Algorithmic Approaches for Biological Data, Lecture #23

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City University of New York
American Museum of Natural History

2 May 2016

Outline

- Project & Last Day Notes

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- Complexity Revisited: NP-hardness, Time & Space Complexity

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- Tree Vectors

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- For those who cannot make Monday, possible to do presentation this Wednesday (see me).

Complexity Revisited: Running Times

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- *Sorting Algorithms demo*

  Not in demo is the built-in Python sort: timSort (invented by Tim Peters in 2002) that is hybrid of merge sort and insertion sort.

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(That is, after some point, $f(n)$ is smaller than $c \cdot g(n)$.)

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  (For big-Oh notation, drop constants and keep only largest terms.)

Complexity Classes: What is NP-hardness?

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- P stands for problems that can be computed quickly (polynomial time).
- NP stands for problems that can be checked quickly (nondeterministic polynomial time).
- Example: given a geometry proof, you can check if its correct quickly, but knowing that, is there a quick way to find proofs?

Millennium Prize Problems

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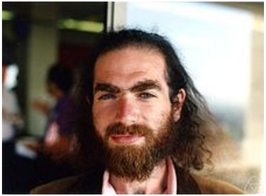
In 2000, the Clay Mathematics Institute announced million dollar prizes for:

- Birch and Swinnerton-Dyer Conjecture
- Hodge Conjecture
- Navier-Stokes Equations
- P vs NP
- Poincaré Conjecture
- Riemann Hypothesis
- Yang-Mills Theory

Millenium Prize Problems



Grigori Perelman, 1993

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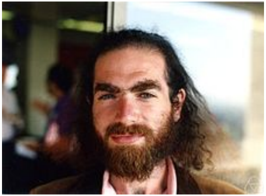

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He turned down the prize.

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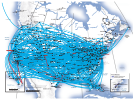
More Examples of NP Problems



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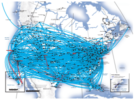

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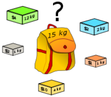

Knapsack Problem: fill your backpack with the most valuable objects without exceeding weight restrictions.

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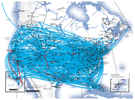

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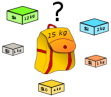

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5	3			7				
6			1	9	5			
	9	8					6	
8				6				3
4			8		3			1
7				2				6
	6					2	8	
			4	1	9			5
				8			7	9

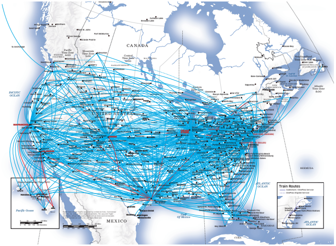
Sudoku: find a solution to a (large) Sudoku puzzle.

$P \stackrel{?}{=} NP$: Why Does It Matter?

wiki

If you could quickly find solutions to NP-hard problems (i.e. P=NP), then

- Many security systems (such as the Data Encryption Standard (DES) used to send ATM/bank data) would be easily breached.



United Airlines

If you could quickly find solutions to NP-hard problems (i.e. P=NP), then

- Scheduling and routing questions (such as the Knapsack question and Traveling Salesman Problem) could be done efficiently.

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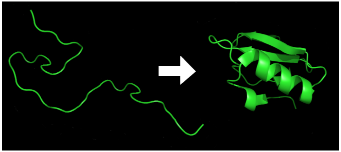

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- Some hard biological questions (such as protein folding) would be tractable.

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- change how algorithms are designed

In Pairs: Analyze Running Time

Give upper bounds on the worst case running time of:

1.
```
def double(n):
    d = 2*n
    return d
```

2.
```
def sum(n):
    s = 0
    for i in range(n):
        s += i
    return s
```

3.
```
def sum2(n):
    return n*(n+1)/2
```

4.
```
def findMin(numList):
    m = numList[0]
    for i in range(1,len(numList)):
        if numList[i] < m:
            m = numList[i]
    return m
```

5. (Code from text):
```
def selectionSort(alist):
   for fillslot in range(len(alist)-1,0,-1):
       positionOfMax=0
       for location in range(1,fillslot+1):
           if alist[location]>alist[positionOfMax]:
               positionOfMax = location

       temp = alist[fillslot]
       alist[fillslot] = alist[positionOfMax]
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alist = [54,26,93,17,77,31,44,55,20]
selectionSort(alist)
print(alist)
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6. (Code from text):
```
def insertionSort(alist):
   for index in range(1,len(alist)):

     currentvalue = alist[index]
     position = index

     while position>0 and alist[position-1]>currentvalue:
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- Can measure space usage as we did for time complexity.

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5.
```
def findMaxDist(numList):
    n = len(numList)
    d = np.zeros(n,n)
    for i in range(1,n):
        for j in range(1,n)
            d[i,j] = abs(i,j)
    return np.amax(d)
```

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def findMaxDist2(numList):
    n = len(numList)
    m = 0
    for i in range(1,n):
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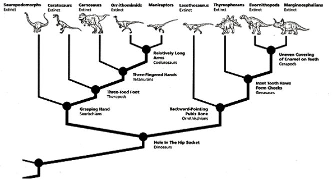
- Though NP-hard, some problems can be solved in time polynomial in the size of the input size but exponential in the size of a fixed parameter.
- Often, the parameter, k, will be the distance between the trees.
- For example, the distance between the two trees can be calculated by shrinking the common regions and focusing on the differences, which can be bounded by k.

Recap: Small Parsimony Problem



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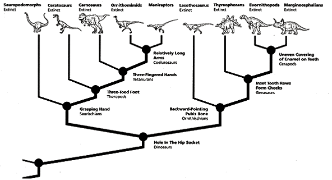
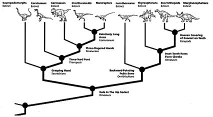


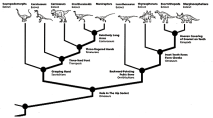
- Last Week: given a tree with leaves labeled by sequences, computed the parsimony score of the tree.
- Thinking in terms of time complexity: How long does it take?

- How do you code this?



AMNH

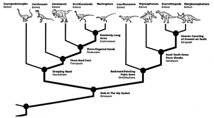
Algorithm Design: Scoring Trees Under Parsimony



AMNH

- How do you code this?
  - Input: A tree and sequences on the leaves.

Algorithm Design: Scoring Trees Under Parsimony



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  - Input: A tree and sequences on the leaves.
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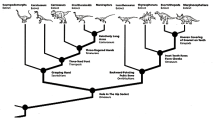

AMNH

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  - Input: A tree and sequences on the leaves.
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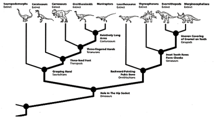
- What data structures do you need?

Algorithm Design: Scoring Trees Under Parsimony



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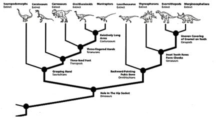
  - Tree structure

Algorithm Design: Scoring Trees Under Parsimony



AMNH

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  - Input: A tree and sequences on the leaves.
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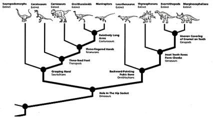
Algorithm Design: Scoring Trees Under Parsimony



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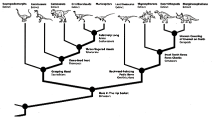

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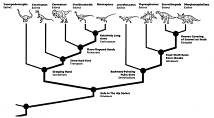
Fitch's Algorithm: Pseudocode



AMNH

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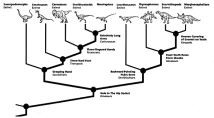

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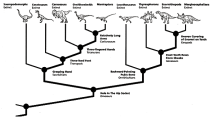

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  - Go position by position:

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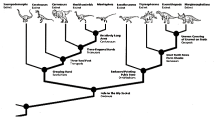

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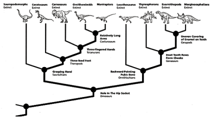
Fitch's Algorithm: Pseudocode



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    ```
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    ```
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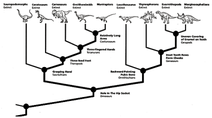
    - ★ If overlap, use that label.
    - ★ If no overlap, use the union.

Fitch's Algorithm: Pseudocode



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  - Useful Python container type: `set`

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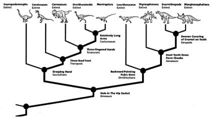

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  - Go position by position:
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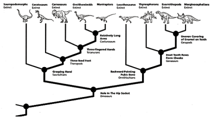
  - Useful Python container type: `set`
    - Has functions for union and intersection of sets.

Fitch's Algorithm: Pseudocode



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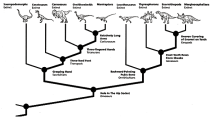
    ```
    A T A T G
    A A T T G   →   A AT AT T G
    ```

  - Go position by position:
    - ★ If overlap, use that label.
    - ★ If no overlap, use the union.
  - Useful Python container type: `set`
    - ★ Has functions for union and intersection of sets.
    - ★ `s1 = set(l1)`
      `s2 = set(l2)`

Fitch's Algorithm: Pseudocode



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    ```
    A T A T G
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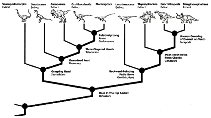
    ```
  - Go position by position:
    - If overlap, use that label.
    - If no overlap, use the union.
  - Useful Python container type: `set`
    - Has functions for union and intersection of sets.
    - ```
      s1 = set(l1)
      s2 = set(l2)
      print s1.intersection(s2)
      ```
      ```

Fitch's Algorithm: Pseudocode



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      ```
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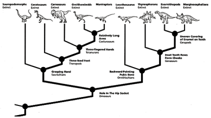
Fitch's Algorithm: Pseudocode



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  - Given labels for children, compute label for the parent:

    ```
    A T A T G
    A A T T G   →   A AT AT T G
    ```
  - Go position by position: for-loop
    - ★ If overlap, use that label. if-statement
    - ★ If no overlap, use the union.
  - Useful Python container type: `set`
    - ★ Has functions for union and intersection of sets.
    - ★ set operations

      ```
      s1 = set(l1)
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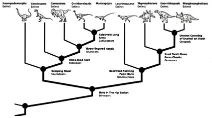
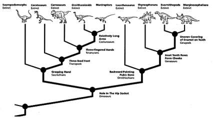
Fitch's Algorithm: Pseudocode



AMNH

- Second pass: Starting at the root, choose a labeling, then work towards the leaves minimizing the conflicts.

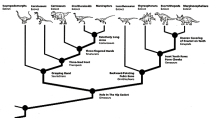
Fitch's Algorithm: Pseudocode



AMNH

- Second pass: Starting at the root, choose a labeling, then work towards the leaves minimizing the conflicts.
  - At root, choose one labeling:

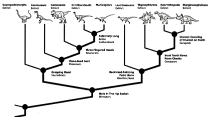
Fitch's Algorithm: Pseudocode



AMNH

- Second pass: Starting at the root, choose a labeling, then work towards the leaves minimizing the conflicts.
  - At root, choose one labeling:
    `A AT AT T G` $\rightarrow$ `A A T T G`
  - For all other nodes, compare to the parent:

Fitch's Algorithm: Pseudocode



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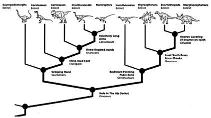
    `A T A T G`
    `AT AT G ACT G`

Fitch's Algorithm: Pseudocode



AMNH

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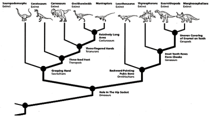
Fitch's Algorithm: Pseudocode



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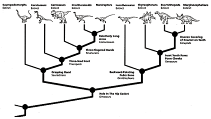

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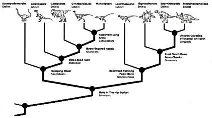

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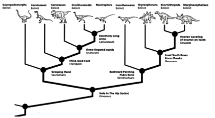
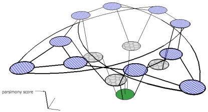


AMNH

What is the running time and space requirements for:

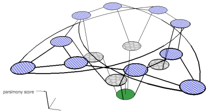
- First pass: Starting at the leaves, label the internal leaves (with possible multiple labels).
- Second pass: Starting at the root, choose a labeling, then work towards the leaves minimizing the conflicts.
- Print out all tree on *n* leaves.

Searching for Optimal Trees



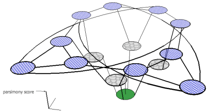
- Large Parsimony Problem: Given sequences for leaves, find the optimal scoring tree.

Searching for Optimal Trees



- Large Parsimony Problem: Given sequences for leaves, find the optimal scoring tree.
- Visually: think of the trees on a 2D map and the height above sea level is the score.

Searching for Optimal Trees



- Large Parsimony Problem: Given sequences for leaves, find the optimal scoring tree.
- Visually: think of the trees on a 2D map and the height above sea level is the score.
- Works for any optimality criteria (i.e. same analogy works for maximum likelihood).

Analogy: Find the Highest Point

polymaps.org

Analogy: Find the Highest Point

Sampling:

- Choose 1000 random points.

Analogy: Find the Highest Point

Sampling:

- Choose 1000 random points.
- Find height at each point.

Analogy: Find the Highest Point

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- Choose 1000 random points.
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- Output the sampled point with largest height.

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- Will you reach the highest point?

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- Choose 1000 random points.
- Find height at each point.
- Output the sampled point with largest height.
- Will you reach the highest point?
- Only if very lucky or a very dense sample.

Hill Climbing:

- Start at the harbor.

Analogy: Find the Highest Point

Hill Climbing:

- Start at the harbor.
- Can see 25 meters in all directions.

Analogy: Find the Highest Point

Hill Climbing:

- Start at the harbor.
- Can see 25 meters in all directions.
- Walk upwards, repeat.

Analogy: Find the Highest Point

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- Maybe, but maybe not.

Analogy: Find the Highest Point

Hill Climbing:

- Start at the harbor.
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- Walk upwards, repeat.
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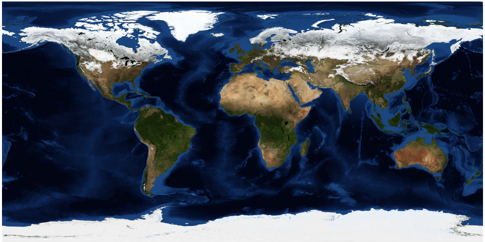
- Maybe, but maybe not.
  - Could reach small peaks, but miss the larger ones.

Analogy: Find the Highest Point

Hill Climbing:

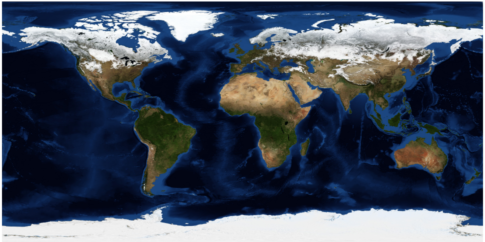
- Start at the harbor.
- Can see 25 meters in all directions.
- Walk upwards, repeat.
- Will you reach the highest point?
- Maybe, but maybe not.
  - Could reach small peaks, but miss the larger ones.
  - Start in multiple places to see more.

Local Search Techniques



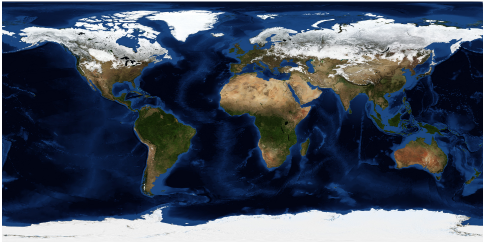
- **Goal:** Find the point with the optimal score

Local Search Techniques



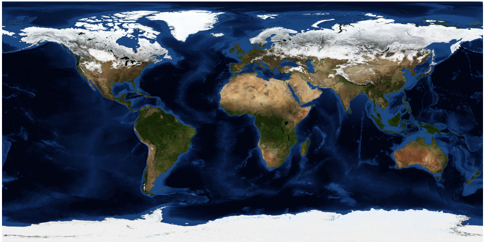
- **Goal:** Find the point with the optimal score
- Local search techniques prevail:

Local Search Techniques



- **Goal:** Find the point with the optimal score
- Local search techniques prevail:
  - Begin with a point

Local Search Techniques



- **Goal:** Find the point with the optimal score
- Local search techniques prevail:
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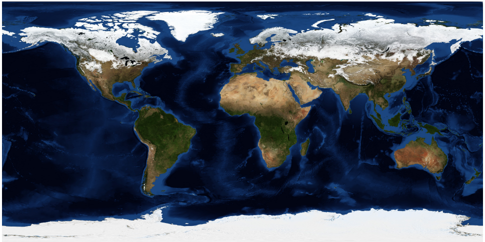
  - Choose the next point from its neighbors (e.g. best scoring)

Local Search Techniques



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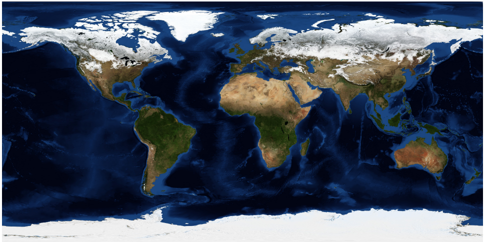
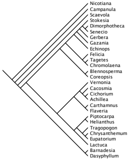
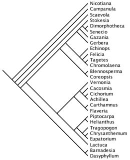


- **Goal:** Find the point with the optimal score
- Local search techniques prevail:
  - Begin with a point
  - Choose the next point from its neighbors (e.g. best scoring)
  - Repeat
- Many variations on the theme: branch-and-bound, MCMC, genetic algorithms,...

Popular Tree Metrics

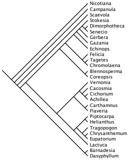


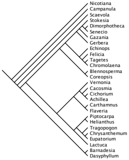


Those based on tree rearrangements:

- Subtree Prune and Regraft (SPR)
- Tree Bisection and Reconnection (TBR)
- Nearest Neighbor Interchange (NNI)

Popular Tree Metrics





Those based on tree rearrangements:

- Subtree Prune and Regraft (SPR)
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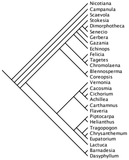

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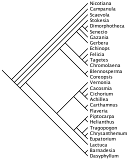

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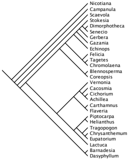

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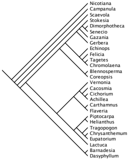

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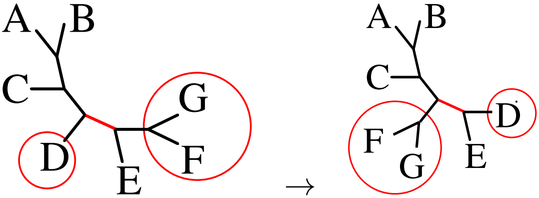
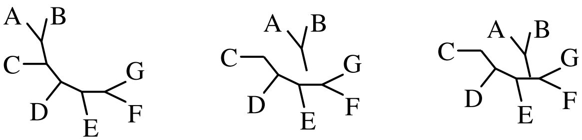
NNI Metric



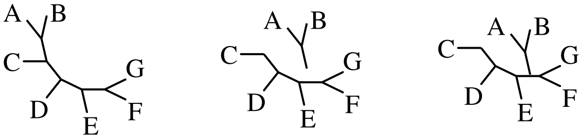
The NNI distance between two trees is the minimal number of moves needed to transform one to the other (NP-hard, DasGupta *et al.* '97).

SPR Distance



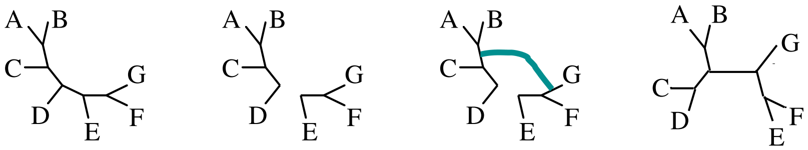
- SPR distance is the minimal number of moves that transforms one tree into the other.

SPR Distance



- SPR distance is the minimal number of moves that transforms one tree into the other.
- SPR for rooted trees is NP-hard (Bordewich & Semple '05).
- SPR for unrooted trees is NP-hard (Hickey *et al.* '08).
- SAT-based heuristic (Bonet & S '09).

TBR Distance



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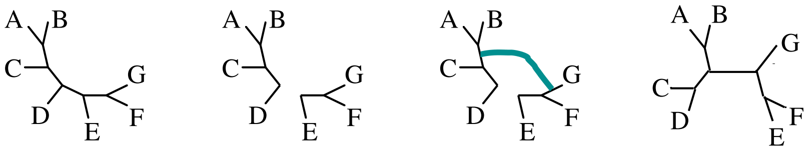

- TBR distance is the minimal number of moves that transforms one tree into the other.
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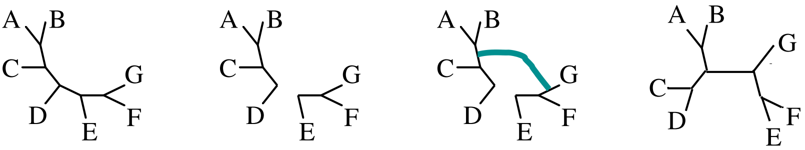
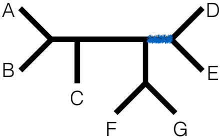
TBR Distance



- TBR distance is the minimal number of moves that transforms one tree into the other.
- TBR is NP-hard and FPT. (Allen & Steel '01)
- TBR has a linear time 5-approximation and a polynomial time 3-approximation (Amenta, Bonet, Mahindru, & S '06; Bordewich, McCartin, & Semple '08)

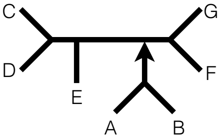
Tree Rearrangements

Tree Rearrangements



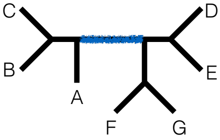
Nearest Neighbor Interchange

(NNI)



Subtree Prune & Regraft

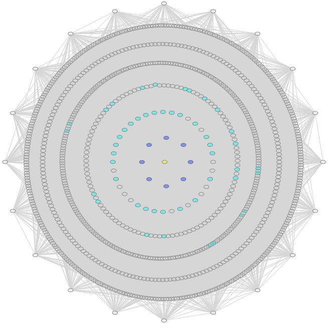
(SPR)



Tree Bisection & Reconnection

(TBR)

Metrics Matter



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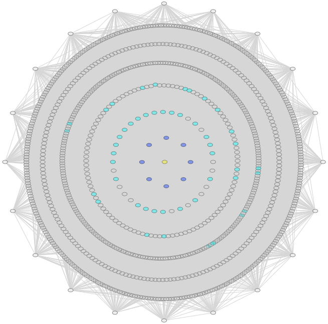
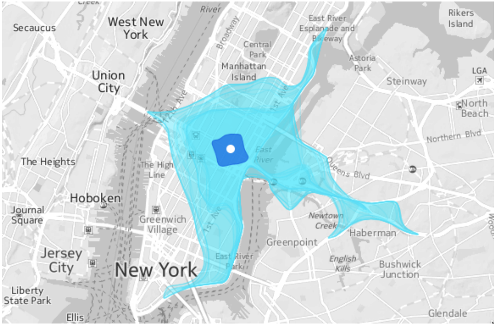
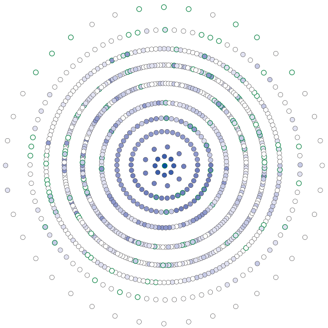


NNI & SPR



Isoscope

Landscapes



Parsimony score for compatible characters for $n = 7$ (Urheim, Ford, & S, submitted)

A treespace with assigned scores is often called a landscape.

What does the landscape look like?

Each landscape depends on the number of taxa and the score of each tree (usually derived from the inputted character sequences).

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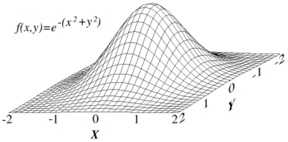

(from wikipedia)

If very smooth, 'hill climbing' will work well.

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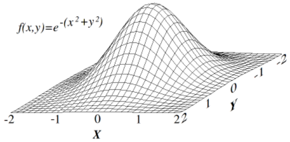

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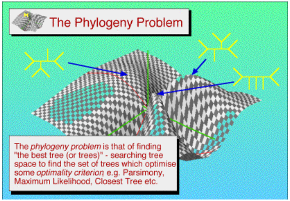
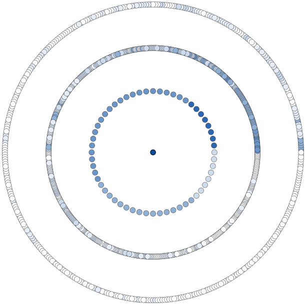
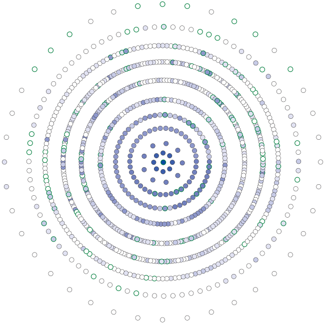


If very rugged, need more sophisticated searches that use the underlying structure of the space.

Adjusting Search Space



SPR metric

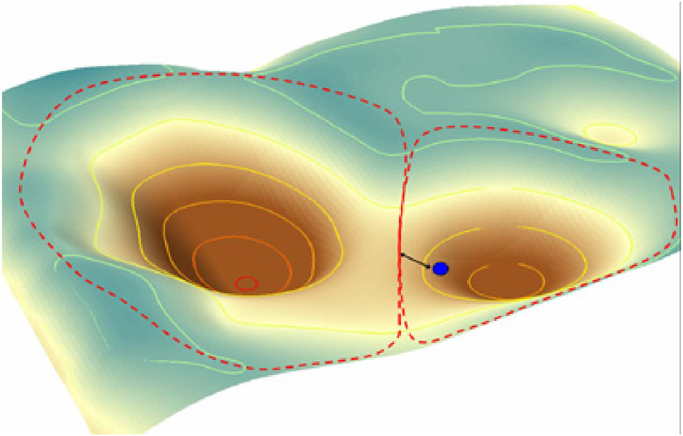


NNI metric

Parsimony score for compatible characters for $n = 7$ (Urheim, Ford, & S, submitted)

The same data, organized by different tree metrics.

Attraction Basins



resalliance.org

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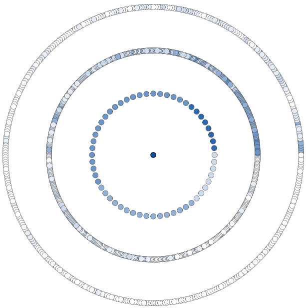

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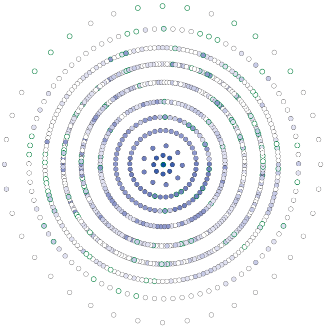

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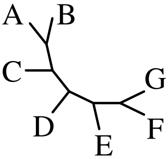
Parsimony score for compatible characters for $n = 7$ (Urheim, Ford, & S, submitted)

Simplest Case: for compatible character sequences ('perfect data'):

- Under SPR, there is a single attraction basin.
- Under NNI, multiple attraction basins occur even for perfect data.

In Pairs: Tree Rearrangements



For the tree on the left:

1. What are the NNI neighbors?

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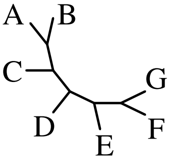

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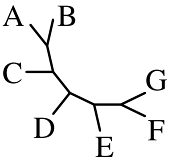

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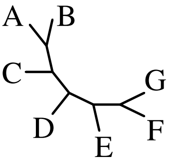

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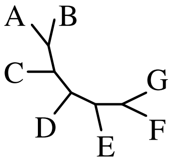

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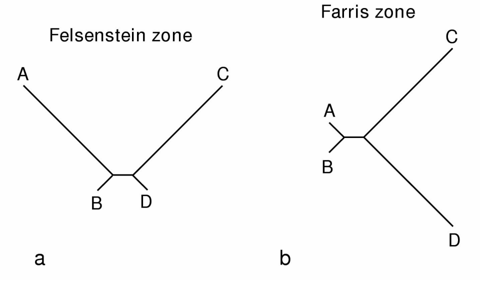
4. Find a tree that is NNI distance 3 but SPR distance 1.
5. Write an algorithm for given a tree T and a specific edge/node, the two NNI neighbors around that edge.

Weighted Trees



Philippe *et al.*, '05

- Branch weights are part of the model.

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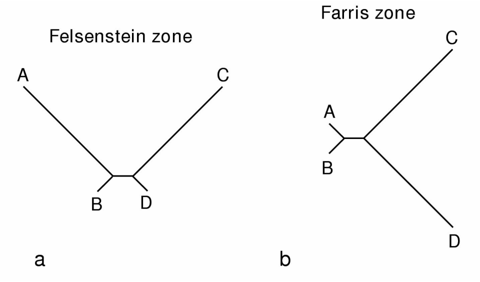

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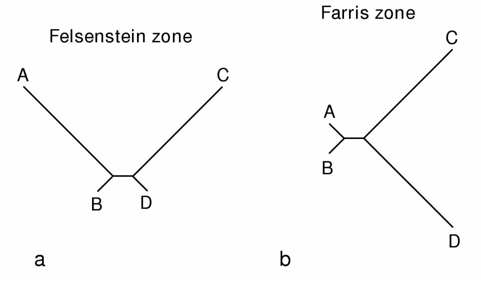

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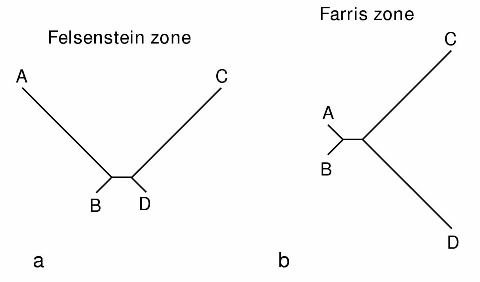

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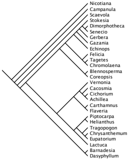
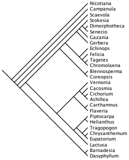
- Two classic trees with same underlying topology.
- The metrics and search spaces above treat them as identical.

Popular Tree Metrics





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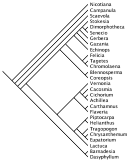

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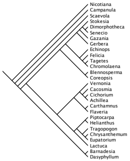

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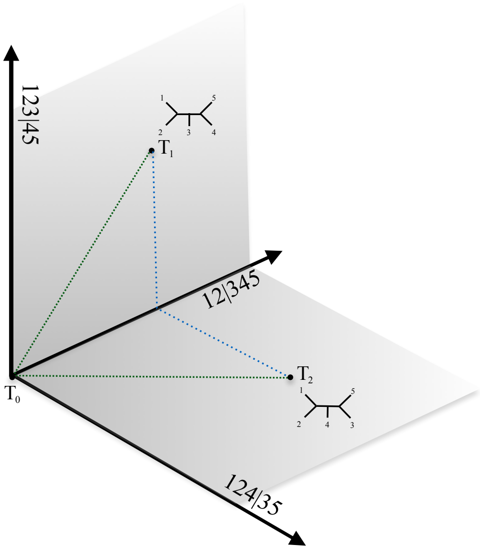
Trees as Vectors



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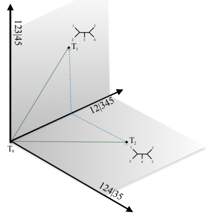
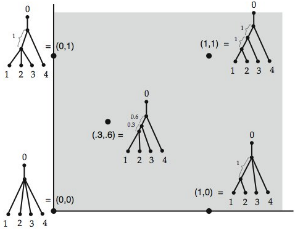


	1|2345	2|1345	3|1245	4|1235	5|1234	12|345	13|245	14|235	15|234	23|145	24|135	25|134	34|125	35|124	45|123
$T_0 = (1,2,3,4,5)$	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0
$T_1 = ((1,2),(3,(4,5))$	1	1	1	1	1	1	0	0	0	0	0	0	0	0	1
$T_2 = ((1,2),(4,(3,5))$	1	1	1	1	1	1	0	0	0	0	0	0	0	1	0

BHV Distance



Billera, Holmes, Vogtmann '01

- Billera, Holmes, and Vogtmann '01 have a continuous metric space of trees.

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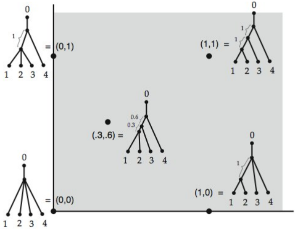

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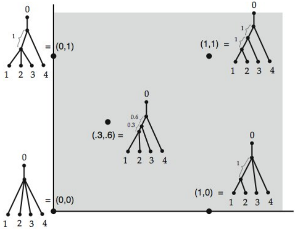

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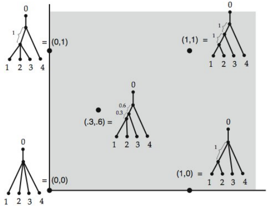
- Identify edges of orthants to form space

Identify Edges of Orthants



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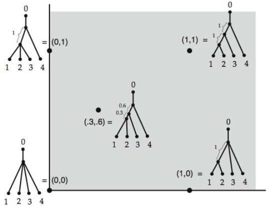

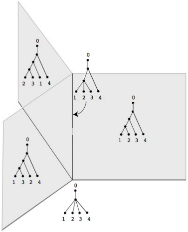

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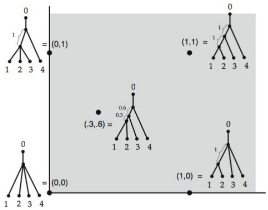
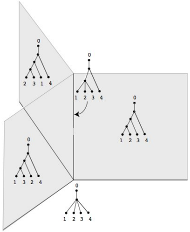
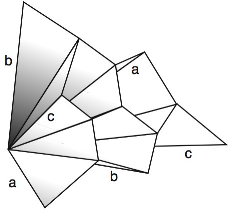
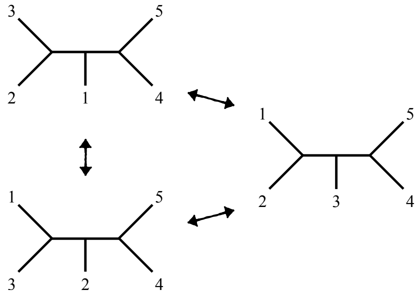


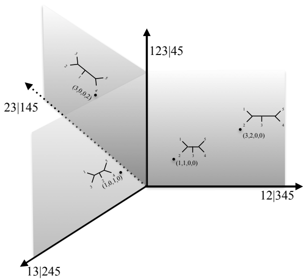




(All images from Billera, Holmes, Vogtmann '01)

BHV & NNI Distances





- Simplest move between orthants: shrink coordinate/edge and expand.

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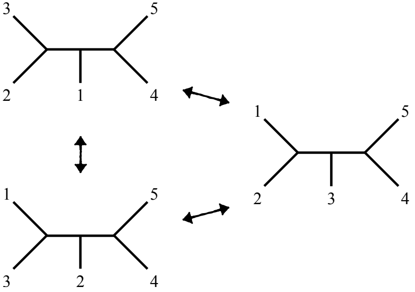
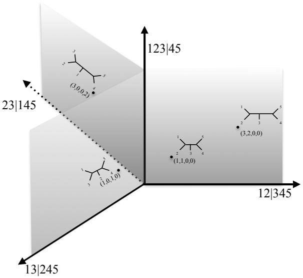
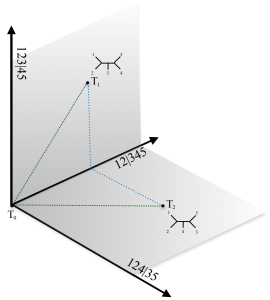
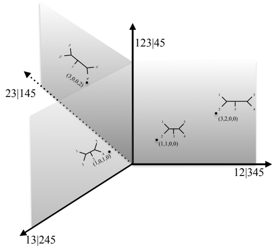




- Simplest move between orthants: shrink coordinate/edge and expand.
- Corresponds to a Nearest Neighbor Interchange (NNI) move on the topology.

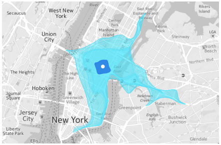
In Pairs: Continuous Treespace





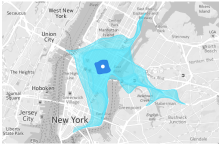
1. What is the distance between T_1 and T_2?
2. What is the average (tree at the midpoint) of T_1 and T_2?
3. Give three trees that have distance 1 to the origin, T_0 (star tree).
4. Lower figure: what is the distance between (3,0,0,2) and (1,1,0,0)?
5. What is a good average/consensus for the four trees?

Recap



- Efficiency (in time and space) matters when data gets large.

Recap



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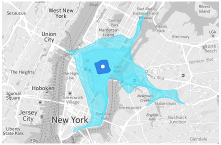
- More on tree searching next lecture.

Recap



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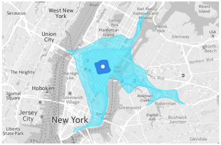
Recap



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- Challenges available at `rosalind.info`.