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Supplemental information

Antigenic cartography of well-characterized human sera shows SARS-CoV-2 neutralization differences based on infection and vaccination history

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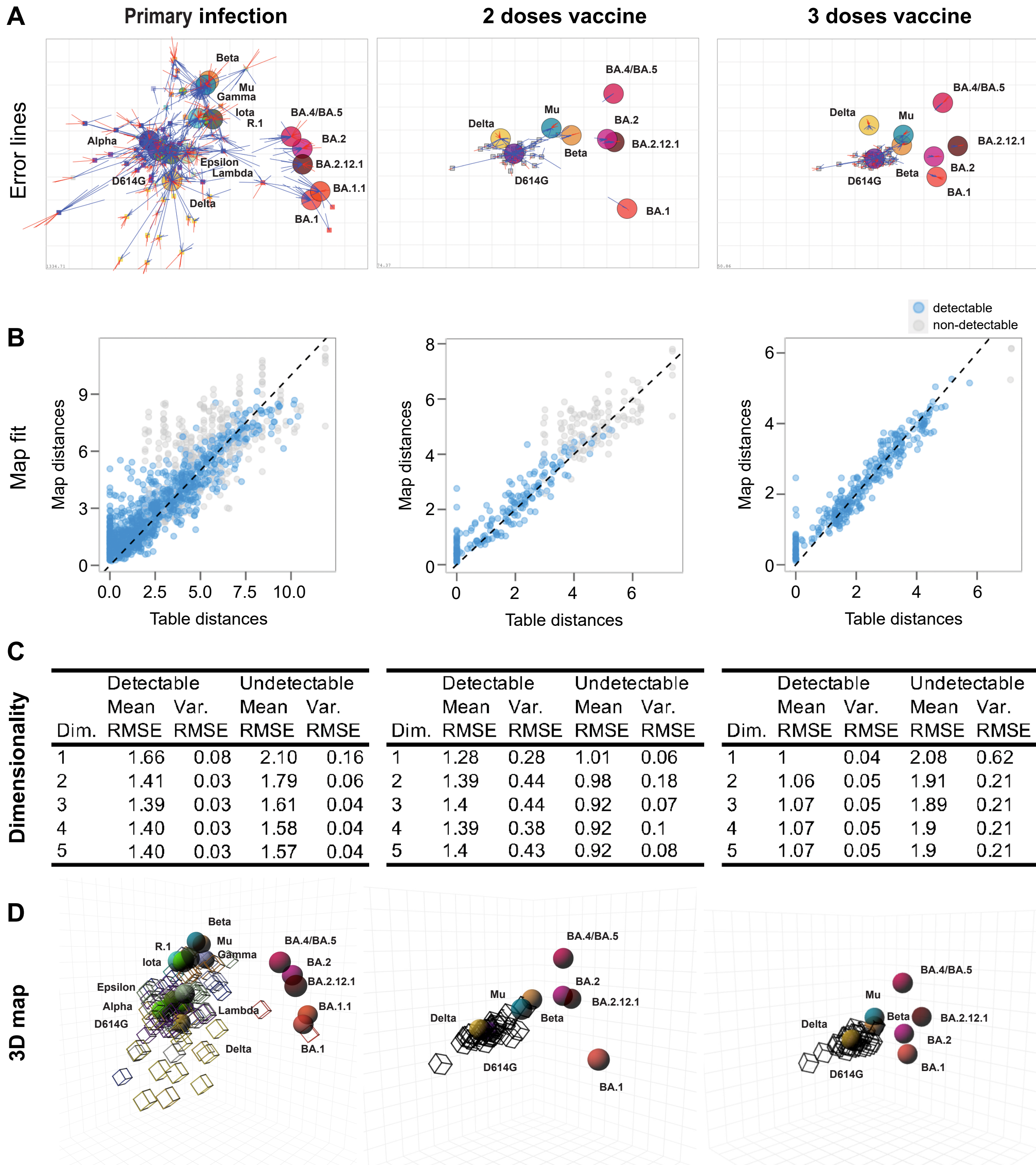


Dim.	Detectable Mean RMSE	Detectable Var. RMSE	Undetectable Mean RMSE	Undetectable Var. RMSE
1	1.66	0.08	2.10	0.16
2	1.41	0.03	1.79	0.06
3	1.39	0.03	1.61	0.04
4	1.40	0.03	1.58	0.04
5	1.40	0.03	1.57	0.04

Dim.	Detectable Mean RMSE	Detectable Var. RMSE	Undetectable Mean RMSE	Undetectable Var. RMSE
1	1.28	0.28	1.01	0.06
2	1.39	0.44	0.98	0.18
3	1.4	0.44	0.92	0.07
4	1.39	0.38	0.92	0.1
5	1.4	0.43	0.92	0.08

Dim.	Detectable Mean RMSE	Detectable Var. RMSE	Undetectable Mean RMSE	Undetectable Var. RMSE
1	1	0.04	2.08	0.62
2	1.06	0.05	1.91	0.21
3	1.07	0.05	1.89	0.21
4	1.07	0.05	1.9	0.21
5	1.07	0.05	1.9	0.21

Figure S1. Evaluation of goodness of fit and dimensionality for antigenic maps made with primary infection sera (left column), two doses vaccine sera (middle column), and three dose svaccine sera (right column), related to Figure 2. Sera are shown as small colored squares, viruses as large circles. The grid corresponds to a two-fold dilution in the neutralization assay. **(A)** antigenic map with error lines. The distance between the ends of error lines indicates the measured titer: red lines indicate that the map distance is less than the measured titer, blue l nes that the map distance is greater than the measured titer.
(B) difference between the table distance (estimated from the measured titer) and the fitted

map distance. The dotted horizontal line shows what would be perfect a perfect fit of the data.
(C) results of dimensionality testing. Cross-validation (excluding 10% of titers as a test set in 100 independent repeats) was used to determine the optimal number of dimensions. Lower root mean squared error (RMSE) for both detectable titers (above the assay limit of detection) and undetectable (below the assay limit of detection) indicate the optimal number of dimensions for fitting the antigenic map.
(D) antigenic maps made in three dimensions.

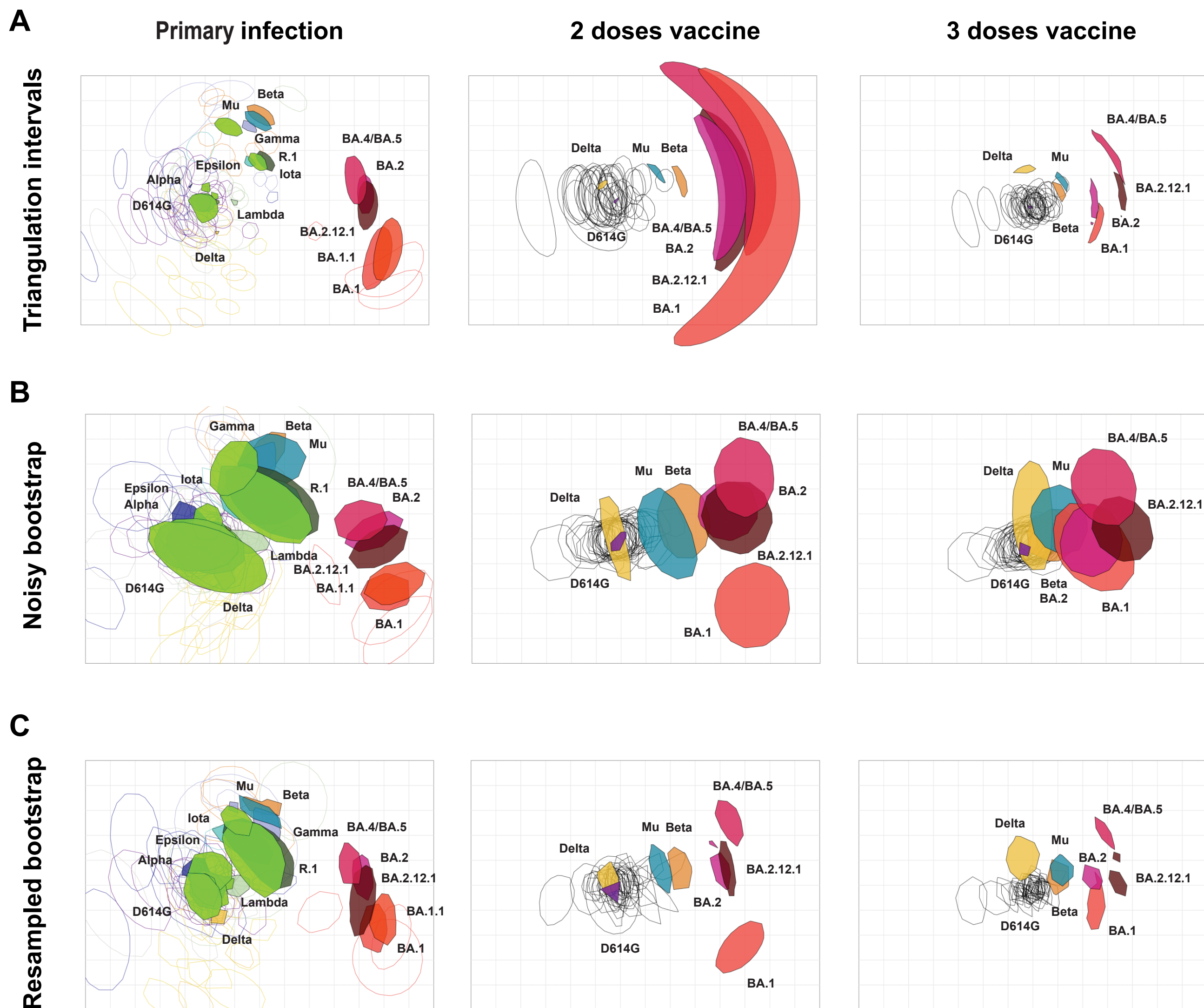


Figure S2. Evaluation of robustness in positioning for viruses and sera on antigenic maps made with primary infection sera (left column), two-dose vaccinee sera (middle column), and three-dose vaccinee sera (right column), related to Figure 2. Sera are shown as open shapes, viruses as colored shapes. The grid corresponds to a two-fold dilution in the neutralization assay. **(A)** Triangulation/coordination confidence intervals, indicating confidence in positioning of points. Each shape marks the area that the point can occupy before increasing the total map error by more than 1 antigenic unit.
(B) Bootstrapped maps considering titer error for the neutralization assay. The shapes correspond to the positions of points on resampled maps assuming titers have random noise added with the measured assay standard deviation of log2 0.29 (1.2-fold).
(C) Confidence in coordination of points following bootstrapping of the sera and viruses.

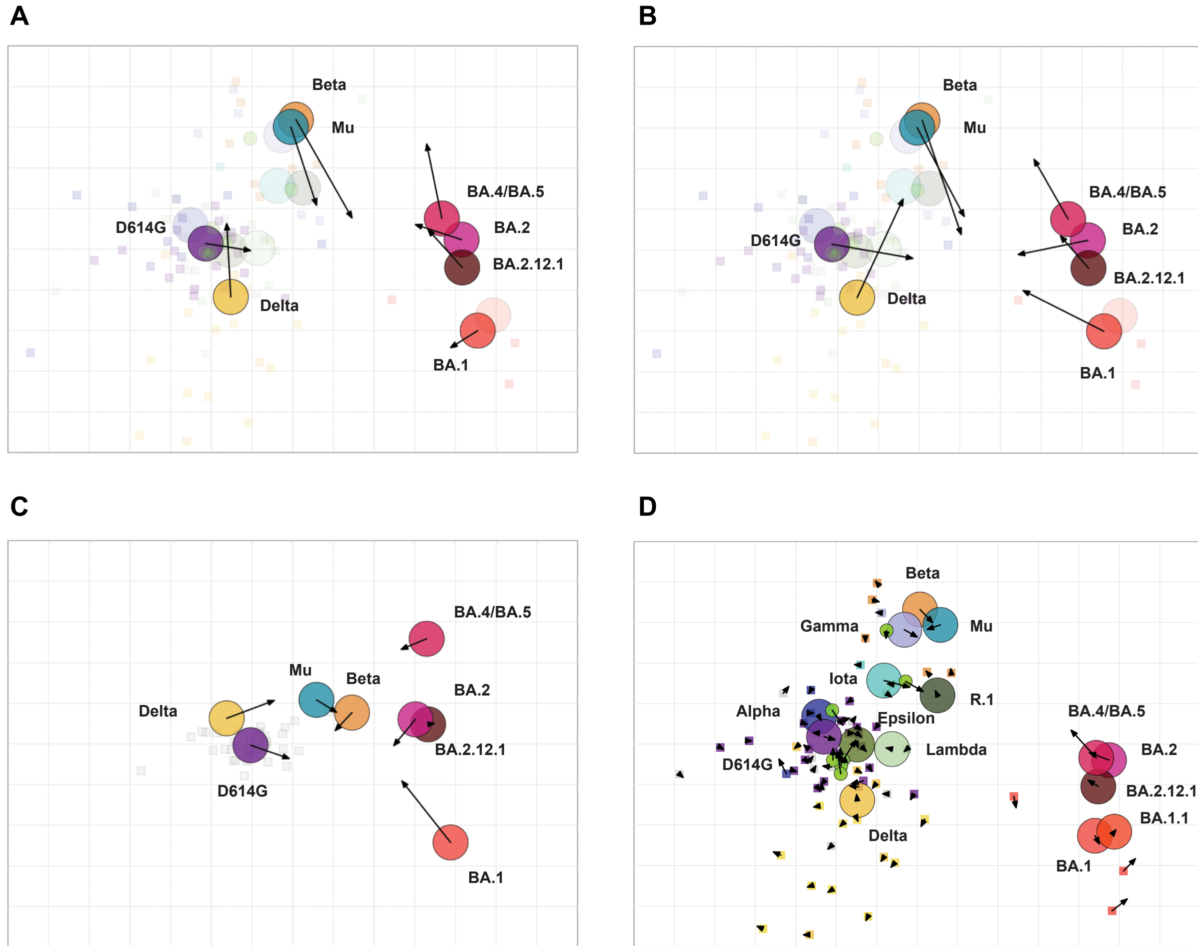
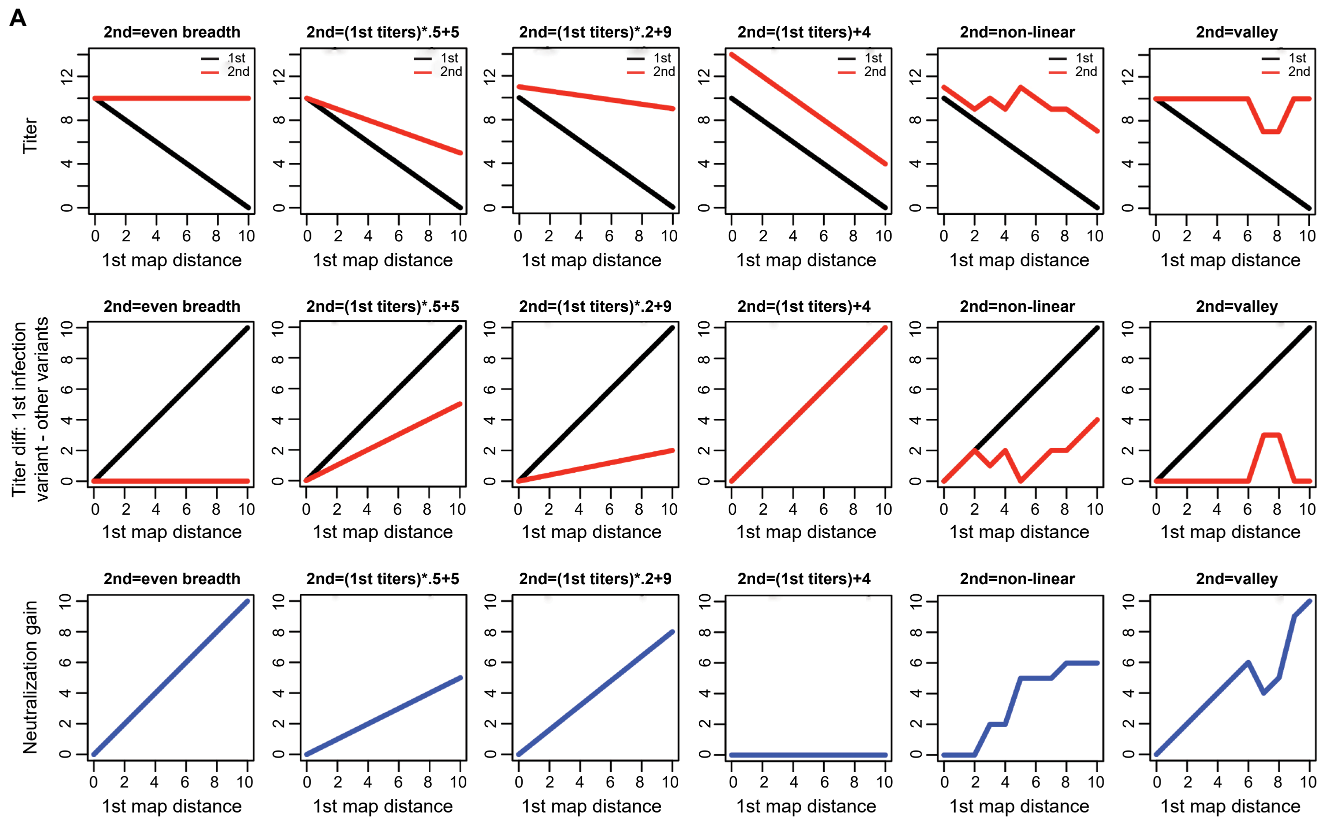


Figure S3. Comparison of virus positions between antigenic maps, related to Figure 2.
Arrows point to virus positions from one map to another:
(A) primary infection to 2 dose vaccine,
(B) primary infection to 3 doses vaccine,
(C) 2 doses to 3 doses vaccine
(D) primary infection map excluding sera collected <6 days post symptom onset (n=21 of 83 sera excluded) to the full primary infection map.
Sera are shown as small squares, viruses as colored circles. The grid corresponds to a two-fold dilution in the neutralization assay.



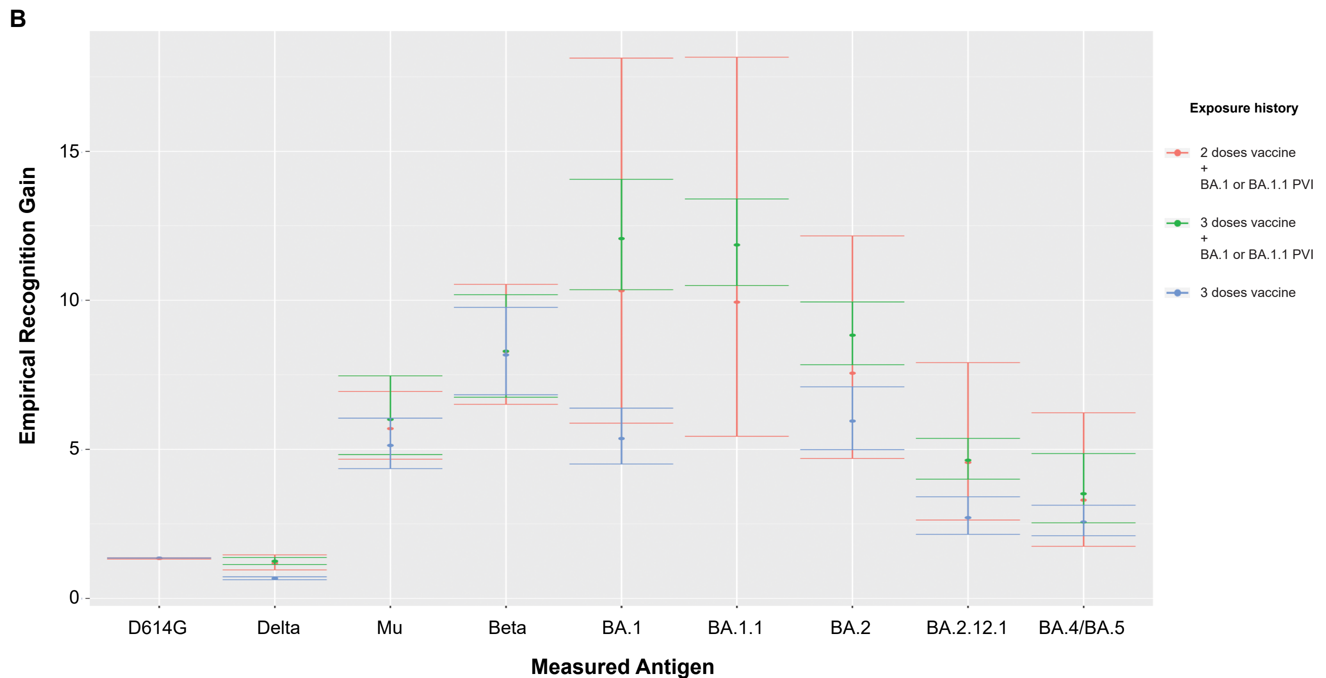


Figure S4. Explanation of the neutralization gain plot, related to Figure 4.
(A) Explanation and intuition of the neutralization gain plot. **Top panel**: Example neutralization titers following primary and secondary infection. The x-axis shows antigenic distance of the tested antigen from the first infecting antigen. The y-axis shows the titer (in antigenic units, i.e. log2(titer/10)) for each group. Across all examples, the same response for primary

infection and different secondary infection responses is shown. The titles of these plots indicate the kind of secondary neutralization titers shown. **Middle panel**: for primary and secondary responses, the difference in titer between the first infecting antigen and each other antigen is plotted. **Bottom panel**: The neutralization gain plot, i.e. how much additional neutralization is observed after secondary infection compared to primary infection.
(B) Empirical neutralization gain plot, where the primary infection differences are estimated directly from the data instead of from the antigenic map. For each secondary exposure serum, the fold neutralization gain (y-axis) against each measured antigen (shown on the x-axis) relative to the average response amongst primary wild-type sera against that measured antigen is calculated. For summary statistics and comparisons, sera are grouped by exposure history (denoted by colors). Points denote the mean fold neutralization gain, while error bars denote confidence interval bounds (mean +/- 2 times the standard error).