Phylodynamics of Ebola in West Africa

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Motivation

- The 2013-2016 West African Ebola virus disease (EVD) epidemic was the largest in history;
- A massive international collaboration produced the most comprehensive data set for an acute virus to date (over 5% sampling);
- Our challenge is to combine different sources of information (epidemiological, genetic, climatic, etc) to trace the epidemic and explain its mode and tempo.
- Investigate the role of particular mutations in disease severity;

Contributions

Here I present my contributions to Dudas et al. (2016) and Diehl et al. (2016):

- Generalised linear model (GLM) to study the association between a particular mutation, viral load and fatality rates;
- More GLMs, this time coupled with Stochastic Search Variable Selection (SSVS) to investigate the factors that drove the epidemic;
- Construction of (approximately) conditionally independent clusters combining incidence and phylogenetic data;

Methods

In total 1610 genomes were sequenced so far. We take a Bayesian approach and estimate time-calibrated phylogenies with **BEAST**.

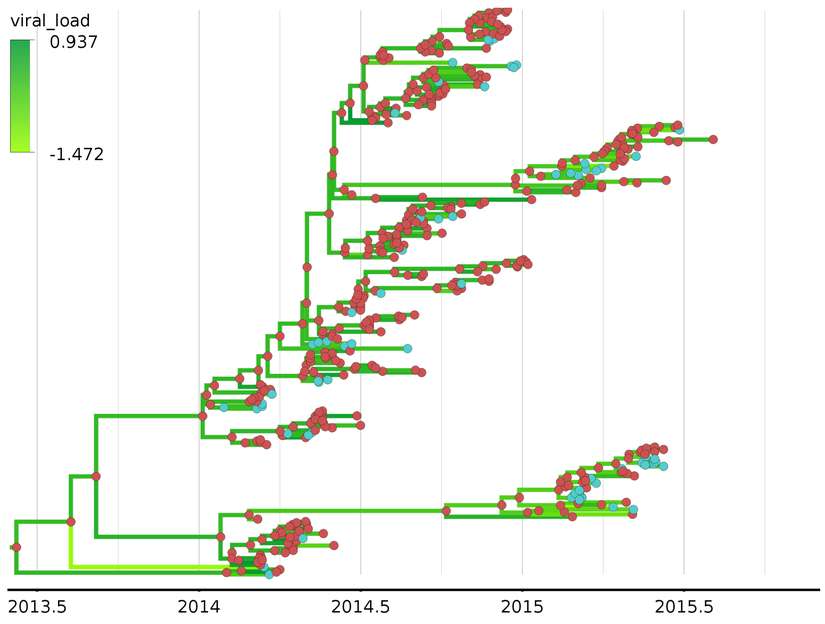
- We had viral load ($C(t)$ values) and outcome (death/survival) information for 236 patients $\rightarrow$ binomial GLM;
- Case counts ($\mathbf{Y}$) along climatic and socio-economic covariates ($\mathbf{X}$) for 56 locations $\rightarrow$ negative binomial GLM + SSVS:

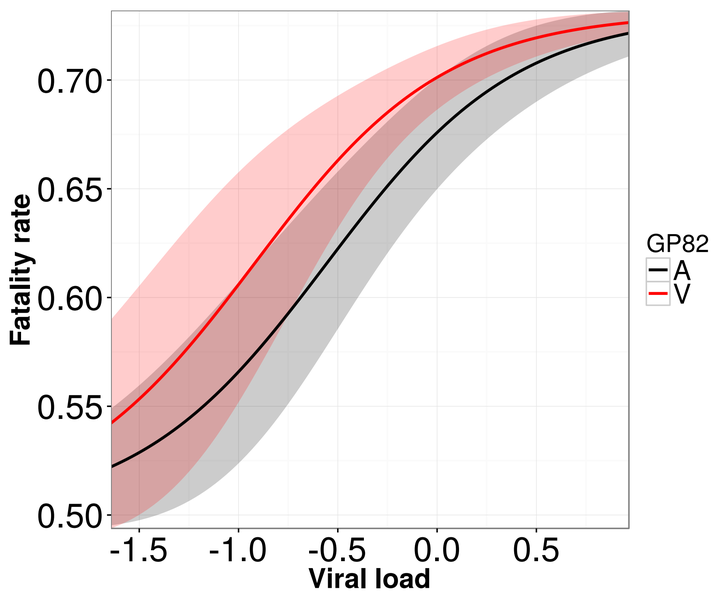
$$Y_i \sim \text{NegBin}(p_i, r)$$
$$p_i = \frac{r}{(r + \lambda_i)}$$
$$\log(\lambda_i) = \alpha + \beta_1 \delta_1 x_{i1} + \ldots + \beta_P \delta_P x_{iP}$$

- Constructing outbreak clusters: every time a location receives a viral introduction that leads to >20 sampled cases, split the series before and after the introduction.

Results

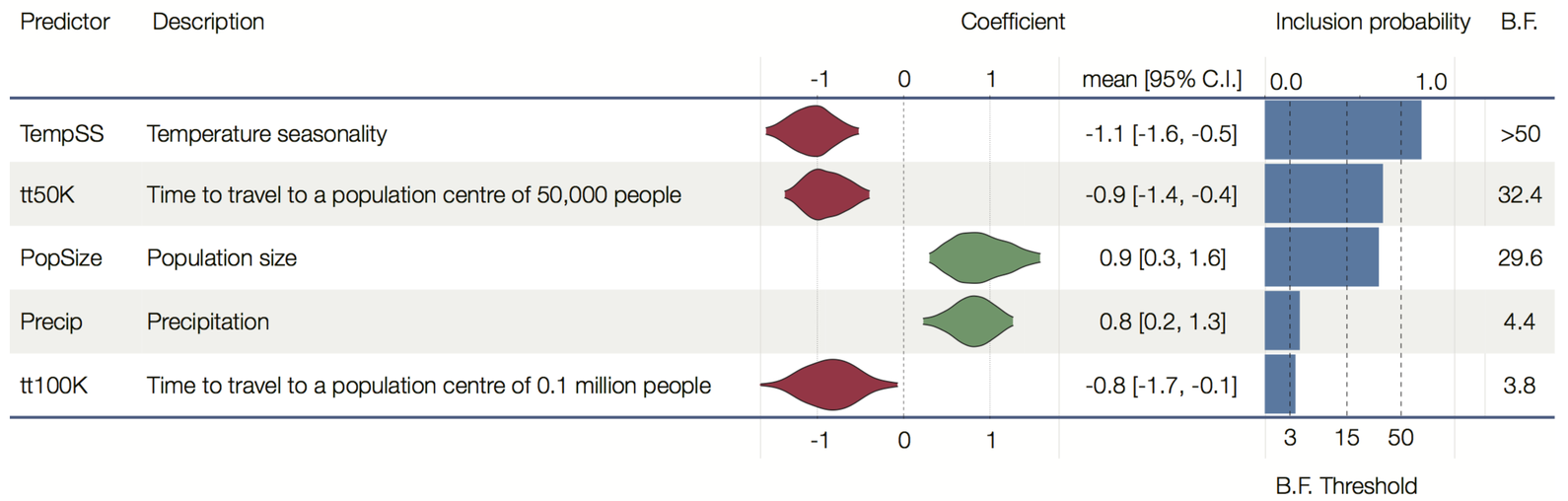
Did the GP-A82V mutation increase mortality?



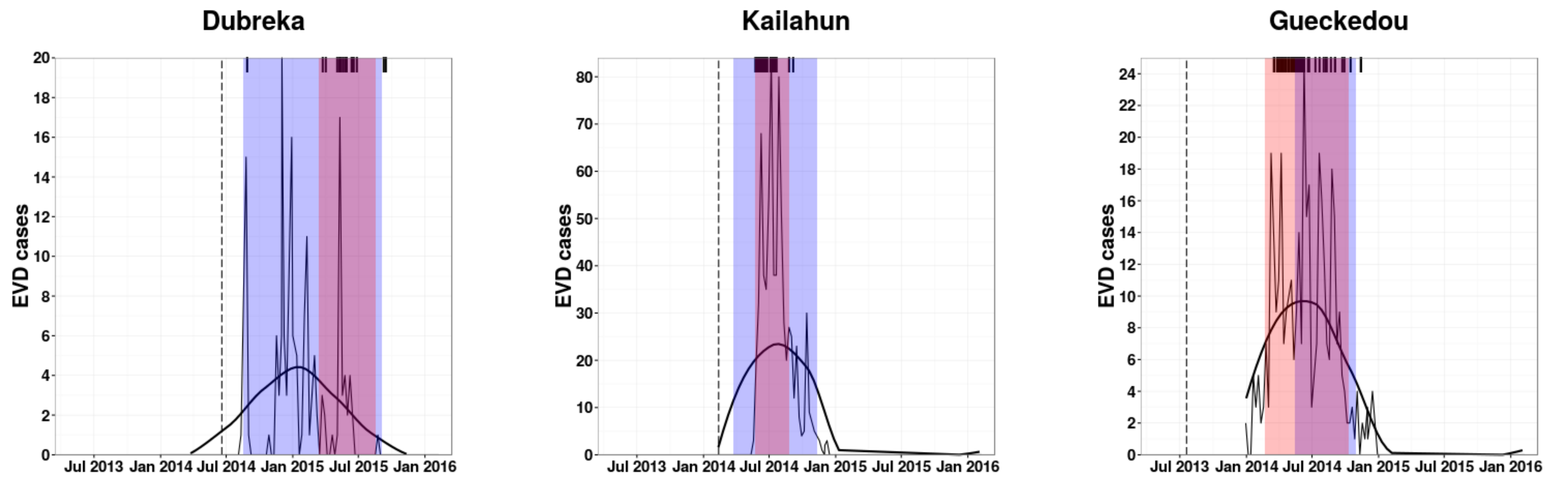


Answer: Yes, there is some evidence that A→V conferred increased infectivity intra-host. That does not mean the mutation had any bearing in transmission, however.

What drove the epidemic?



Combining epidemiological and phylodynamic data



What's next?

- What impact did intervention have? $\rightarrow$ hierarchical SIR model;
- Study the correlation between viral load and fatality using a latent liability model;
- Investigate possible differences in rates of evolution across time and space;

Thanks for reading!

I'm very grateful to IEB and SBS for topping up my annual stipend. Thanks! Source code and a cool animation showing the spread of A82V in West Africa are available at `https://github.com/maxbiostat/diehl_ebola_cell_2016`. A digital copy of this poster can be found at `https://github.com/maxbiostat/second_year_poster`.