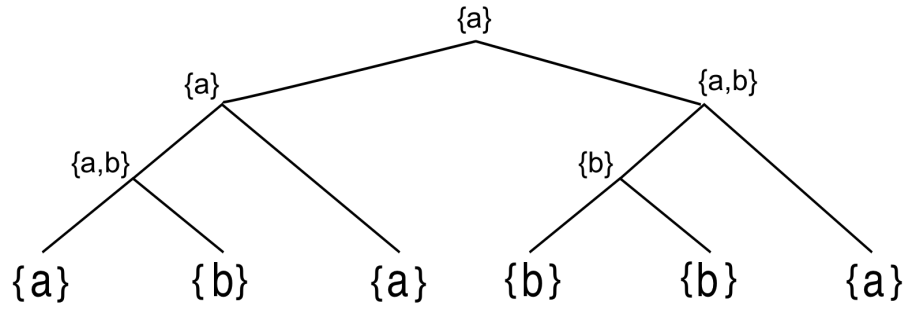
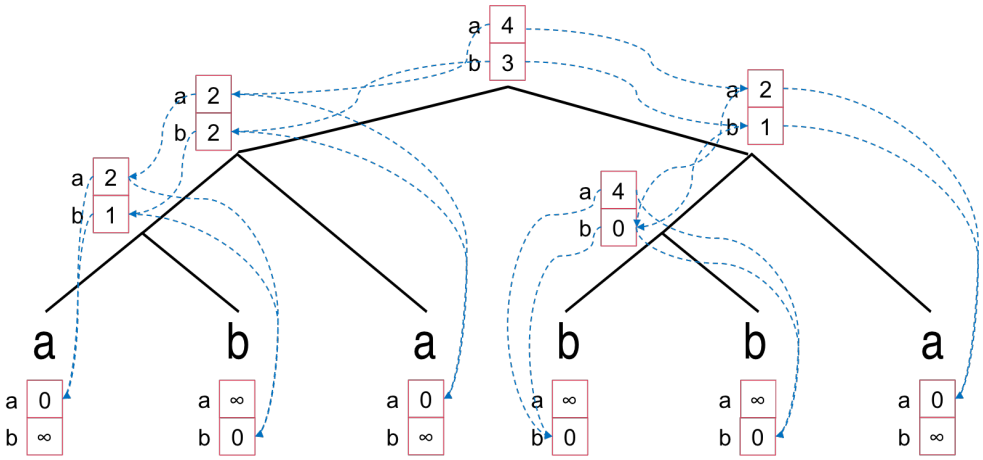
Ancestral Reconstruction Review

1. In the figure below, the "bottom-up" phase of Fitch's algorithm has been completed. Perform the "top-down" phase to assign a state to each internal vertex, and show where mutations have occurred on the tree. What is the total mutation score?



2. In the figure below, the "bottom-up" phase has again been completed, but for Sankoff's algorithm with the scoring matrix σ. Perform the traceback phase to assign a state to each internal vertex, and show where mutations have occurred on the tree. What is the total mutation score?

σ	a	b
a	0	2
b	1	0



3. What is the runtime of Fitch's algorithm in terms of the number of samples n and the number of character states k? What is the runtime of Sankoff's algorithm?

4. Is there any way to relate Fitch's algorithm and Sankoff's algorithm? Is one a special case of the other?

Population Genetics Review

The diagram below shows five sequences (rows), with mutations marked in orange X's.

1. What is n (the number of sequences)? What is S (the number of segregating sites)?

2. Compute the site frequency spectrum: ξ_i = number of sites with i copies of the mutant/derived allele, for $i = 1, \cdots, n-1$.

3. Compute the folded site frequency spectrum: η_i = number of sites with a i / $(n-i)$ split (don't know ancestral vs. derived) for $i = 1, \cdots, \lfloor n/2 \rfloor$.

4. Using the folded site frequency spectrum, compute π:

$$\pi = \frac{1}{\binom{n}{2}} \sum_{i=1}^{\lfloor n/2 \rfloor} i(n-i)\eta_i$$

5. Putting this all together, compute Tajima's $d = \pi - S/a_1$ where $a_1 = \sum_{i=1}^{n-1} \frac{1}{i}$.

6. Is d positive, negative, or zero? What could this indicate about the data?

Viterbi Algorithm Review

Suppose we have an HMM with $K = 2$ hidden states representing two weighted coins (coin 1 and coin 2). Our emissions are represented as the observed outcomes (H or T) of coin tosses. At first, say we are given the following transition and emission probabilities:

$$\begin{pmatrix} a_{11} = \frac{1}{2} & a_{12} = \frac{1}{2} \\ a_{21} = \frac{1}{5} & a_{22} = \frac{4}{5} \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} e_1(H) = \frac{2}{3} & e_1(T) = \frac{1}{3} \\ e_2(H) = \frac{1}{4} & e_2(T) = \frac{3}{4} \end{pmatrix}$$

Note that the rows sum to 1. Also say we are given the initial state probabilities $\pi_1 = \frac{1}{2}$ and $\pi_2 = \frac{1}{2}$. Now we want to find the most likely path (Viterbi path) of hidden states for a given dataset using dynamic programming. Let $V_k(i)$ be the probability of the most probable path that ends in hidden state k at position i in the data. We will initialize the Viterbi recursive data structure with:

$$V_k(1) = \pi_k \cdot e_k(x_1)$$

And fill in each subsequent column using the previous column:

$$V_k(i) = e_k(x_i) \cdot \max_l \{V_l(i-1) \cdot a_{lk}\}$$

1. Given the observed sequence $\vec{x} = (H, T, H)$ and the probabilities above, fill in the table for V below, then use backpointers to find the most likely sequence of hidden states.

	H	T	H
1			
2			

2. Now suppose we have the opposite information - we are given the hidden state sequence $\vec{z}$ and want to estimate the probabilities. What are the new transition and emission probabilities a_{kl} and $e_k(b)$?

hidden state sequence $\vec{z}$	2	1	2	1	1	1	2	2	2	2	2	2	2	2	1	2	2
observed sequence $\vec{x}$	T	H	H	H	T	H	T	T	H	T	T	T	T	H	H	T	T