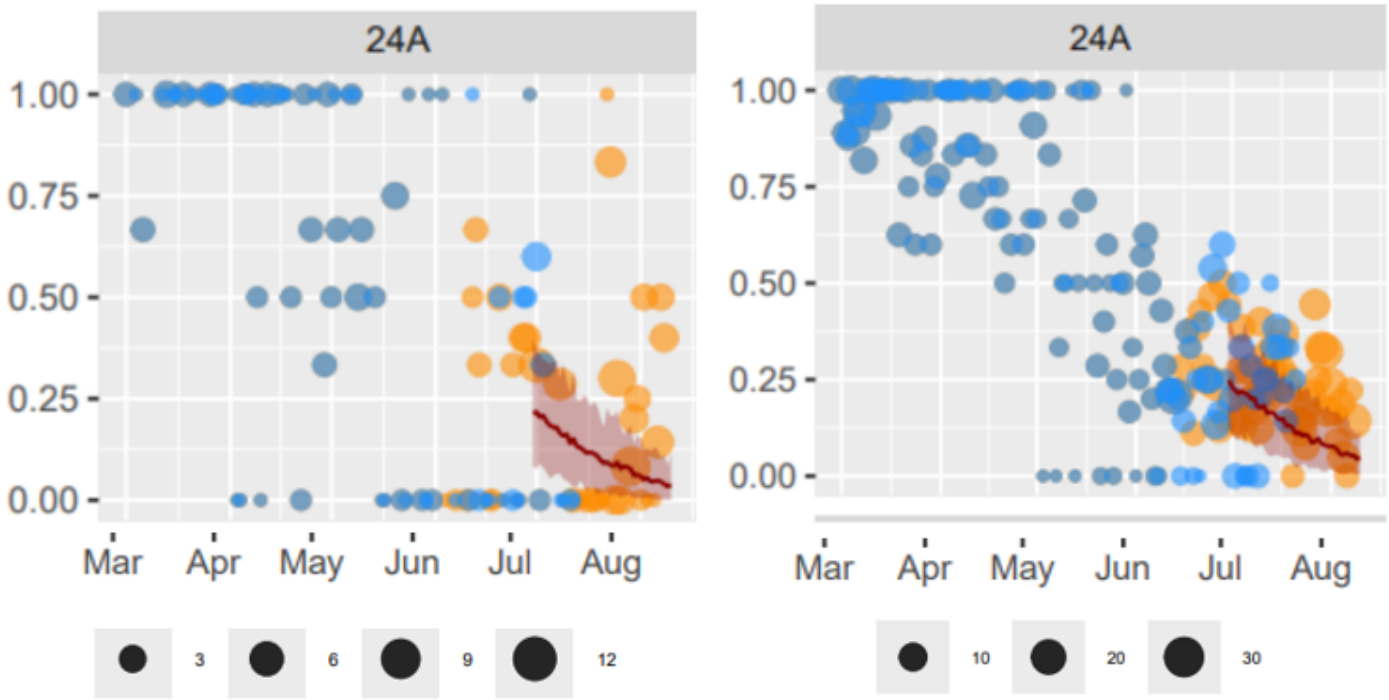


- Hierarchical model accommodates common trends
- Dirichlet-Multinomial accommodates overdispersion

Model Fitting and Specifications

- Choose a target "nowcast" date
- Fix training data to the 150 days prior to "nowcast" date
- Use STAN to simulate from the posterior distribution of the parameters
- Construct "nowcasts" for "nowcast" date and 30 days prior
- Construct forecasts for 10 days after "nowcast" date

MA and MN Proportion 24A for July 31, 2024



Evaluating the Model

- Abousamra et. al (2024) used MAE relative to seven day retrospective average
  - Does not reflect dependence of proportions
  - Focuses on quality of point prediction
  - Requires definition of a notion of retrospect "truth"
- We use approximate energy scores

The Energy Score

- The energy score is a proper scoring rule for comparing how similar two distributions are that was introduced in Gneiting et al. (2008)
- If we let $\mathbf{y} = (y_1, y_2, \ldots, y_V)$ be the observed values for a given location and time and $\mathbf{x}_1, \ldots \mathbf{x}_m$ be the forecasted values for the forecasted distribution F, then the energy score is then computed as:

$$\mathrm{ES}(F, \mathbf{y}) = \frac{1}{m} \sum_{i=1}^{m} ||\mathbf{y} - \mathbf{x}_i|| - \frac{1}{2m^2} \sum_{i=1}^{m} \sum_{j=1}^{m} ||\mathbf{x}_i - \mathbf{x}_j||$$

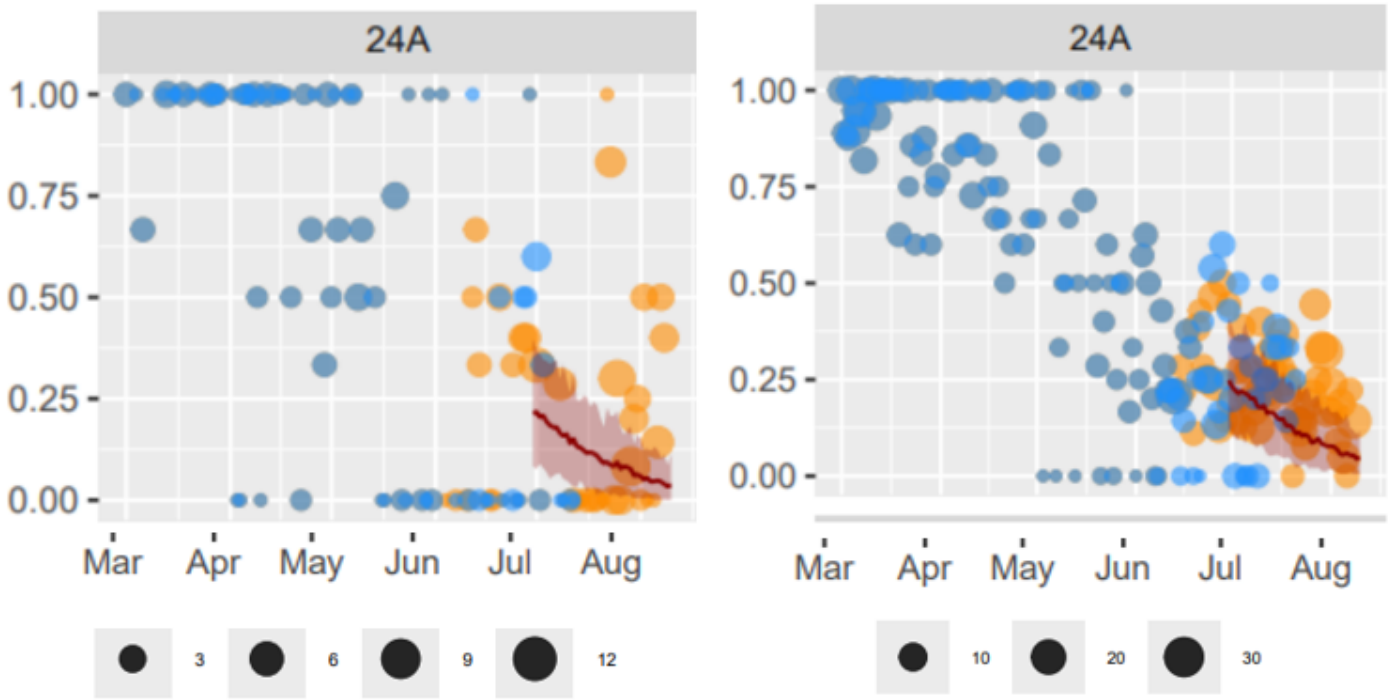
where $||.||$ is the Euclidean norm on R^V, and m is the total number of samples from the predictive distribution.

Computing the Energy Score

- From our model, we obtain posterior distributions of variant proportions on the forecast and nowcast dates
- 90 days after our target "nowcast" date, we have observed the number of samples obtained for each forecast and nowcast date
- We simulate forecasts and nowcasts of counts by drawing multinomial random variables with the observed totals and posterior predictive variant proportions

$$\text{ES}(F, \mathbf{y}) = \frac{1}{m} \sum_{i=1}^{m} ||\mathbf{y} - \mathbf{x}_i|| - \frac{1}{2m^2} \sum_{i=1}^{m} \sum_{j=1}^{m} ||\mathbf{x}_i - \mathbf{x}_j||$$

MA and MN Proportion 24A for July 31, 2024



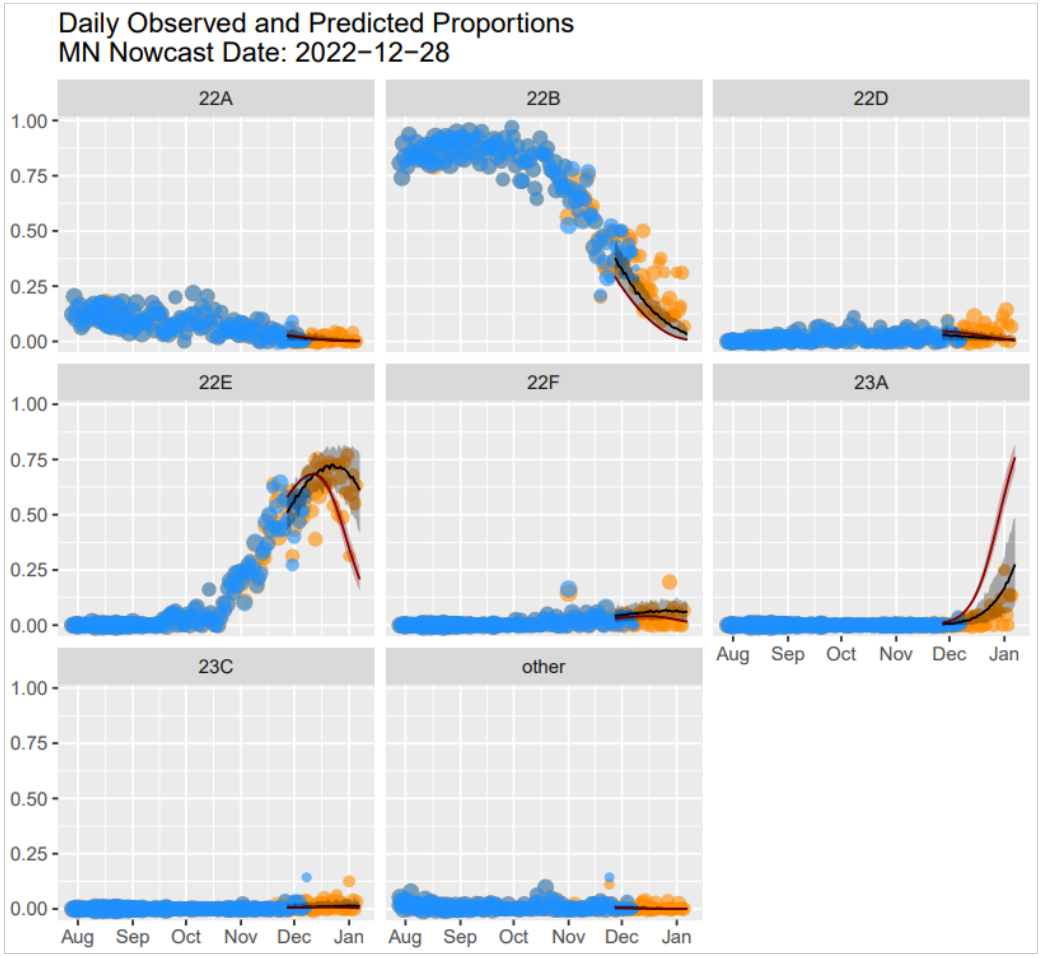
Model Comparison

- The energy score measures both the accuracy and variance of the forecasted distribution and a higher score is worse, but the energy score is hard to interpret.
- Thus to evaluate the performance of the HMLR model, we want to choose a baseline model that we can use as a comparison.
- We have chosen a baseline MLR model that predicts at the country level and makes the same prediction at each state.

Model Testing

- To test the HMLR model, we accrued historical versions of Nextstrain datasets for Mondays.
- These datasets run from August 2022 to August 2024
- Each Monday dataset was used to predict the following Wednesday, for a total for 106 predictions.
- Each forecast was scored using the data 91 days after the dataset used.

Example Forecasts

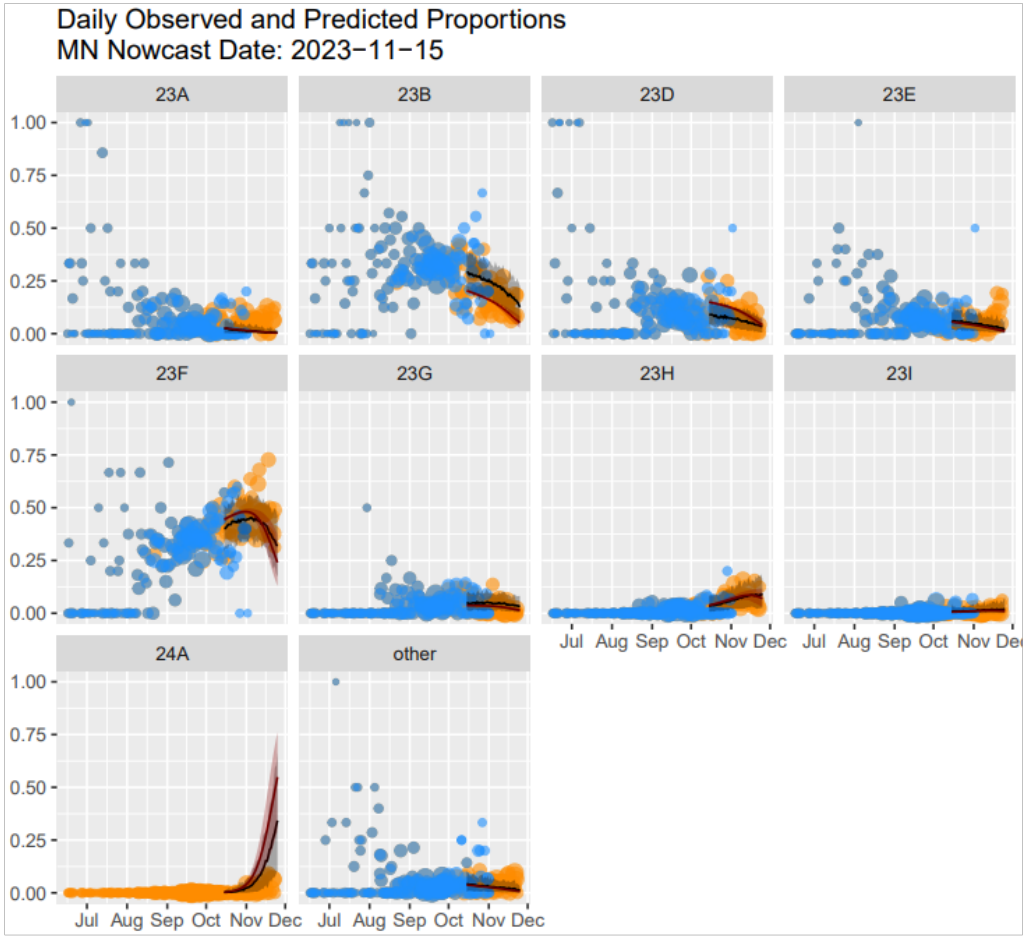


Mean energy scores: HMLR = 4.37, Baseline = 9.45

Example Forecasts

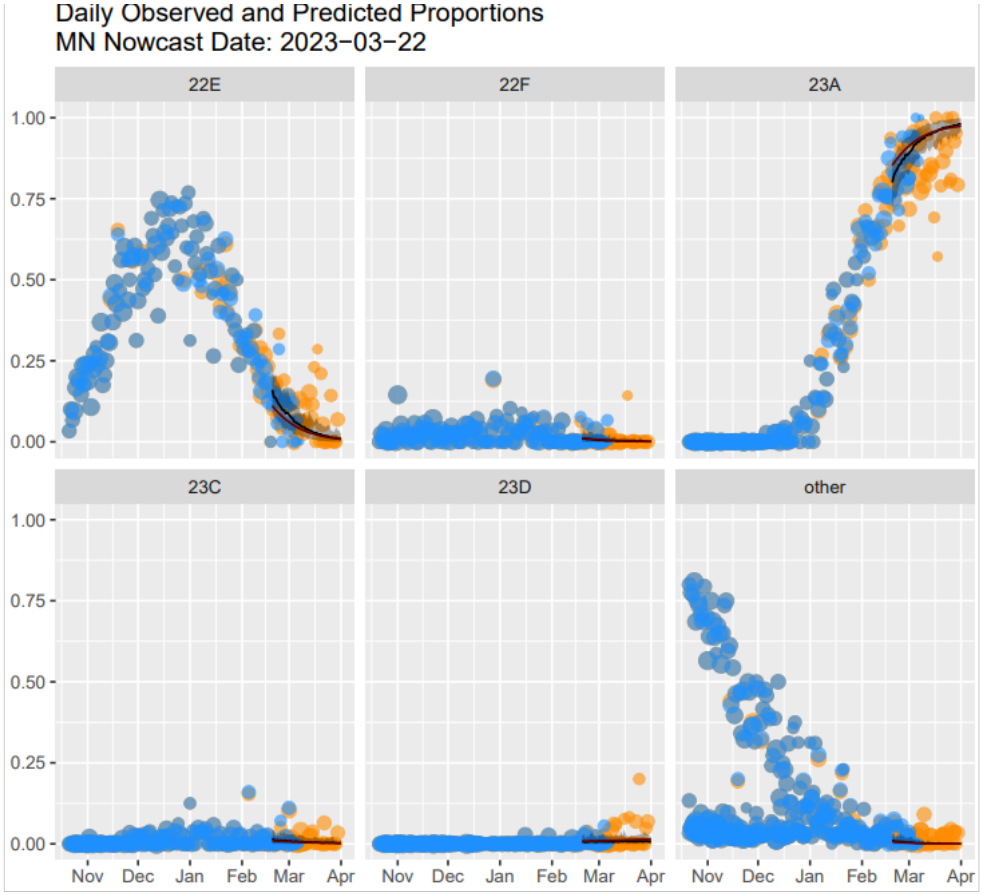
Mean energy scores: HMLR = 0.78, Baseline = 0.81

Example Forecasts



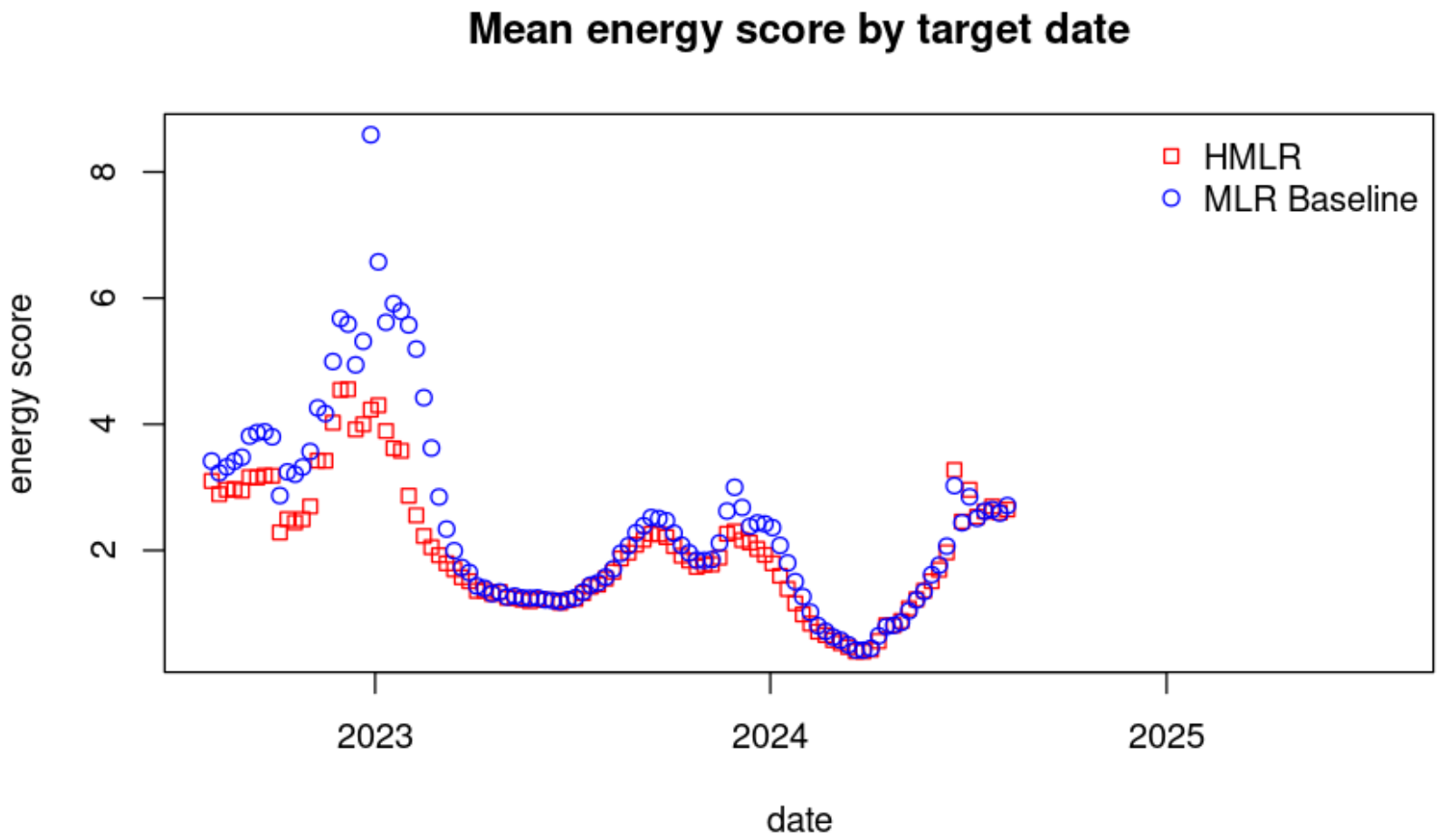
Mean energy scores: HMLR = 4.86, Baseline = 6.48

Example Forecasts

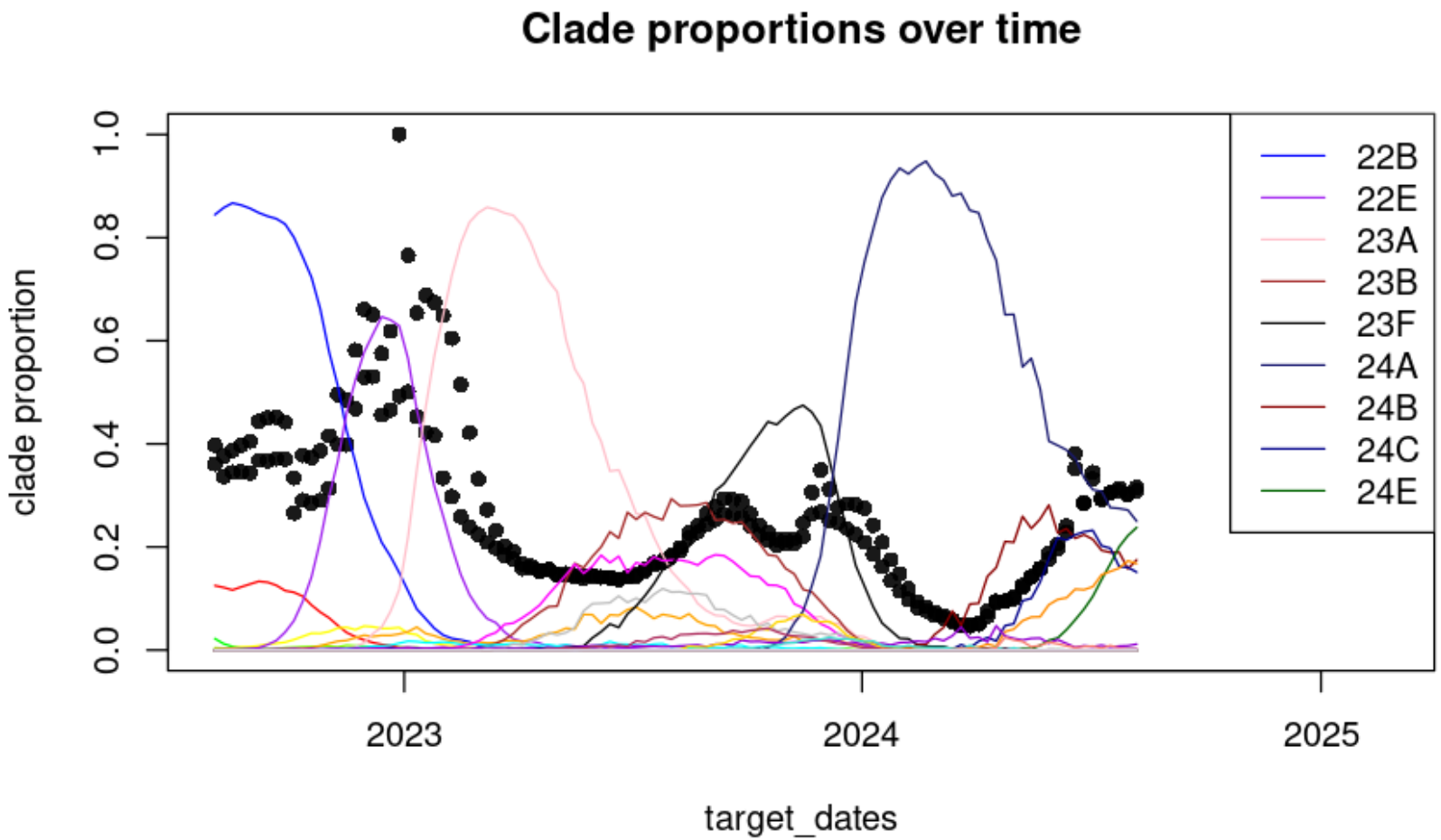


Mean energy scores: HMLR = 2.76, Baseline = 3.02

Mean Energy Scores



Energy Score Trends



Conclusions

- Sharing information tends to provide improved forecasts
- Allowing for overdispersion with a Dirichlet-Multinomial model improves forecasts
- Energy scores seem to summarize meaningful differences in model performance

Future Work

- Sharing information across states
- Sharing information across variants
- Moving away from ad-hoc subsetting of data
- Applications to other viral illnesses and ecology
- *Smoothing multinomial data with limited observations*