Phylodynamics of infectious diseases

Recent advances

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Outline

What is phylodynamics?

Concepts and tools.

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Examples

Influenza, West Nile Virus, Ebola. In space* and time.

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Where are we headed?

We should prepare for an era of plenty.

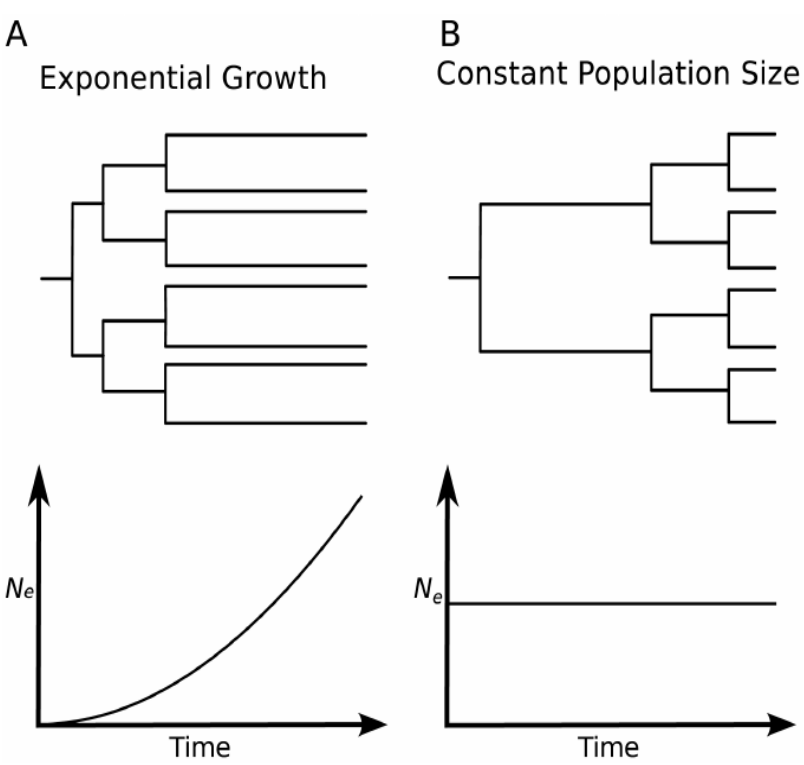
Motivation

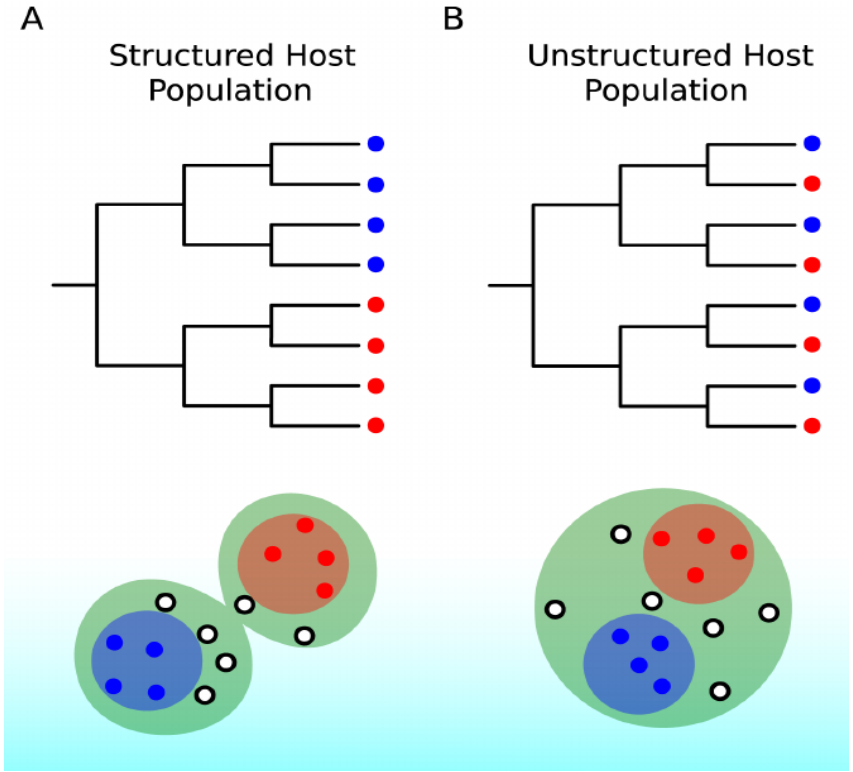
Phylodynamics of fast-evolving pathogens

Inferring spatial and temporal dynamics from genomic data:

Phylogenies*!

* plus complicated models





Trees and the coalescent

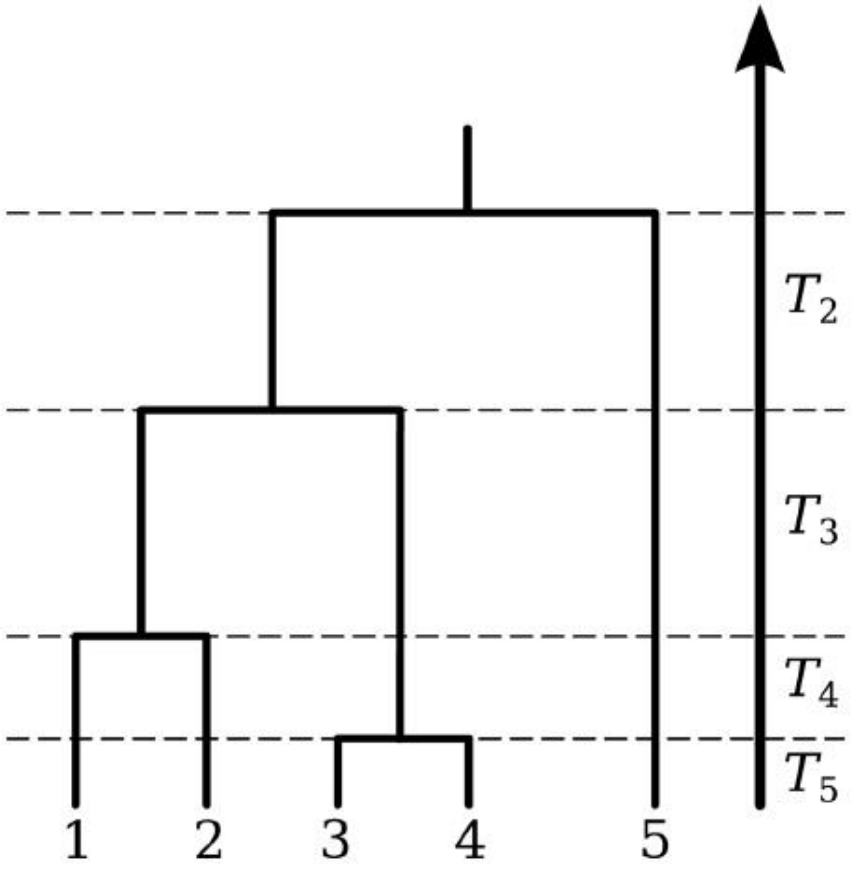


Figure: Figure 4 from Volz et al. (2013).

Let T_n denote the time for n lineages to *coalesce*, i.e., merge into one ancestral lineage, in a population of size N_e. Then:

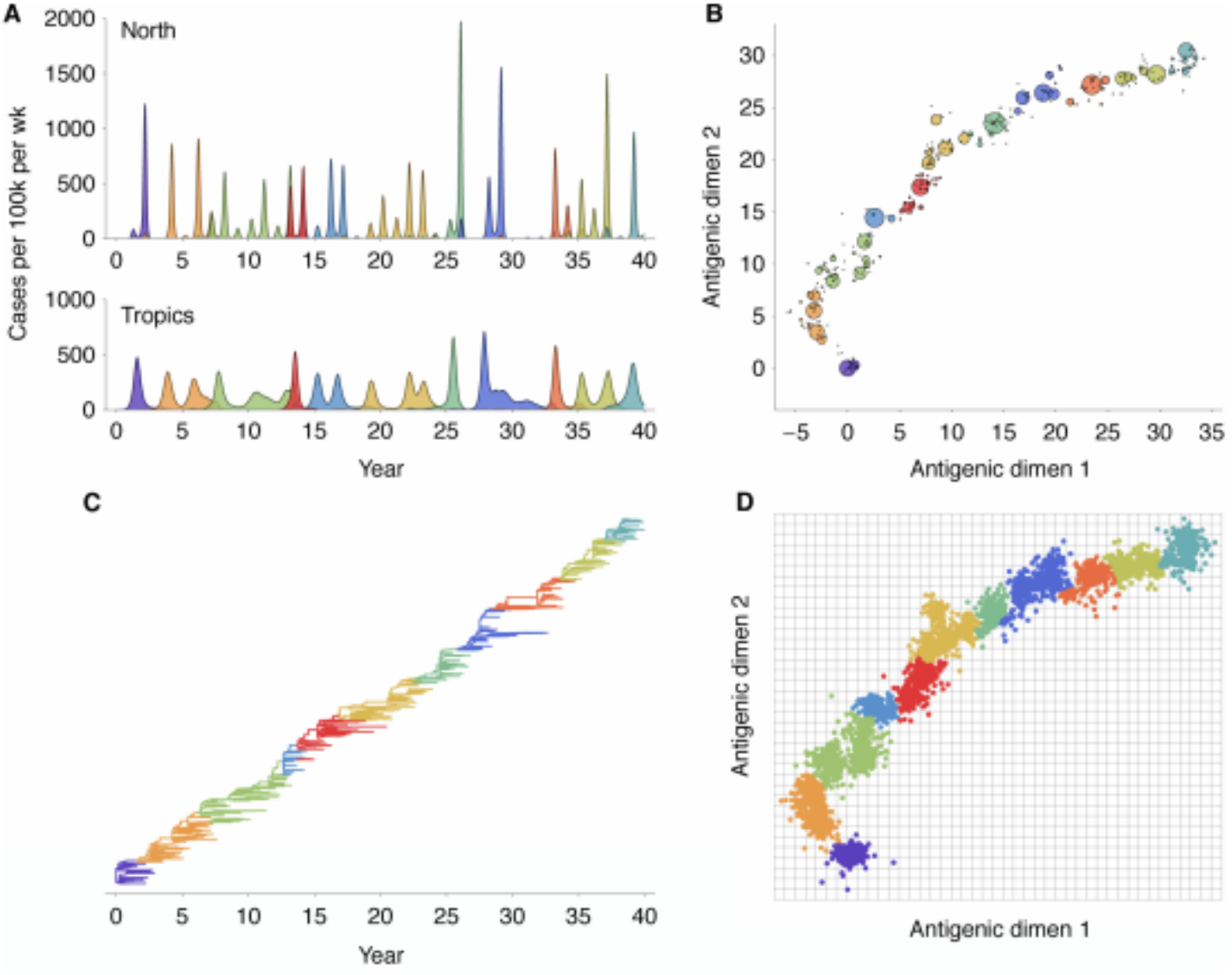
$$Pr(T_n = t) = \lambda_n e^{-\lambda_n t}$$

$$\lambda_n = \binom{n}{2} \frac{1}{N_e} = \binom{n}{2} \frac{1}{N_e \tau}$$

where N_e is the effective population size and τ is the generation time. Let T_{mrca} denote the age of the most recent common ancestor:

$$\begin{aligned} \mathbb{E}[T_{\text{mrca}}] &= \mathbb{E}[T_n] + \mathbb{E}[T_{n-1}] + \ldots + \mathbb{E}[T_2] \\ &= 1/\lambda_n + 1/\lambda_{n-1} + \ldots + 1/\lambda_2 \\ &= 2N_e \left(1 - \frac{1}{n}\right) \end{aligned}$$

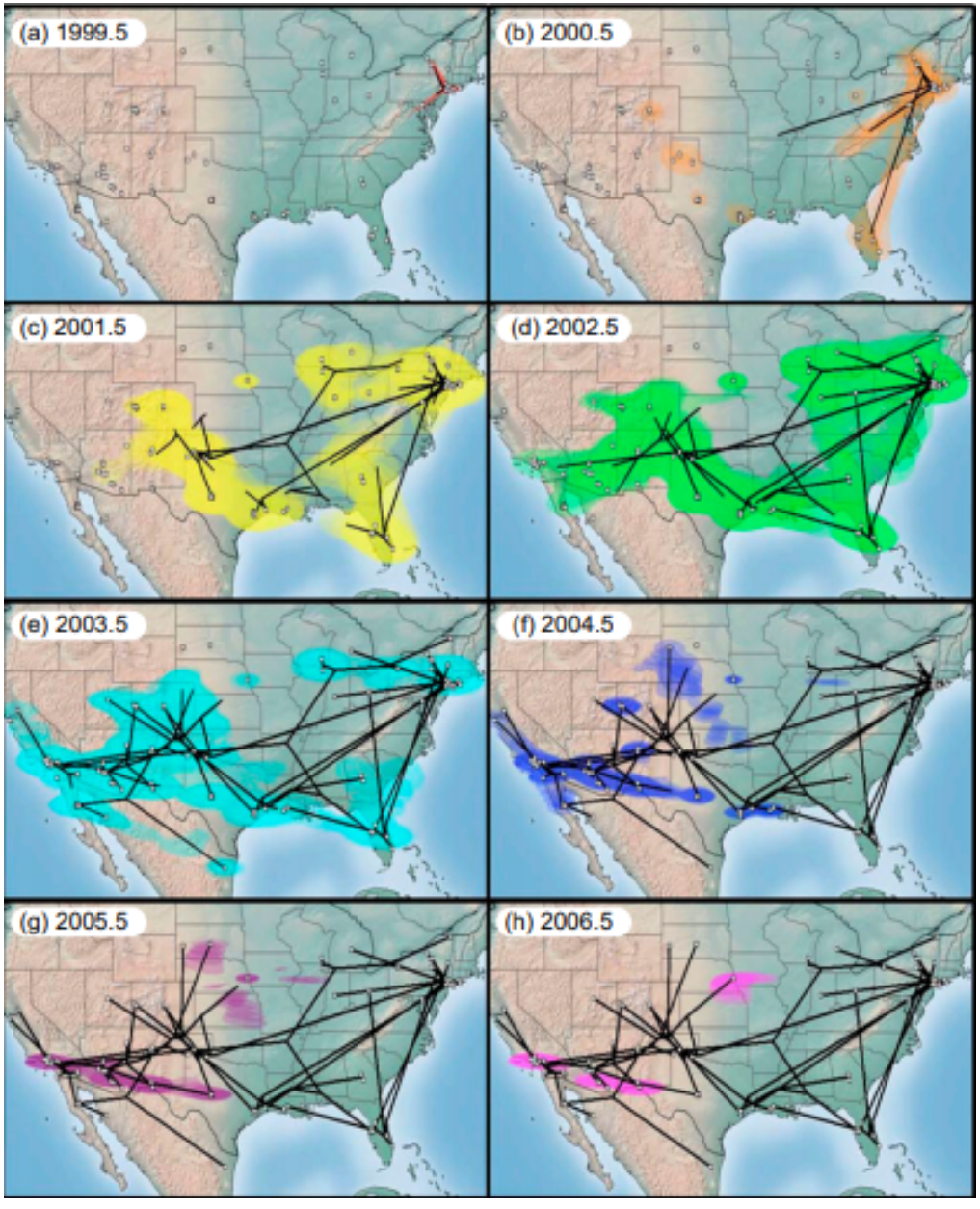
Example I: Antigenic evolution in Influenza H3N2



Antigenic evolution in Influenza H3N2: details

Antigenic evolution in Influenza H3N2: findings

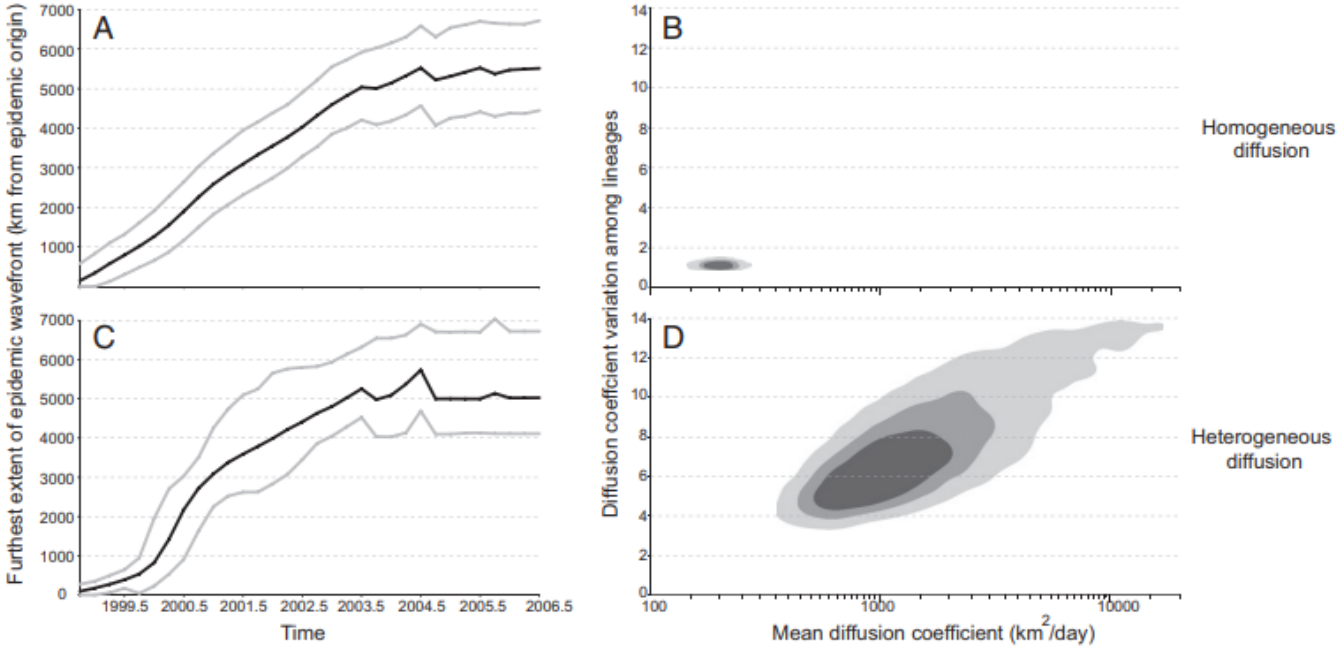
Example II: West Nile Virus in the United States of America



West Nile Virus in the USA: details

- Study from 2012, used 104 complete WNV genomes (11,029 nt);
- Employed a random walk diffusion model.

$$D \approx \frac{1}{n} \sum_{i=1}^{n} \left(\frac{d_i}{2t_i} \right)^2 \tag{1}$$



West Nile Virus in the USA: findings

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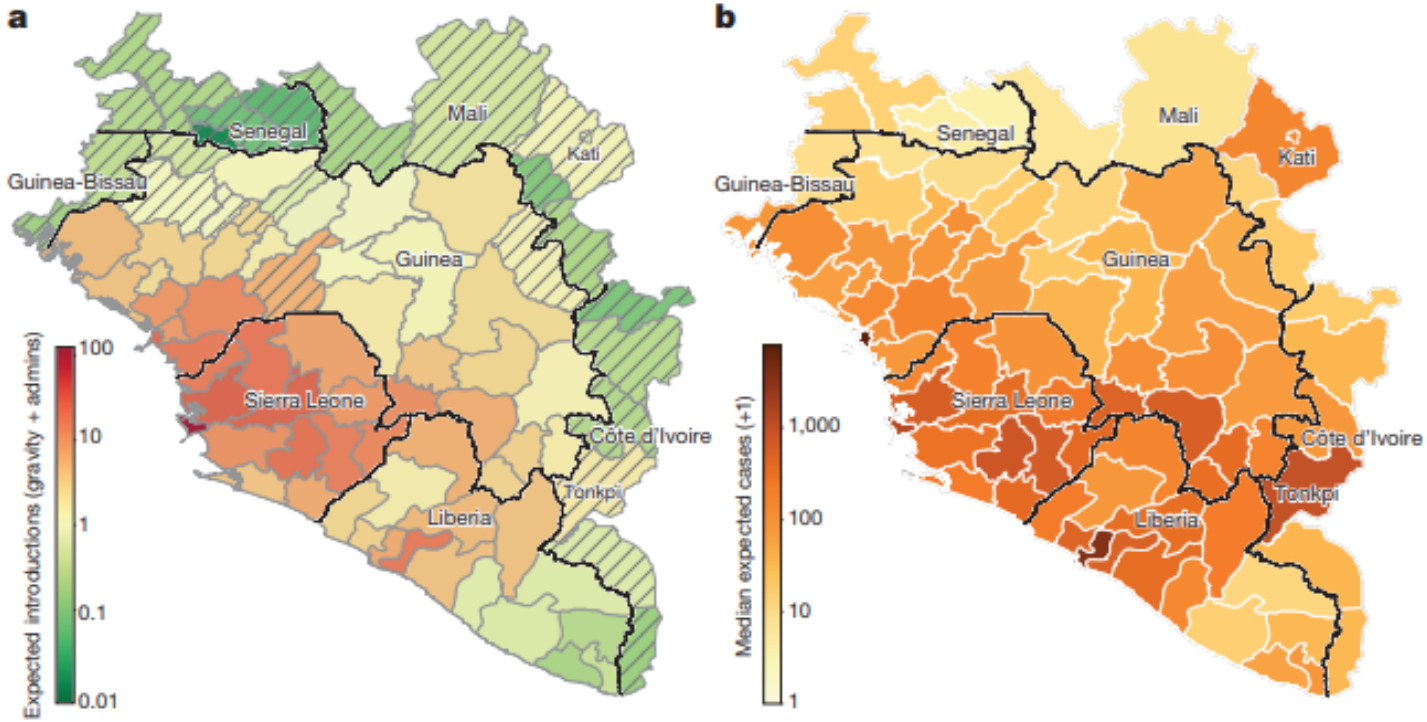
- Epidemic acceleration rate estimated from genomic data is almost **identical** to what was estimated from large-scale patterns of spatiotemporal WNV incidence;
- Rare, long range movements **unlikely to be detected in the field**;
- Traditional approaches overestimate R_0 by ignoring heterogeneity between lineages.

Example IIIa: Ebola epidemics in West Africa

[animation]



Ebola epidemics in West Africa: details

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- Study from 2017, used 1610 (!) full EBOV genomes (18,992 nt);
- Employed a phylogeographic generalised linear model:

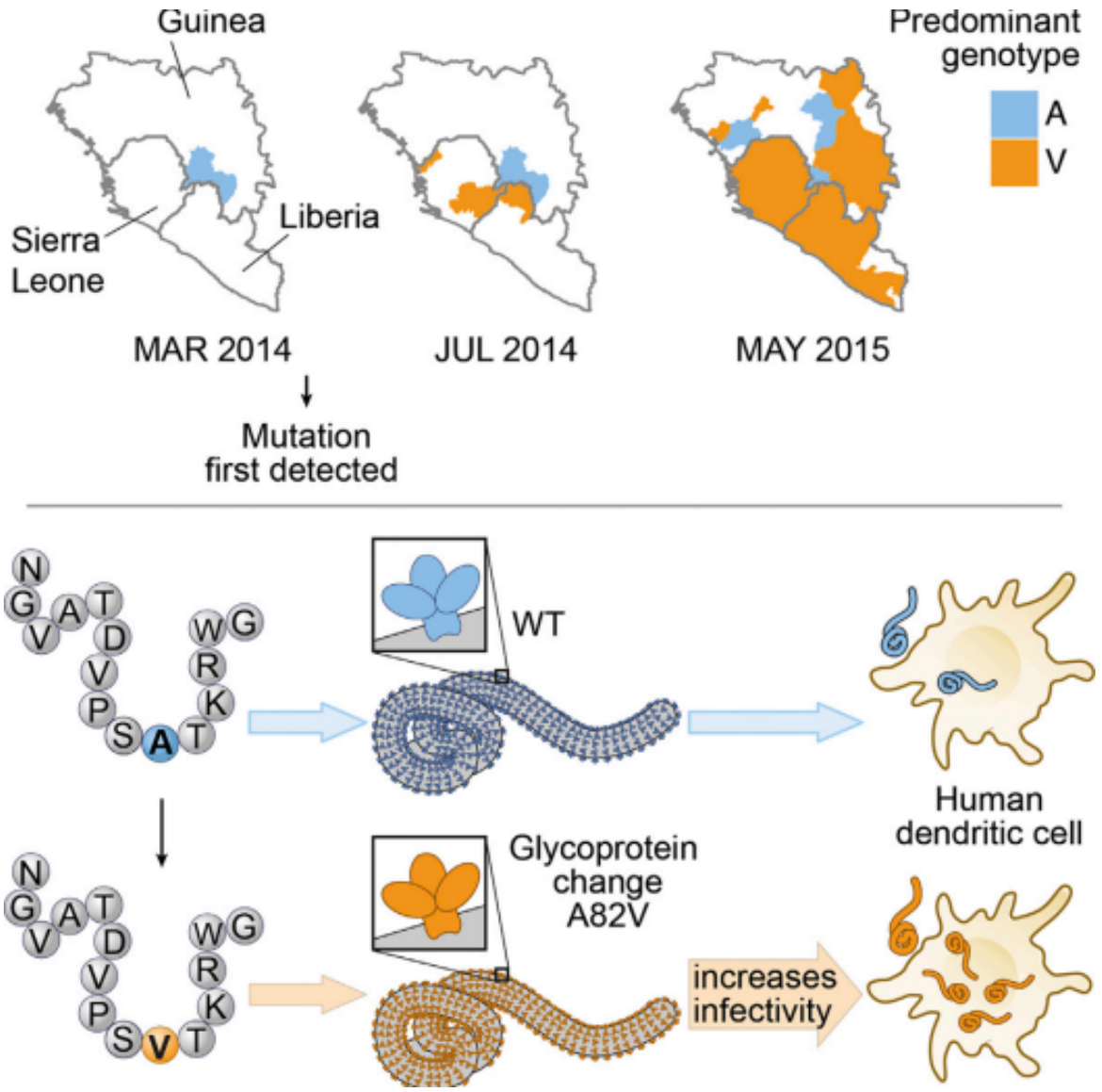
$$\log \Lambda_{ij} = X_{ij}^T \delta\boldsymbol{\beta} + \epsilon_i + \epsilon_j,$$
$$\epsilon_k \sim \text{Normal}(0, \sigma^2) \text{ for } k = 1, \ldots, K, \text{ with}$$
$$\sigma^2 \sim \text{Inverse-Gamma}(0.001, 0.001),$$
$$\beta_j \sim \text{Normal}(0, 16).$$

Table 2 | Summary of generalized linear model results with case counts as the response variable

Predictor*	Description	Coefficient†	95% CI‡	Inclusion§	BF‖
TempSS	Temperature seasonality	−1.1	−1.6, −0.5	0.83	>50
TT50K	Time to travel to a population centre of 50,000 people	−0.9	−1.4, −0.4	0.62	32.4
PopSize	Population size	0.9	0.3, 1.6	0.60	29.6
Precip	Precipitation	0.8	0.2, 1.3	0.18	4.4
TT100K	Time to travel to a population centre of 0.1 million people	−0.8	−1.7, −0.1	0.16	3.8

*Predictors included in the model with Bayes factor >3.
†Mean coefficient.
‡95% highest posterior density credible interval (CI).
§Probability that the predictor was included in the model.
‖BF, Bayes factor.

Example IIIb: GPA82V mutation and mortality



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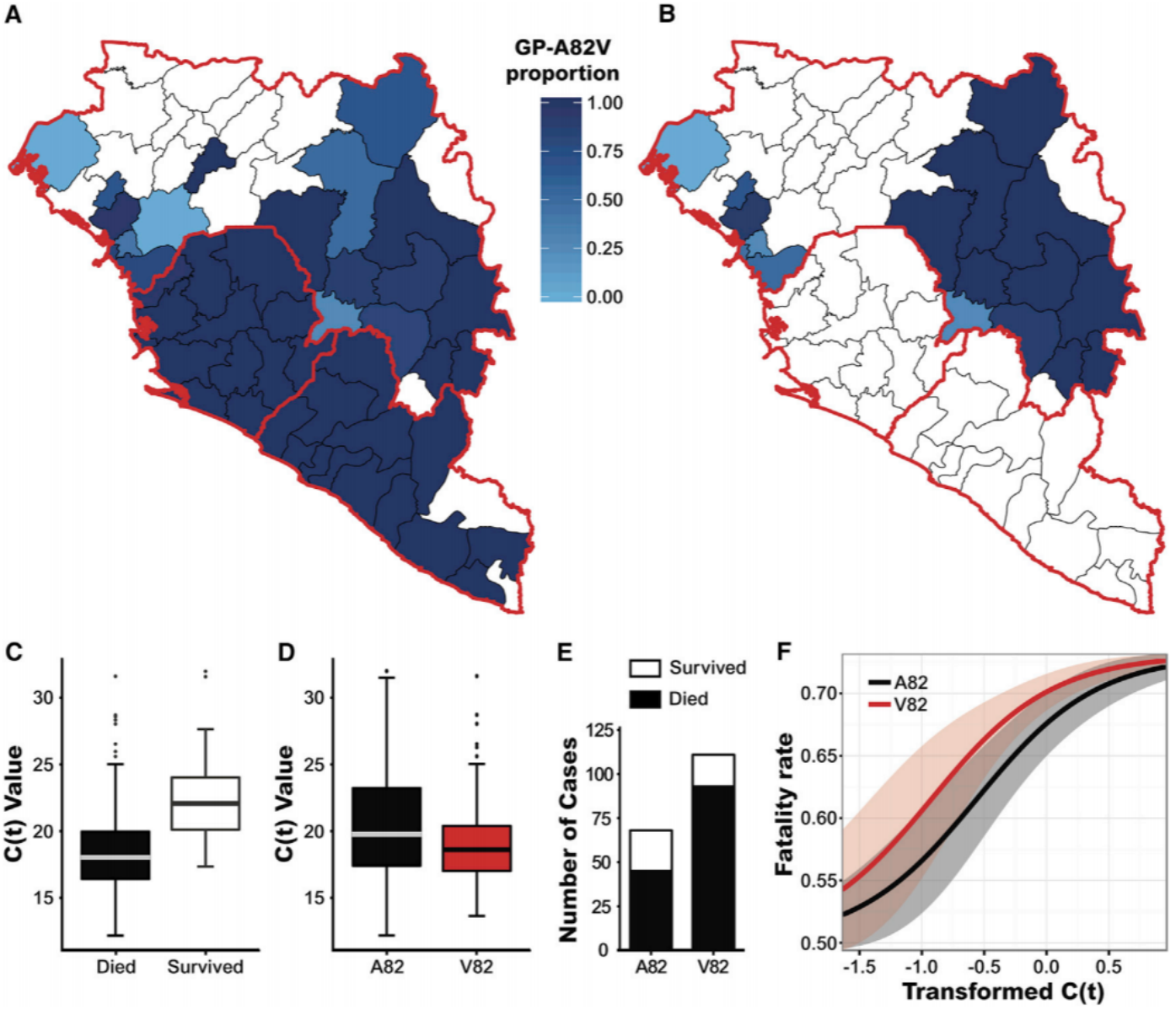

Lessons learned so far

Phylodynamics can help us

- Integrate genetic and antigenic data to understand immune escape;

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- Integrate genetic and antigenic data to understand immune escape;
- Uncover previously undetectable routes of pathogen spatial spread;
- Estimate the rate of spatial spread of an epidemic, its R_0 and drivers of spread;
- Study clinical outcomes while controlling for underlying dependencies.

New developments: ARTIC network

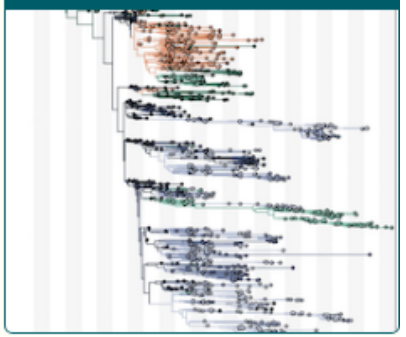
http://artic.network/

The field laboratory

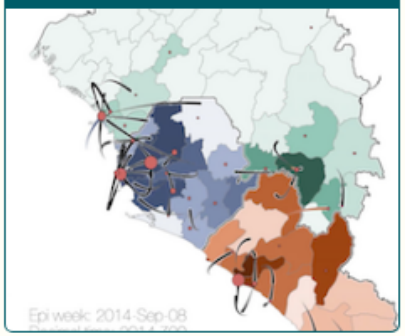
Portable sequencing

Deployable bioinformatics

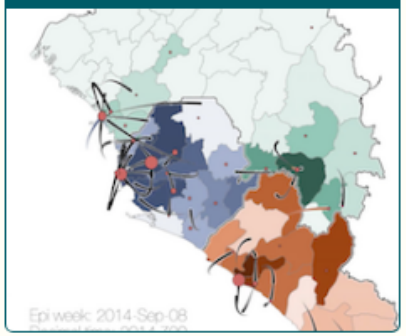
Real-time phylodynamics



Visualisation and interpretation



Tools and resources



Funded by the Wellcome Trust

Collaborators Award 206298/Z/17/Z --- ARTIC network

Lab in a suitcase

- Develop portable sample inactivation and reagent/sample preparation;

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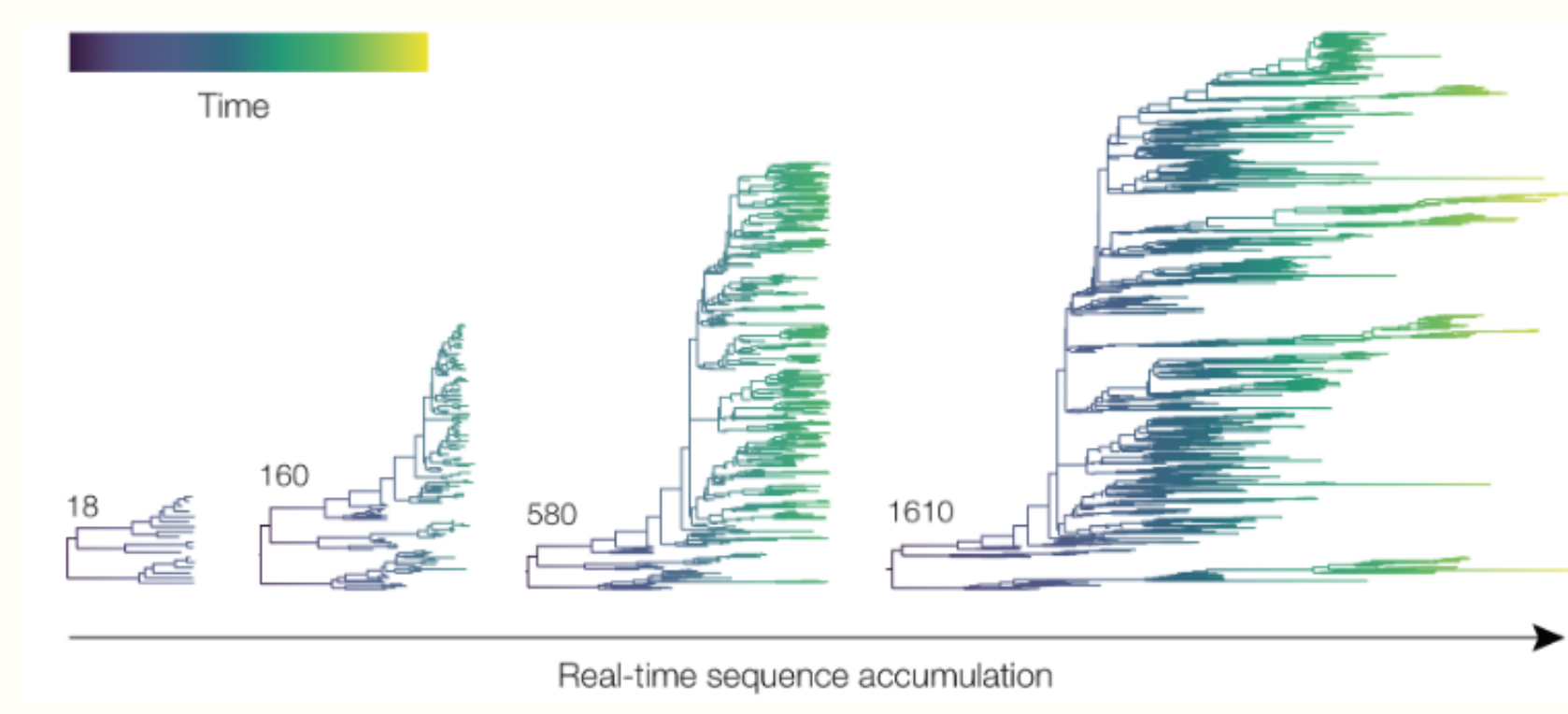
- Reducing contamination risk.

Real time phylodynamics



- Build trees and make inferences as sequences arrive;

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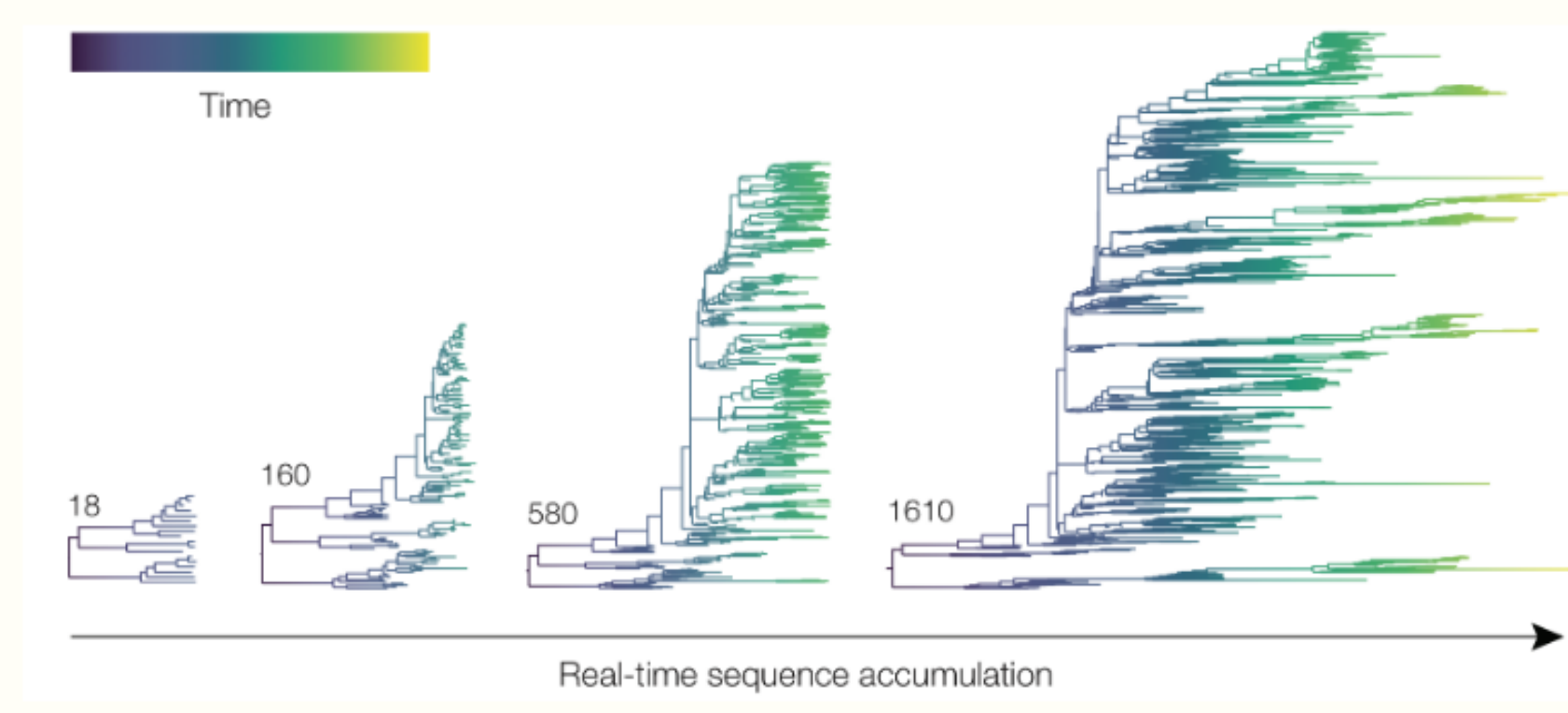

- Build trees and make inferences as sequences arrive;
- Sequential Monte Carlo (SMC).

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DNA sequences from pathogens +
environmental/socio-economic data can give us insight

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Developing better statistical models and computational tools is crucial.

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We need more and better data.

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Nature is complicated

We need better models to go along.

THE END