

The second midterm (Nov 26 in-class) covers in-class material days 8-21, labs 5-8, reading weeks 5-11. You may bring a 1 page (front and back), hand-written study guide, but no other notes or resources. You will not need a calculator. I have put vocab in blue.

### 1. Phylogenetic Trees

- Study vocab from the end of class 8 + idea of pairwise differences
- What is a [phylogenetic tree](#) and what can we learn from them?
- What is the input and output of a phylogenetic tree algorithm? Input: [dissimilarity map](#), Output: tree topology (often binary) AND branch lengths
- Vocab: [tree metric](#) (usually induced), [ultrametric](#), [rooted](#), [unrooted](#)
- What are we trying to minimize with phylogenetic tree algorithms?
- [UPGMA](#) algorithm, how to run it and interpret the results
- [Neighbor Joining](#) algorithm, how to run it and interpret the results (how to root tree?)
- How do UPGMA and NJ compare? Runtime? Advantages/disadvantages depending on the situation?

### 2. Ancestral State Reconstruction

- What is ancestral state reconstruction? What can we learn from it?
- Multiple mutations at the same site are rare. Could be [convergent evolution](#).
- [Fitch's algorithm](#) (small [parsimony](#)): what is the input, method, output, and interpretation
- [Sankoff's algorithm](#) (weighted parsimony): same as above + how is it different from Fitch?
- Runtime for Fitch and Sankoff
- [Perfect phylogeny](#): what is the input (data from many sites), what is the goal (yes/no answer, ideally + tree and mutation history)
- Notation (i.e.  $O_i$ ) and interpretation (containment, disjoint, etc, what do they mean?)
- Naive algorithm for perfect phylogeny (check all pairs of sites)
- [Gusfield's algorithm](#): how to run it and interpret the results + why does it work?
- Why do we use [radix sort](#)? What is the runtime of Gusfield's algorithm?

### 3. Bayesian Phylogenetics

- Likelihood framework (i.e. probabilistic) for trees
- [Felsenstein's peeling algorithm](#) (basic ideas, not details)
- [Bootstrapping](#): how it can be used to resample sites and estimate uncertainty of tree inference
- [MCMC](#): Markov chain Monte Carlo for moving through tree space (basic ideas, not details)

#### 4. Population Genetics

- What is [population genetics](#)? What changes when we consider a single species?
- What is [recombination](#) and what affect does it have on population genetic analysis?
- [Wright-Fisher model](#) of evolution within a population
- Notation:  $N$  for population size,  $n$  for sample size, etc
- [Neutrality](#) assumptions: constant  $N$ , random mating, no [natural selection](#)
- Measures of sequence diversity:  $S$ ,  $\pi$ , and the [site frequency spectrum](#) (SFS)
- Finding a [common ancestor](#) and how we use that to derive the [coalescent](#)
- Idea that coalescent times ( $T_n, T_{n-1}, \dots, T_2$ ) are [exponentially](#) distributed (not details)
- [Tajima's  \$d\$](#) : how to compute it and why we expect it to be 0 under neutrality
- How to interpret  $\pi$  and Tajima's  $d$  in terms of deviations from neutrality (e.g. selection)
- How [deep learning models](#) ([CNNs](#) in particular) can be used to identify regions under selection

#### 5. Hidden Markov Models

- What is a [Markov chain](#)? What are [transition probabilities](#)? [Stationary distribution](#)?
- Difference between a [state diagram](#) and a [state sequence](#) for a Markov process
- Probability concepts: [conditional probability](#), probabilities “sum to 1”
- What is a [hidden Markov model](#) (HMM)? Observed sequence  $\vec{x}$ , hidden state sequence  $\vec{z}$
- [Transition](#), [emission](#), and [initial](#) state probabilities (notation, meaning, etc)
- [Viterbi algorithm](#): input, method (fill in recursive data structure + backtrace to get best path), output and interpretation
- [Forward and Backward algorithms](#) and how we use them to get the [posterior decoding](#) and [posterior mean](#)
- Parameter estimation for HMMs when the state sequence is known
- [Baum-Welch algorithm](#) for parameter estimation when the state sequence is unknown (basic idea, not details)
- HMM example in genetics: time to most recent common ancestor (TMRCA) for  $n = 2$
- Skip: details of log-space (just know why we need to use it), and formulas for  $A_{kl}$  and  $E_k(b)$  in Baum-Welch