

Maximally distant genomes under the DCJ operation

Manda Riehl

Permutation Patterns, 2010

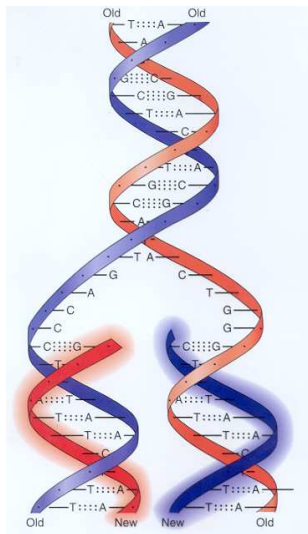
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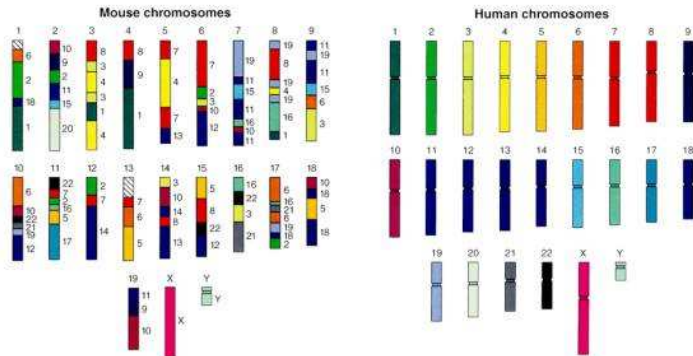
Replication



Mouse and Human Genomes

90.2% of the human genome and 93.3% of the mouse genome lie in conserved syntenic segments.

Mouse and Human Genetic Similarities



YCA 98-07582

Courtesy Lisa Stubbs
Oak Ridge National Laboratory

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 - ▶ Direction matters:
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 - ★ UAG is STOP.
 - ▶ Even so, Christie (1996), Pevzner (1998), Labarre (2005) have also considered unsigned versions.

Chromosomes as SIGNED Permutations

- $1\ 2\ -4\ -3$ indicates the substring $3\ 4$ was attached to $1\ 2$ “backwards”.

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- Fundamental Answer:
It depends on your operation.

(Note: Because in this talk, we are using a multichromosomal model, our signed permutations are more like “broken” permutations, or ordered set partitions)

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- $(2h,1t)$, $(1h,4h)$, and $(5h,5t)$ are internal vertices.

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(Yancoupoulos 2005)

A DCJ operation involves making two cuts in a genome and rejoining the pieces in one of the following ways:

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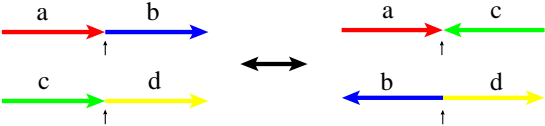
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- An internal vertex (a,b) can be replaced by two external vertices (a) and (b) .

The example below shows how a DCJ operation can transform one genome into another.



DCJ Distance

- The DCJ distance between two genomes on the same set of genes is defined to be the fewest number of Double-Cut-and-Join operations that it takes to transform one genome into the other.

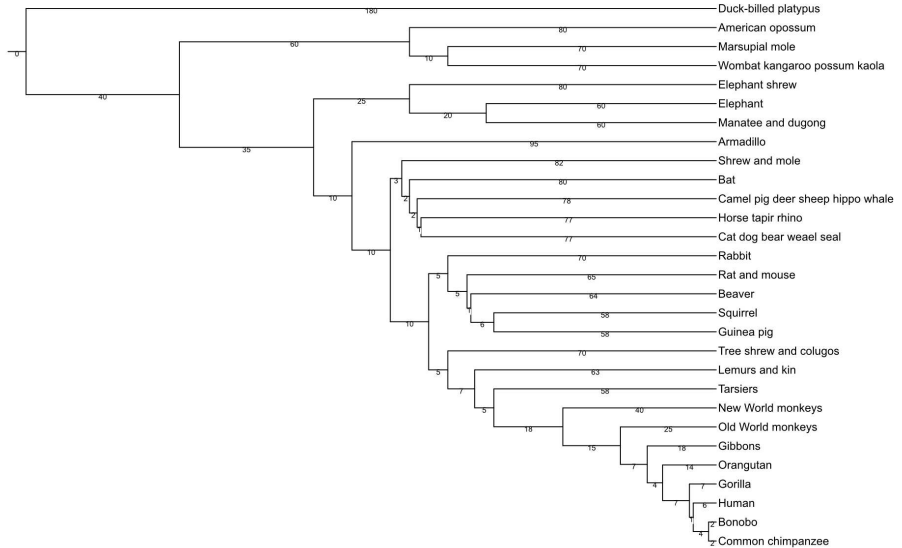
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- Audience Poll: Which has a more recent common ancestor: humans and rabbits, humans and camels, or humans and pigs?

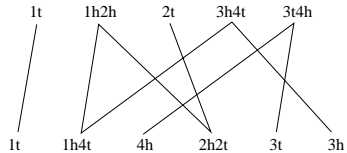
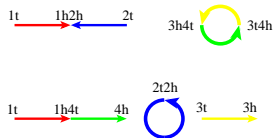
- 1



Adjacency/Breakpoint Graph

Any genome can be represented by a distinct arrangement of sets of internal vertices and external vertices.

A bipartite adjacency graph is constructed with vertices corresponding to the sets of internal and external vertices of the two genomes. Two vertices are connected with an edge for every head or tail that they share.



Distance Formula

Theorem

(Bergeron, Mixtacki, Stoye 2008) The DCJ distance between two genomes, A and B, defined on the same set of N genes is given by

$$d_{DCJ}(A, B) = N - (C + I/2),$$

where C is the number of cycles and I is the number of odd paths in the adjacency graph of A and B.

Example

$$d_{DCJ}(1\ 2\ 3\ 4\ 5, 1\ -4\ 2\ \quad 5\ -3)$$

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- Questions:
 - ▶ Are “most” genomes near A or far from A ?
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 - ▶ Are there symmetry properties of this distribution?

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- This means that there are no cycles and no odd paths in the adjacency graph of two maximally distant genomes.

Maximum Distance

By considering an arbitrary starting genome, A , defined on N signed genes and counting the number of distinct adjacency graphs that could be created from it containing only even paths we showed:

Theorem

The number of maximally distant genomes is given by

$$G_{max}(m, n) = (2m - 1)!! \sum_{k=0}^n \binom{n + m - 1}{k} \binom{n}{k} 2^k k!,$$

where $2m$ is the number of telomeres, and n is the number of adjacencies in A .

Show me the values!

$m \ n$	0	1	2	3	4	5
0	N/A	1	5	37	361	4361
1	1	3	17	139	1473	19091
2	3	15	111	1083	13083	188103
3	15	105	975	11265	155535	2495865
4	105	945	10605	142485	2228625	39757305
5	945	10395	137025	2104515	36893745	726753195

Theorem

$$G(m, 1) = G(m + 1, 0)$$

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- Conjecture: $G(m, n) \neq G(s, t)$ otherwise.

Generating Functions (for fixed m)

Theorem

The exponential generating function for the sequence $\{g_m\}$ is given by

$$f_m(x) = (2m - 1)!! \frac{e^{\frac{x}{1-2x}}}{(1 - 2x)^m},$$

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- The method of BMS breaks down thoroughly.
- Python program to generate data.

Number of unsigned genomes distance D from a single linear chromosome of length N

$N \setminus D$	0	1	2	3	4	5
1	1	1				
2	1	4	1			
3	1	10	12	1		
4	1	18	64	39	1	
5	1	28	208	387	149	1
6	1	40	501	2096	2478	661

Column when $n = 1$ is A028552 in OEIS.

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- Find a new data structure!
- Must incorporate the symmetries.

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- Imagine an infinite source of circles at $(0, 0)$.

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- Take a circle, move it in its row or column.

Recording these moves gives a sequence of unsigned DCJ operations. When all crosses have been destroyed, you have reached your destination genome.

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- OR: Take two circles $(0, a)$, $(0, b)$ and create one circle (a, b) , or vice versa.

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- No single is better than any other!

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- Basically, large loops of dependencies terminate.
- Not only shows that the maximum distance is n , but also gives the sequences of DCJ's.

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- Is there a better data structure that yields a distance without the work of finding the sequence of moves?
- The total number of these unsigned genomes is not known. Is there a smart way to count them?

Thank you to the organizers for allowing me to speak and all their hard work.

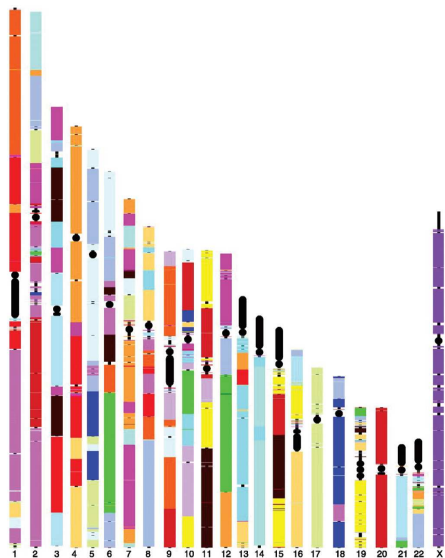


FIGURE 13.33. Gene order is conserved across wide evolutionary distances. The colored segments show blocks of genome that have maintained the same order between mouse and humans. Each color corresponds to a mouse chromosome, overlaid onto the human chromosomes. Note that gene content on the X chromosome is completely conserved (far right).