**Infection round 1: Antigenic shift and drift**

Each round consists of 3 actions:

1. Acquire a new ‘flu virus [in the first round, do this by drawing randomly from the pool of available viruses; in subsequent rounds, do this by passing viruses clockwise in your group]
2. Determine the outcome of the virus infection [roll the die]
3. Replicate the virus (or not) depending on the outcome of the roll.

You should play until you have **six** viral genotypes recorded in Table 2.

**Table 1. Dice rules for determining the outcome of a ‘flu virus infection.**

|  |  |
| --- | --- |
| **Roll** | **Outcome** |
| 1 | **Pre-existing immunity:** virus does not infect/replicate [do not record in Table 2; return virus to the general pool] |
| 2, 4, 5 | **Infection**: the virus is able to replicate. Record starting genome state in Table 2 & add a mutation to 1 segment randomly (+0.1 to the allele number) before passing it on |
| 3 | **Co-infection!**: draw a new virus packet from the general pool 🡪 mix your two viruses and draw 1 of each segment at random 🡪 assemble new viral genome. Record genome in Table 2 & add a mutation to 1 segment randomly (+0.1 to the allele number) before passing it on |
| 6 | **Superspreader!** virus infects and replicates in several hosts. [record genome 2x in Table 2 & add a mutation to 1 segment randomly (+0.1 to the allele number) before passing it on |

Give each virus isolate a **unique** name (e.g., AB1, AB2…) **Record the allele number** for each genome section, for each infectionin Table 2.

**Table 2. ‘Flu virus alleles**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| virus isolate # | PB2 | PB1 | PA | NP | HA | NA | M | NS |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |

**Construct a phylogenetic tree** representing your viruses.

Fill in Table 3 with the unique names of your virus isolates (e.g., AB1, AB2) and calculate the pairwise Hamming distances based on the number of allele differences.

**Table 3.** Hamming distance matrix for the ‘flu viruses in Table 2 (A)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | \_\_\_\_\_1 | \_\_\_\_\_\_2 | \_\_\_\_\_3 | \_\_\_\_\_4 | \_\_\_\_\_5 | \_\_\_\_\_6 |
| \_\_\_\_\_1 | 0 |  |  |  |  |  |
| \_\_\_\_\_2 |  | 0 |  |  |  |  |
| \_\_\_\_\_3 |  |  | 0 |  |  |  |
| \_\_\_\_\_4 |  |  |  | 0 |  |  |
| \_\_\_\_\_5 |  |  |  |  | 0 |  |
| \_\_\_\_\_6 |  |  |  |  |  | 0 |

**Identify** the two viruses that are most similar (have the smallest Hamming distance) and calculate the branch length to their common answer (H/2). **Sketch** the first two branches of your phylogenetic tree.

**Combine** the two most similar viruses and **calculate** a new Hamming distance matrix

**Table 4.** Hamming distance matrix for the ‘flu viruses in Table 2 (B)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | \_\_\_\_\_ | \_\_\_\_\_\_ | \_\_\_\_\_ | \_\_\_\_\_ | \_\_\_\_\_ |
| \_\_\_\_\_ | 0 |  |  |  |  |
| \_\_\_\_\_ |  | 0 |  |  |  |
| \_\_\_\_\_ |  |  | 0 |  |  |
| \_\_\_\_\_ |  |  |  | 0 |  |
| \_\_\_\_\_ |  |  |  |  | 0 |

**Identify** the two viruses that are most similar (have the smallest Hamming distance) and calculate the branch length to their common answer (H/2). **Sketch** the next two branches of your phylogenetic tree.

**Combine** the two most similar viruses and **calculate** a new Hamming distance matrix

**Table 5.** Hamming distance matrix for the ‘flu viruses in Table 2 (C)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | \_\_\_\_\_ | \_\_\_\_\_\_ | \_\_\_\_\_ | \_\_\_\_\_ |
| \_\_\_\_\_ | 0 |  |  |  |
| \_\_\_\_\_ |  | 0 |  |  |
| \_\_\_\_\_ |  |  | 0 |  |
| \_\_\_\_\_ |  |  |  | 0 |

**Identify** the two viruses that are most similar (have the smallest Hamming distance) and calculate the branch length to their common answer (H/2). **Sketch** the next two branches of your phylogenetic tree.

**Combine** the two most similar viruses and **calculate** a new Hamming distance matrix

**Table 6.** Hamming distance matrix for the ‘flu viruses in Table 2 (D)

|  |  |  |  |
| --- | --- | --- | --- |
|  | \_\_\_\_\_ | \_\_\_\_\_\_ | \_\_\_\_\_ |
| \_\_\_\_\_ | 0 |  |  |
| \_\_\_\_\_ |  | 0 |  |
| \_\_\_\_\_ |  |  | 0 |

**Identify** the two viruses that are most similar (have the smallest Hamming distance) and calculate the branch length to their common answer (H/2). **Sketch** the next two branches of your phylogenetic tree.

**Combine** the two most similar viruses and **calculate** a new Hamming distance matrix

**Table 6.** Hamming distance matrix for the ‘flu viruses in Table 2 (E)

|  |  |  |
| --- | --- | --- |
|  | \_\_\_\_\_ | \_\_\_\_\_\_ |
| \_\_\_\_\_ | 0 |  |
| \_\_\_\_\_ |  | 0 |

**Calculate** the branch length to their common answer (H/2). **Sketch** the final version of your phylogenetic tree, being sure to include branch lengths.