



**Figure S1: Evolutionary rates of the influenza virus hemagglutinin head and stalk domains. (A)** Linear schematic of the HA molecule and partitions used for analysis. The stalk domain amino acid demarcations are shown on the figure for H1 and H3 on the left (black) and influenza B on the right (blue). **(B-C)** Evolutionary rates of influenza A virus or influenza B whole hemagglutinin (peach), stalk/transmembrane/cytoplasmic domains (STC) (grey), head (blue) and, stalk (green) domains. The mean (indicated by black dots) and 95% credible interval of BEAST runs (using a single dataset) are shown in nucleotide substitutions/site/year (n/s/t).

**Table S1: Summary of evolutionary rates of head and stalk domains of sH1N1, pH1N1, H3N2, B/Yamagata/16/88-like and B/Victoria/2/87-like viruses based on a functional partitioning model.** Bayes factor is defined as  $\Pr(\text{Head} > \text{Stalk}) / \Pr(\text{Stalk} > \text{Head})$  divided by the prior ( $\sim 1$ ).

| Virus | Mean Whole HA Evolutionary Rate (n/s/y) | Mean STC Evolutionary Rate (n/s/y) | Mean Head Evolutionary Rate (n/s/y) | Mean Stalk Evolutionary Rate (n/s/y) | Bayes Factor |
|-------|---|------------------------------------|-------------------------------------|--------------------------------------|--------------|
| sH1N1 | $2.46 \times 10^{-3}$                   | $2.18 \times 10^{-3}$              | $3.56 \times 10^{-3}$               | $2.42 \times 10^{-3}$                | infinite     |
| pH1N1 | $4.35 \times 10^{-3}$                   | $4.00 \times 10^{-3}$              | $5.64 \times 10^{-3}$               | $5.18 \times 10^{-3}$                | 7.1          |
| H3N2  | $4.16 \times 10^{-3}$                   | $2.55 \times 10^{-3}$              | $4.76 \times 10^{-3}$               | $3.73 \times 10^{-3}$                | infinite     |
| B/Vic | $2.80 \times 10^{-3}$                   | $1.89 \times 10^{-3}$              | $2.98 \times 10^{-3}$               | $2.70 \times 10^{-3}$                | 7.7          |
| B/Yam | $2.73 \times 10^{-3}$                   | $1.58 \times 10^{-3}$              | $3.20 \times 10^{-3}$               | $2.37 \times 10^{-3}$                | infinite     |

**Table S2: Summary of likelihood ratio tests.** These tests were conducted on the non-partitioned, whole HA sequences versus the partitioned (STC, head, stalk) HA sequences. The significance indicates the probability of the partitioned model performing better than the non-partitioned model.

|       |                             |                                 | LRT statistics | degrees of freedom | critical value for chi-square with significance level =0.001 | P-value for supporting Partitional model |
|-------|-----------------------------|---------------------------------|----------------|--------------------|--|--|
| sH1N1 | <b>nucleotide model</b>     |                                 |                |                    |  |  |
|       | Partitioned Log(Likelihood) | Non-partitioned Log(Likelihood) |                |                    |  |  |
|       | -19409.315                  | -20214.554                      | 1610.478       | 2                  | 13.816   | P-Value < 0.00001                        |
|       | <b>codon model</b>          |                                 |                |                    |  |  |
|       | Partitioned Log(Likelihood) | Non-partitioned Log(Likelihood) |                |                    |  |  |
|       | -18845.1                    | -19656.2                        | 1622.2         | 2                  | 13.816   | P-Value < 0.001                          |
| pH1N1 | <b>nucleotide model</b>     |                                 |                |                    |  |  |
|       | Partitioned Log(Likelihood) | Non-partitioned Log(Likelihood) |                |                    |  |  |
|       | -13923.459                  | -14551.487                      | 1256.056       | 2                  | 13.816   | P-Value < 0.00001                        |
|       | <b>codon model</b>          |                                 |                |                    |  |  |
|       | Partitioned Log(Likelihood) | Non-partitioned Log(Likelihood) |                |                    |  |  |
|       | -13428.9                    | -14060.8                        | 1263.8         | 2                  | 13.816   | P-Value < 0.001                          |

|       |                                |                                    |          |   |        |                   |
|-------|--------------------------------|------------------------------------|----------|---|--------|-------------------|
|       | Partitioned<br>Log(Likelihood) | Non-partitioned<br>Log(Likelihood) | 1383.106 | 2 | 13.816 | P-Value < 0.00001 |
|       | -19064.542                     | -19756.095                         |          |   |        |                   |
|       | <b>codon model</b>             |                                    |          |   |        |                   |
|       | Partitioned<br>Log(Likelihood) | Non-partitioned<br>Log(Likelihood) |          |   |        |                   |
|       | -18497.1                       | -19183.5                           | 1372.8   | 2 | 13.816 | P-Value < 0.001   |
| B/Vic | <b>nucleotide model</b>        |                                    |          |   |        |                   |
|       | Partitioned<br>Log(Likelihood) | Non-partitioned<br>Log(Likelihood) |          |   |        |                   |
|       | -10027.183                     | -10410.123                         | 765.88   | 2 | 13.816 | P-Value < 0.00001 |
|       | <b>codon model</b>             |                                    |          |   |        |                   |
|       | Partitioned<br>Log(Likelihood) | Non-partitioned<br>Log(Likelihood) |          |   |        |                   |
|       | -9527.88                       | -9912.66                           | 769.56   | 2 | 13.816 | P-Value < 0.001   |
| B/Yam | <b>nucleotide model</b>        |                                    |          |   |        |                   |
|       | Partitioned<br>Log(Likelihood) | Non-partitioned<br>Log(Likelihood) |          |   |        |                   |
|       | -9291.626                      | -9633.68                           | 684.108  | 2 | 13.816 | P-Value < 0.00001 |
|       | <b>codon model</b>             |                                    |          |   |        |                   |
|       | Partitioned<br>Log(Likelihood) | Non-partitioned<br>Log(Likelihood) |          |   |        |                   |
|       | -8793.41                       | -9135.43                           | 684.04   | 2 | 13.816 | P-Value < 0.001   |