



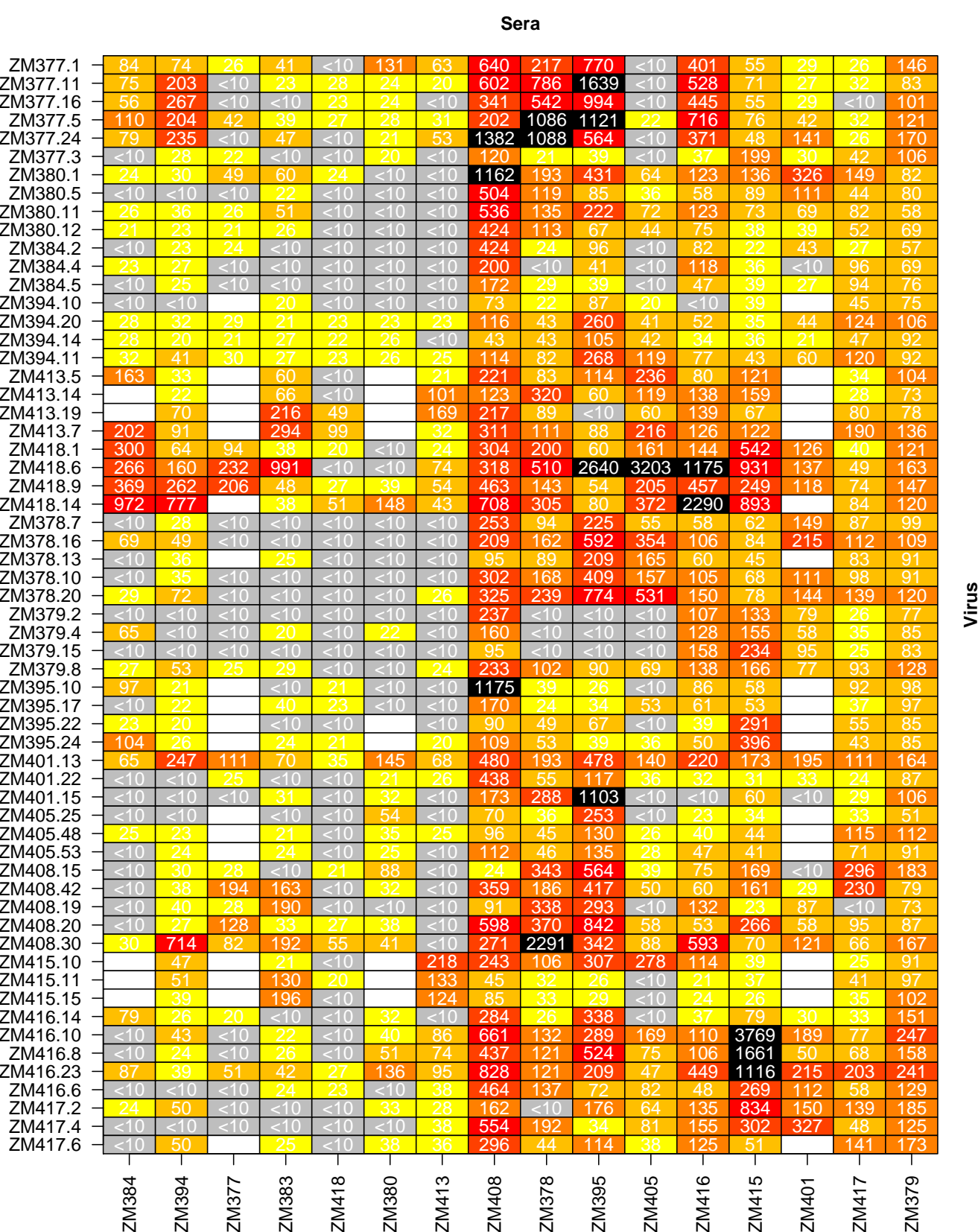
Background

- ▶ Recombinant-virus based assays of neutralisation of HIV-1 envelope are routinely used to measure the sensitivity of viruses to neutralisation, and the ability of sera to neutralise viral isolates.
- ▶ It is difficult to visualise antigenic differences, especially when the number of viruses and sera are large.
- ▶ **I present a statistical model to map viruses and sera into antigenic space, and apply it to data from five published studies of HIV-1 neutralisation.**

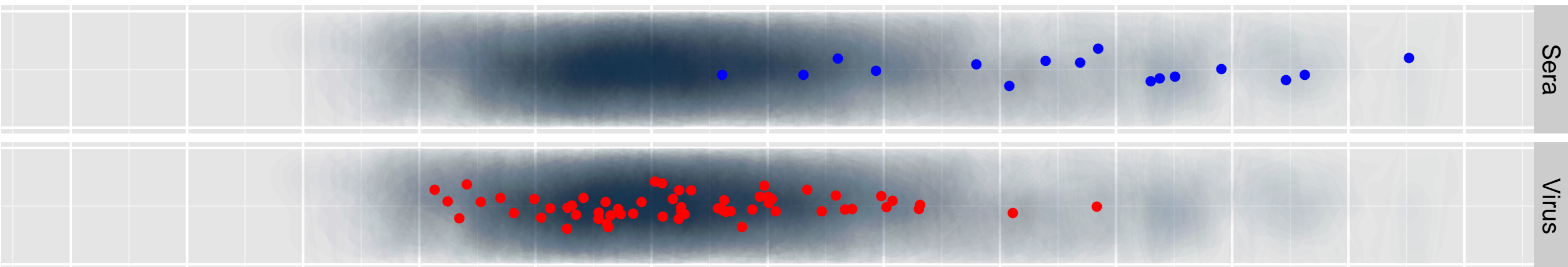
Materials and Methods

- ▶ Data on neutralisation were from published studies were analysed using Bayesian unfolding multidimensional scaling:
- ▶ The model estimates X , a n by p matrix of coordinates in antigenic space of viruses, and Y , a k by p matrix of coordinates in antigenic space of plasma samples.
- ▶ Let y_{ij} denote the \log_2 transformed IC_{50} neutralization titer between virus i and plasma j
- ▶ The observed dissimilarity measure, d_{ij} , was obtained by normalizing the data using the maximum neutralization for each titer, $d_{ij} = \max y_{i.} - y_{ij}$
- ▶ d_{ij} is assumed to follow a truncated normal distribution, $d_{ij} \sim N(\delta_{ij}, \tau), I(d_{ij} > 0)$, where $i = 1, \dots, n, j = 1, \dots, k$
- ▶ δ_{ij} was calculated assuming a two dimensional map.

Analysis of Kirchherr et al. (2011)



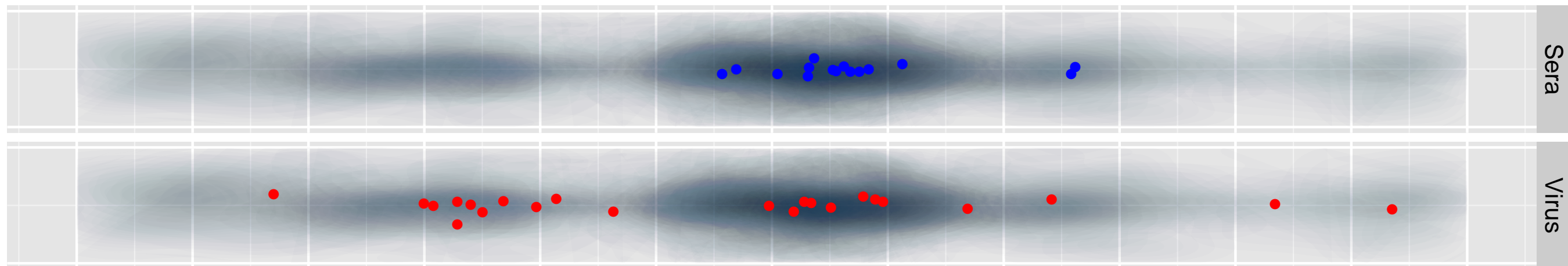
- 60 viruses (including multiple isolates from the same patients), 16 sera
- ▶ Hard to see patterns in the data
 - ▶ Missing data
 - ▶ Measurements below the limit of detection



- ▶ Interpretation of antigenic map
- ▶ Each large square represents a 2-fold difference in neutralisation
- ▶ Distance between viruses represents similarity in neutralisation sensitivity
- ▶ Distance between sera represents similarity in their ability to neutralise diverse viruses (controlling for magnitude)
- ▶ Distances between viruses and sera represent similarity in sensitivity to specific sera, relative to the most sensitive virus in the panel

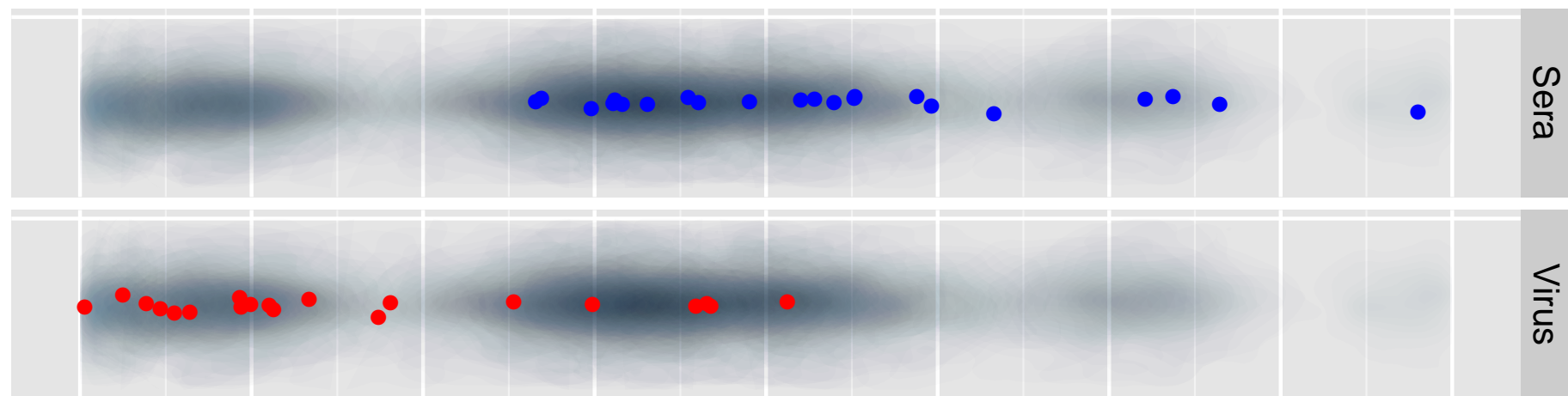
Van Gils et al. (2010)

- ▶ 23 viruses, subtypes A-D, 15 subtype B sera
- ▶ Some apparent clusters of viruses, but *not* related to subtype

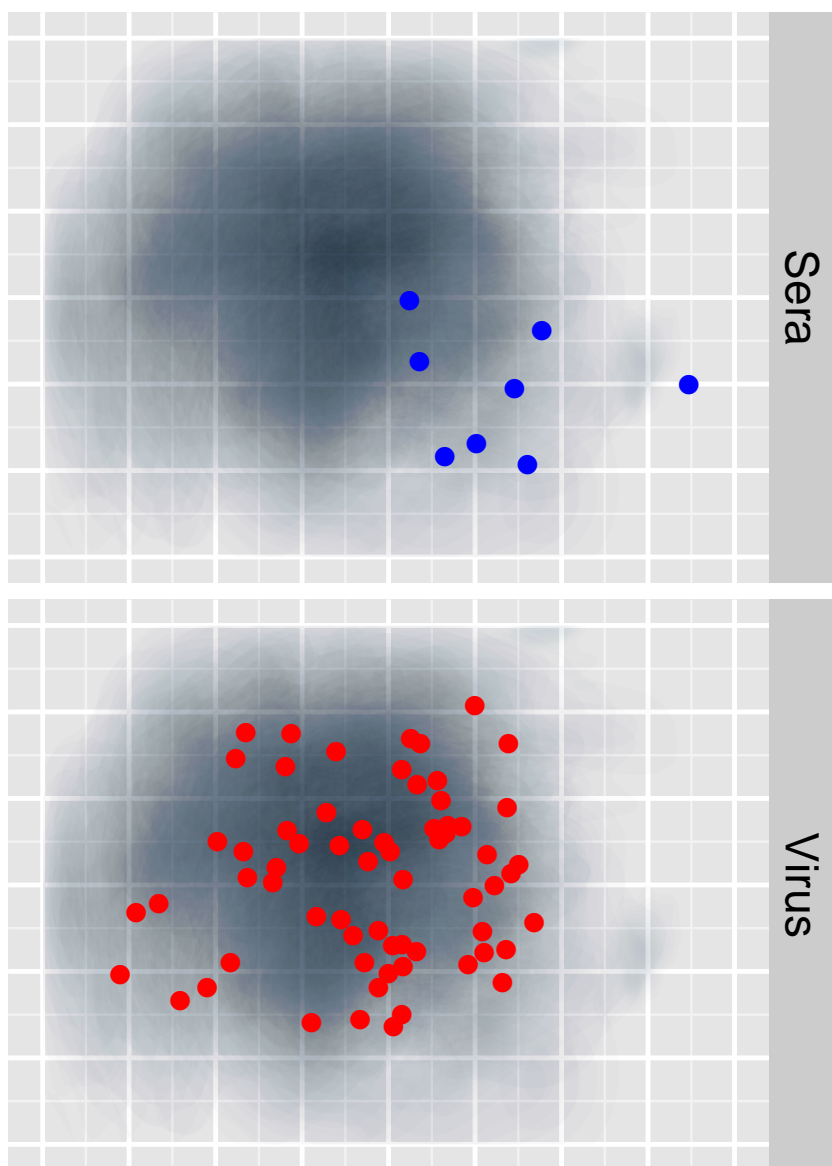


Georgiev et al. (2013)

- ▶ 21 viruses, 22 sera
- ▶ Some clustering of viruses, less antigenic variation than Van Gils et al. (2010)



Ping et al. (2013)



- ▶ 65 viruses, 9 sera (including two immunoglobulin pools)
- ▶ Higher resolution than other datasets; significant two-dimensional variation in the map

Conclusions

- ▶ Differences in neutralisation of HIV-1 can be mapped into 1-2 dimensions without significant loss of information
- ▶ This approach removes confounding of breadth by the overall magnitude of the response
- ▶ Without knowing the number of antibodies in a sample, we cannot compare sera without normalisation
- ▶ 'Broadly-reactive' sera exhibit similar patterns of neutralisation across viral isolates.
- ▶ Extensive, often continuous, antigenic distances between viruses.
 - ▶ Not related to subtype, and only weakly associated with specific positions.

References

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2. J. L. Kirchherr *et al.*, *Virology* **409**, 163–174 (2011).
3. M.-S. Oh, A. E. Raftery, *JASA* **96**, 1031–1044 (2001).
4. L.-H. Ping *et al.*, *J Virol* (2013).
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