



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 → binomial GLM;

§ Case counts (Y) along climatic and socio-economic covariates (X) for 56 locations → negative binomial GLM + SSVS:

$$Y_i \sim \text{NegBin}(p_i, r)$$

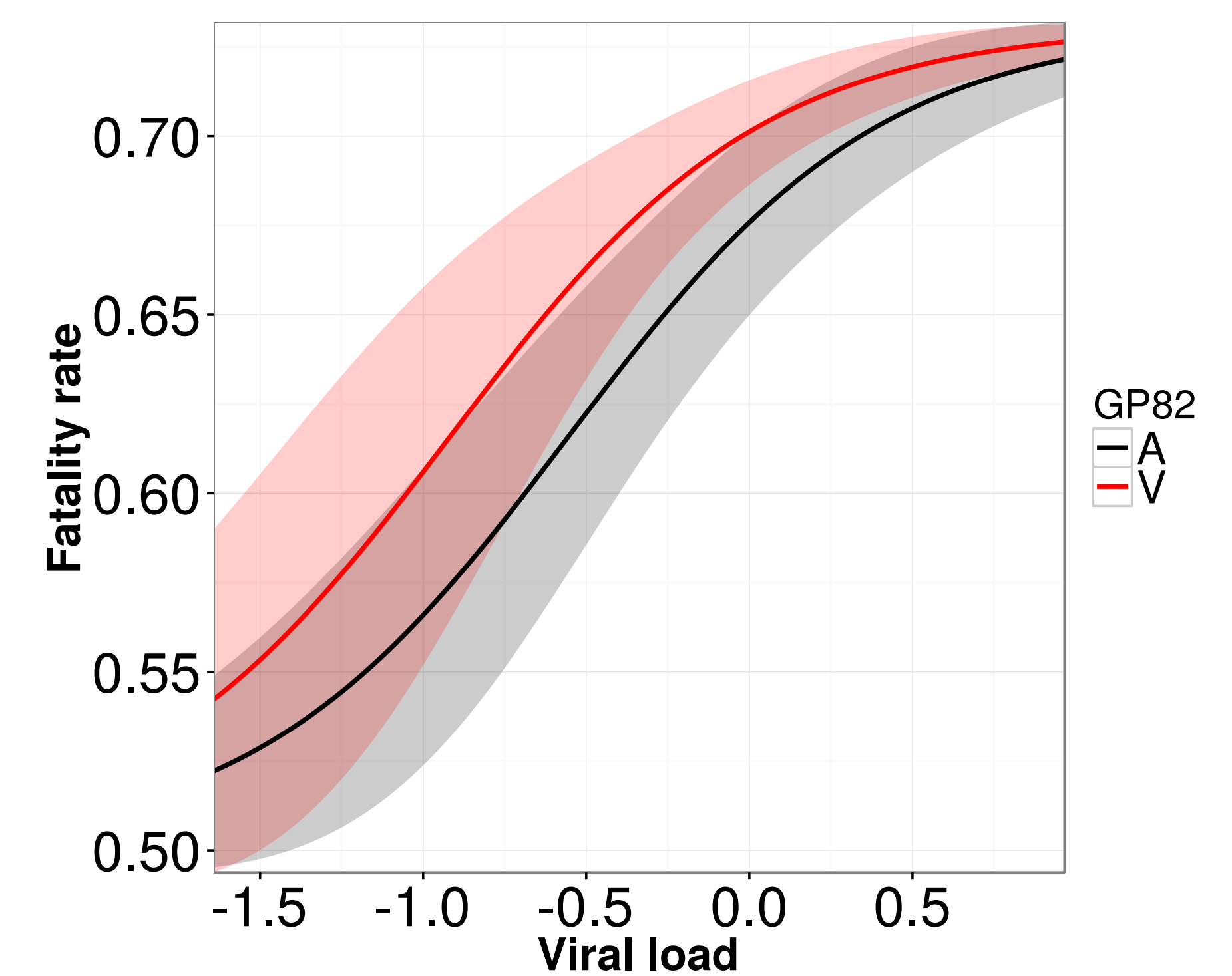
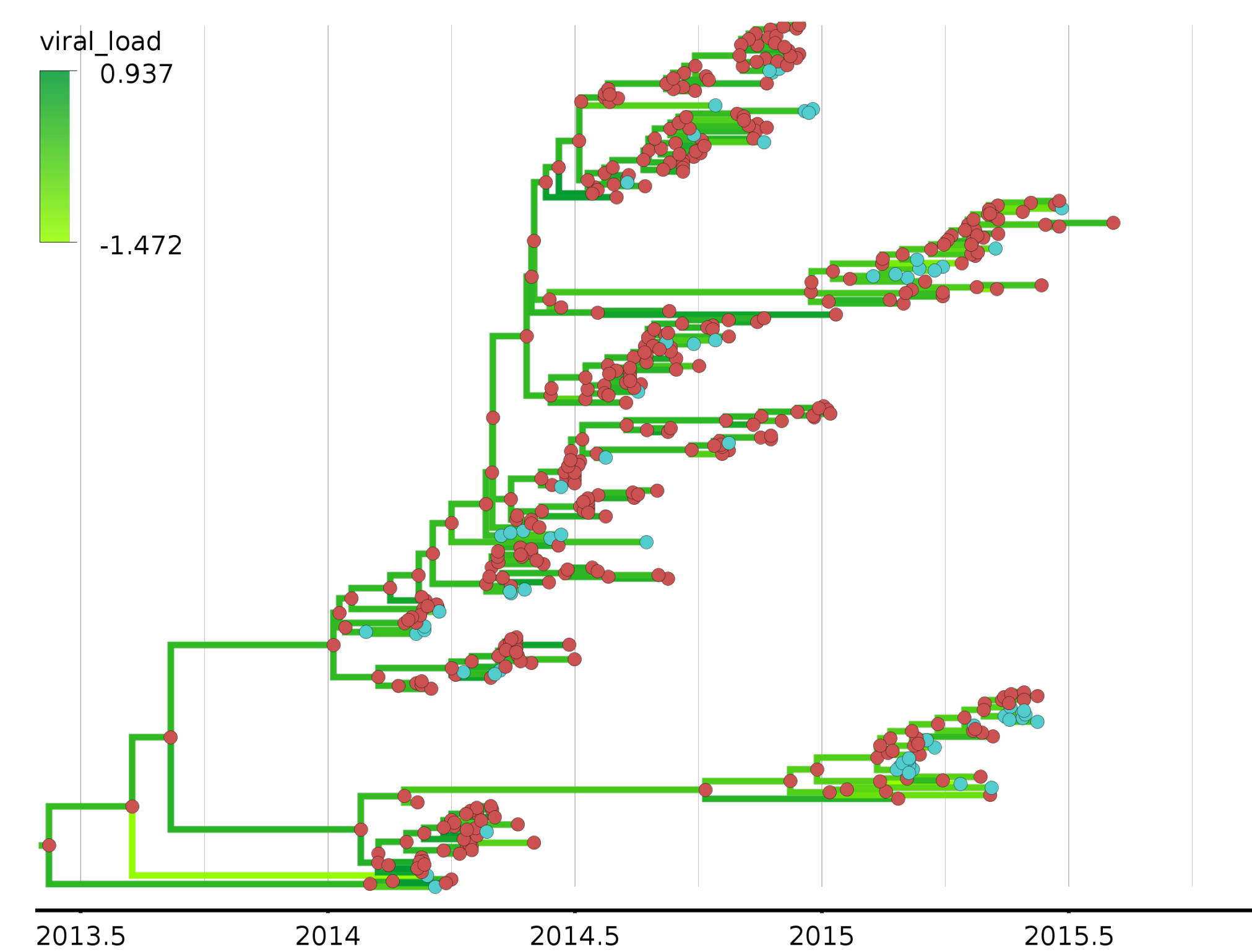
$$p_i = \frac{r}{(r + \lambda_i)}$$

$$\log(\lambda_i) = \alpha + \beta_1 \delta_1 x_{i1} + \dots + \beta_P \delta_P x_{iP}$$

§ 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.








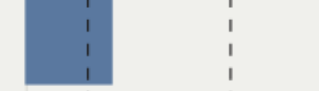


RESULTS

Did the GP-A82V mutation increase mortality?

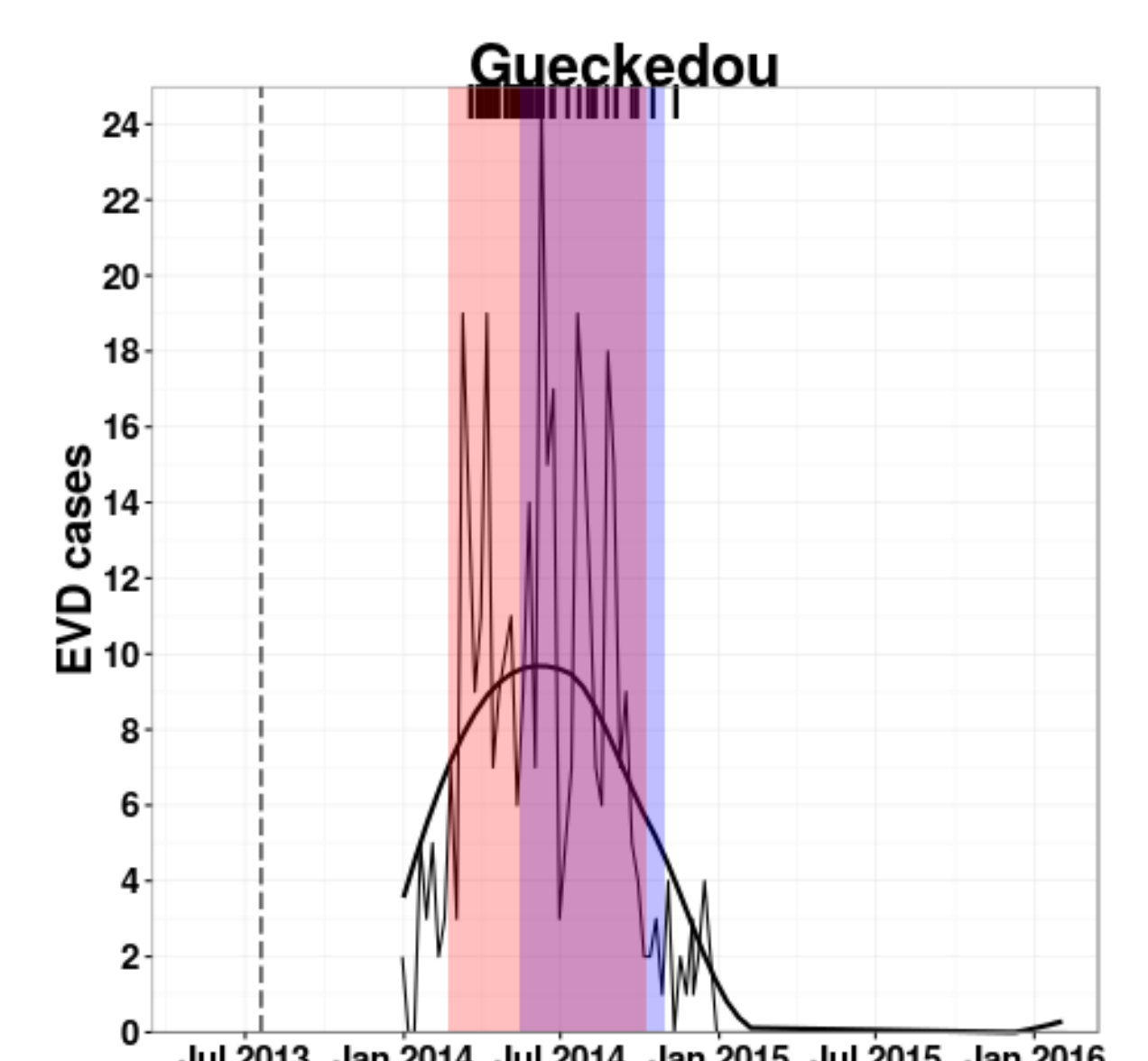
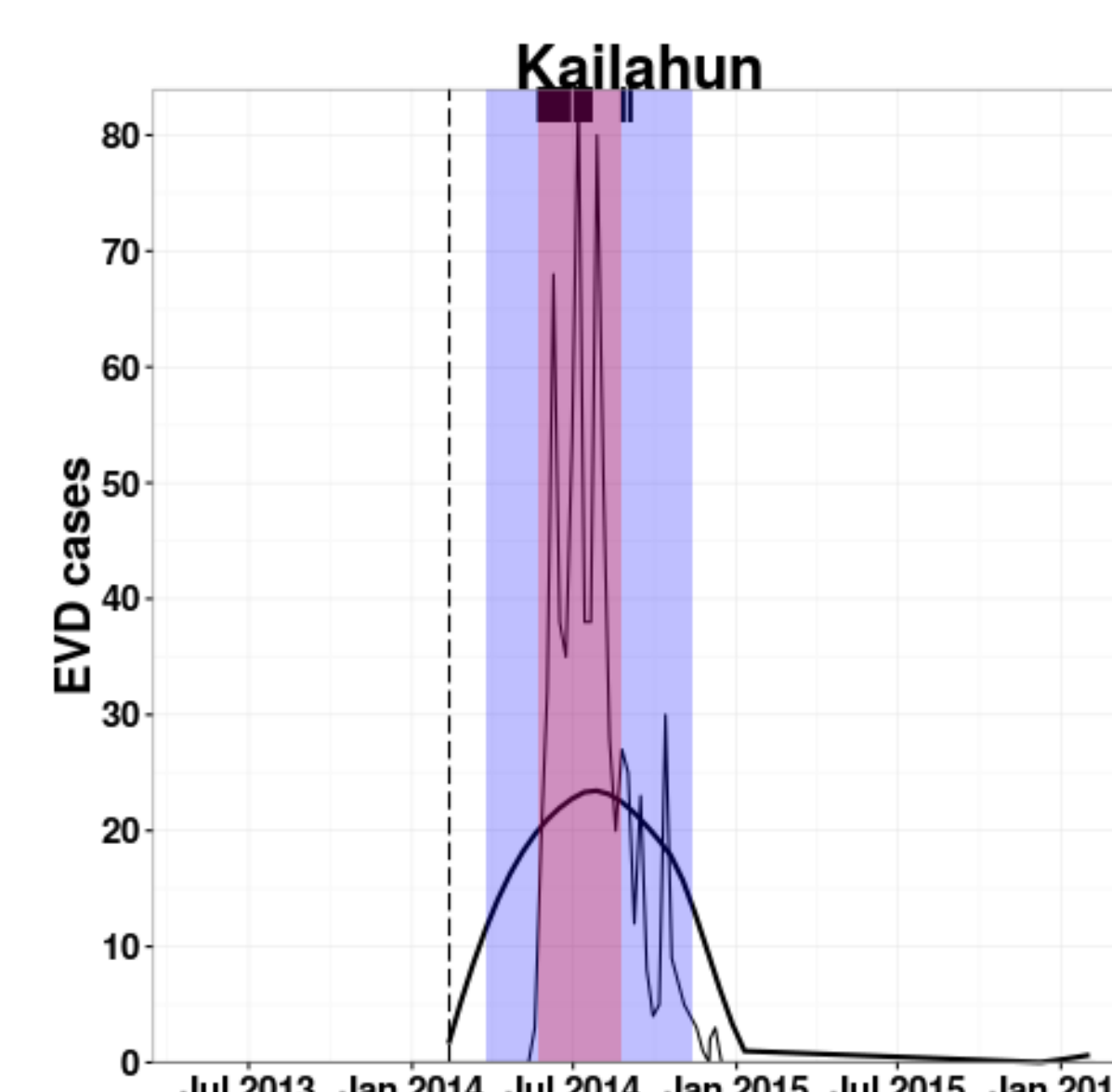
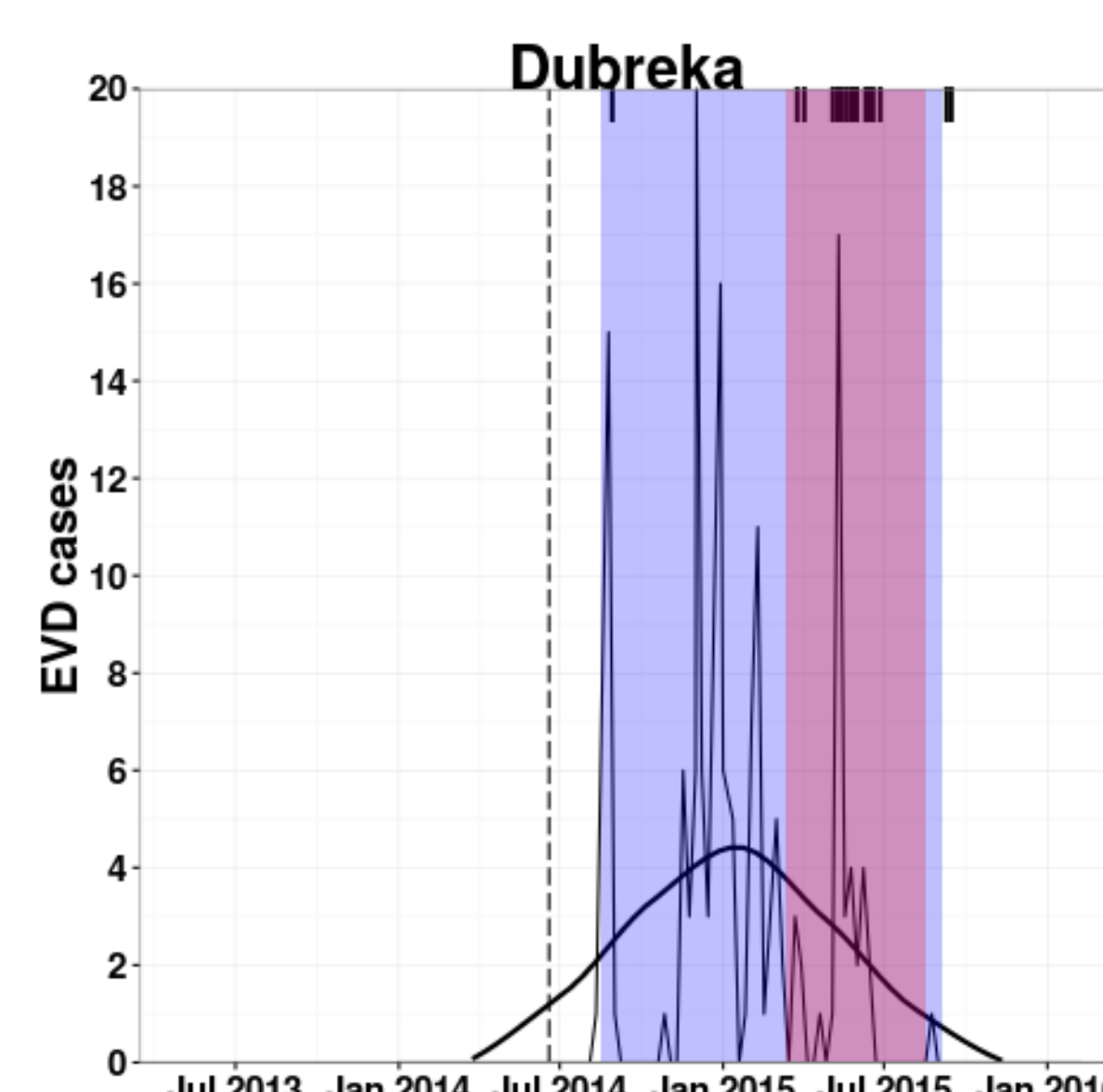


Answer: Yes, there is some evidence that A→V conferred increased infectivity intra-host. That does not mean the mutation had any bearing in transmission, however.

What drove the epidemic?

Predictor	Description	Coefficient		Inclusion probability	B.F.		
		-1	0	mean [95% C.I.]	0.0	1.0	
TempSS	Temperature seasonality			-1.1 [-1.6, -0.5]		>50	
tt50K	Time to travel to a population centre of 50,000 people			-0.9 [-1.4, -0.4]		32.4	
PopSize	Population size			0.9 [0.3, 1.6]		29.6	
Precip	Precipitation			0.8 [0.2, 1.3]		4.4	
tt100K	Time to travel to a population centre of 0.1 million people			-0.8 [-1.7, -0.1]		3.8	
		-1	0		3	15	50
B.F. Threshold							

Combining epidemiological and phylodynamic data



WHAT'S NEXT?

- What impact did intervention have? → 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.