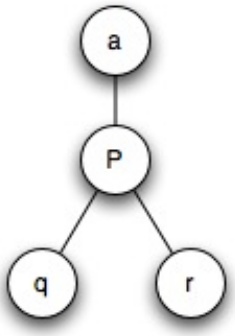
20.181 Lecture 7

Contents

Quick comment on upPass



- not necessary to find the best tree (you won't be tested on it)
- but here's the correct way to do it (via Dr. Fredrik Ronquist's lecture notes on "Parsimony: Counting Changes," from FSU's Computational Evolutionary Biology course) (PDF)

Definitions

1. F_x: the upPass set we want to get to
2. S_x: the downpass set we got to
3. ancestor = a
4. parent = p, node we're looking at
5. children = q,r

Algorithm 2 Fitch uppass algorithm

$F_p \leftarrow S_p \cap F_a$
if $F_p \neq F_a$ **then**
  if $S_q \cap S_r \neq \emptyset$ **then**
    $F_p \leftarrow ((S_q \cup S_r) \cap F_a) \cup S_p$
  else
    $F_p \leftarrow S_p \cup F_a$

Courtesy of Dr. Fredrik Ronquist. Used with permission.

Revisit overall strategy

- Although up until now we've always started with a tree of known topology, a lot of times you wouldn't know the tree topology beforehand

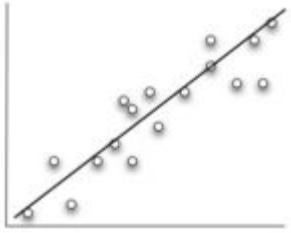
```
for all possible trees:
      compute score (tree)
return best tree
```

Scoring functions

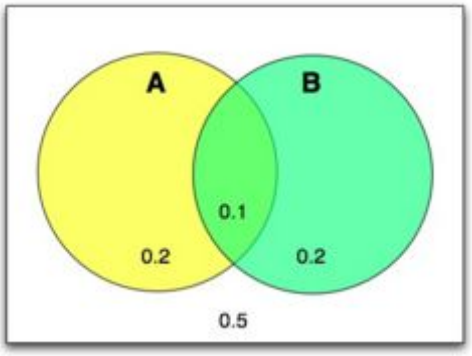
1. max parsimony (fewest mutations)
2. generalized parsimony (Sankoff: weighted mutation costs)
3. Maximum Likelihood

ML intro

- examples of a ML estimator:
    1. for normally distributed random var X, X(bar), the mean of the data you observe, is a ML estimator of the mean of the distribution they were drawn from
    2. A best fit line thru data is a ML estimator.



Probability Refresher



total area of a box = 1

```
p(A)= 0.3 , p(B)= 0.3
p(A,B)= 0.1
p(A|B)= 0.1 / (0.1+0.2) = 1/3 = p(A,B) / p(B)
p(B|A) = 0.1 / (0.1+0.2) = p(A,B) / p(A)
With a little manipulation we can derive Bayes' Rule:
p(A|B) = p(B|A) * p(A) / p(B)
```

ML in trees

- We are looking for the best tree, given some data. What is the best tree T given the data D?

  p(T|D) is what we want to maximize
  Not obvious how we want to do that... use Bayes Law to rearrange into something we can intuitively understand

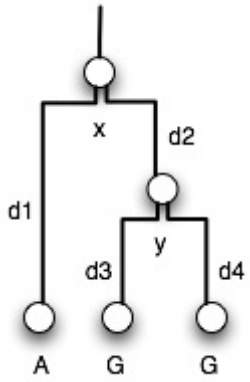
  ```
  p(T|D) = p(D|T) * p(T) / p(D)
  ```

- p(D) is a constant ... we don't have to worry about it
- What is p(T), the a priori probability of the tree ?

  Well, without looking at the data, do we have a way of saying any tree is more likely than another one if they don't have any data associated with them ?
  No... not really

- So what we're left maximizing is just p(D|T) and that sounds like a familiar concept!

NOTE: Tree now consists of topology AND distances We ask, what is the probability of *each* mutation occuring along a branch of a certain length? What is the probability that they ALL occurred, to give us the sequences we see today?




```
p(D|T) = p(x->A|d_1) * p(x->y|d_2) * p(y->G|d_3) * p(y-
>G|d_4)
p(A U B) = p(A) + p(B) - p(A,B)
p(A <intersect> B) = p(A)*p(B)
```

- We treat all of these mutations along the different branches as independent events (that's why you multiply the probabilities, because all the events have to happen independently.)

Jukes-Cantor

- based on a simple cost "matrix"

  probability of changing from one particular nucleotide to another particular nucleotide is 'a'
  probability of any nucleotide staying the same is '1-3a'

```
if x == y :
      [JC eqn you'll derive in the hw]
if x != y :
      [JC eqn you'll derive in the hw]
```

Evolutionary Model

gives us likelihood of (D|T) (need branch lengths)

```
downPass for ML
      compute L(p|q,r,d)
```

q , r = likelihood of the two subtrees, d are the distances to them