Exploring Phylogenetic Relationships in *Drosophila* with Ciliate Operations

Jacob Herlin, Anna Nelson and Marion Scheepers

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What is a phylogenetic relationship?

Phylogenetics is the study of evolutionary relationships between groups of organisms. We define the phylogenetic distance between species to be the time since they diverged into distinct species. For this research, we focused on several organisms in the genus *Drosophila*.

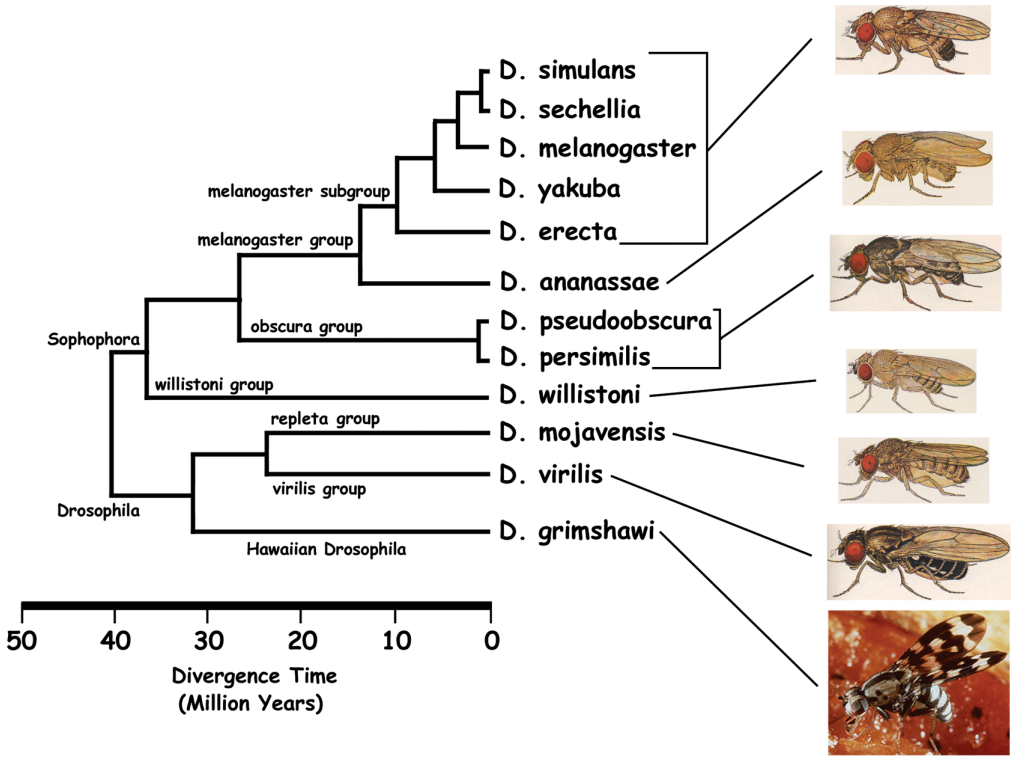

Image courtesy of DroSpeGe: Drosophila Species Genomes. http://insects.eugenes.org/DroSpeGe

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- Using *Drosophila melanogaster* as the canonical reference species, one can use reversals as a measure of evolutionary distance.
- From Hannenhalli and Pevzner, it is known that the shortest signed reversal path can be found in polynomial time.

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- We want to use these operations to relate the DNA of fruitflies in *Drosophila*, and look for a correlation with their known phylogenetic relationsips.

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2. Internal eliminated sequences (IESs) are segments between MDSs that will be removed using the operations
3. Pointers occur on the flanks of the MDSs that preserve the orientation of the genes.

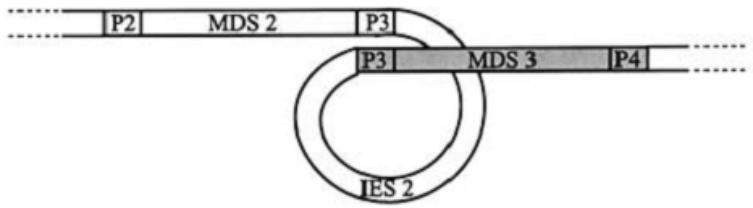
ld operation

The ld operation occurs when a pair of pointers flank an IES between two MDSs. The DNA molecular folds into a simple loop that brings the pairs together. The pairs then join the two MDSs and the removed IES is a closed circle.

$$\ldots\ P_{i,i+1}\ \ldots\ IES_i\ \ldots\ P_{i,i+1}\ \ldots$$

A special case of the ld operation is the boundary ld operation, where a pair of pointers occurs at the ends of a part of the molecule that contains all MDSs.

$$P_{i,i+1}\ \ldots\ MDS_i\ \ldots\ MDS_j\ \ldots\ P_{i,i+1}$$



hi operation

The hairpin (hi) operation occurs when a pair of pointers in which one of the pointers is the opposite sign of the other. The DNA molecule folds so that the two opposite-signed pointers are brought together with the same sign. This operation is analogous to a reversal.

$$\ldots\ P_{i,i+1}\ \ldots\ P_{j,j+1}\ \ldots\ -P_{i,i+1}\ \ldots$$
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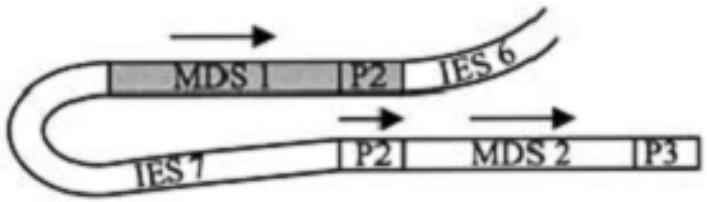

dlad operation

The double-loop (dlad) operation applies to a sequence of DNA when two pairs of pointers are staggered on the strand where one pair of pointers overlap another.

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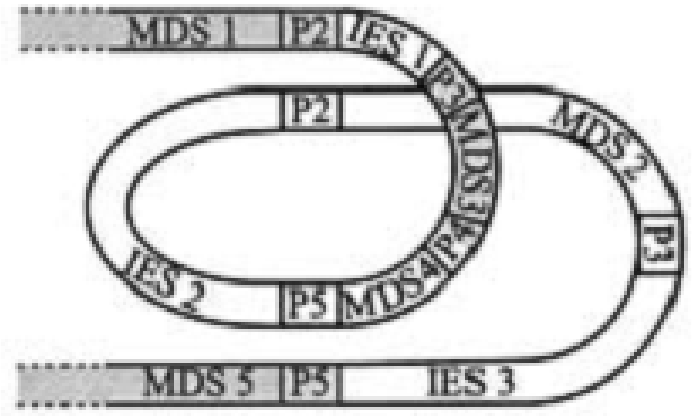

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- The genomes of the species of *Drosophila* are divided into six Muller elements, lettered A-F. We treated each muller element as a seperate permutation.
- We created an algorithm to sort signed permutations in the canonical permutation, and applied this to permutations representing the rest of *Drosophila*, to look for a correlation between the number of requisite steps and their phylogenetic distance from melanogaster.

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where each pair (a, b) represents a section of genome spanning from a pointer a to a pointer b. In our algorithm, we give the pointers signs to represent the orientation of each section, in stead of keeping them in pairs:

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We call this representation a *pointer list*.

Pointer Lists

We define a pointer list formally as a list $L = [x_1, x_2, \ldots x_n]$ that satisfies the following six conditions:

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6. For each odd i, $\nexists$ an odd j such that $x_i < x_j < x_{i+1} < x_{j+1}$.

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The dlad operation is represented by finding a 4-tuple of pointers (x_i, x_j, x_k, x_l) where $x_i = x_j$, and $x_k = x_l$ and $i < k < j < l$. Then, you take the section $x_j x_l$, including the pointers, and the section in-between, but not including, the pointers x_i and x_k, and swapping them, setting up two ld-moves.

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For example,

$$[-2, -1, -3, -2] \Rightarrow [-3, -1]$$

.

A list is considered sorted if it is in the form $[\mu, \lambda]$ or $[-\lambda, -\mu]$ Thus, if a boundary-ld move is done, it will always be the final move in the sorting.

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This algorithm runs in polynomial time in the length of the original permutation. Specifically, the complexity is $O(n^3)$

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- We proved this for lists of length 4 by cases
- For lists of length $n > 4$, we proved this by contradiction, assuming that none of the conditions are met for any of the moves, and showing that the list cannot still be well-formed.
- follows that our algorithm will never crash, and will always find a path to $[\mu, \lambda]$ or $[-\lambda, -\mu]$.

Data Analysis

We obtained, from *Flybase*, data for the locations of every gene on the genomes of the following species of the *Drosophila* genus:

1. Erecta
2. Grimshawi
3. Melanogaster
4. Mojavensis
5. Sechellia
6. Simulans
7. Virillis
8. Yakuba

The algorithm produced these numbers of each move for the Muller *A* element, shown with the known time since their diverenge from *D. melanogaster*.

species	hi	dlad	boundary ld	known divergence time
D. erecta	3	170	0	12.6 mya
D. grimshawi	36	381	1	62 mya
D. sechellia	7	488	0	5.4 mya
D. simulans	8	268	0	5.4 mya
D. yakuba	11	105	1	12.6 mya
D. mojavensis	41	407	0	62 mya
D. virilis	33	403	0	62 mya

The algorithm produced these total numbers for every Muller element added together:

species	hi	dlad	boundary ld	known divergence time
D. erecta	30	658	0	12.6 mya
D. grimshawi	197	1459	3	62 mya
D. sechellia	15	1460	3	5.4 mya
D. simulans	24	508	0	5.4 mya
D. yakuba	47	438	1	12.6 mya
D. mojavensis	189	986	2	62 mya
D. virilis	194	1278	2	62 mya

While this algorithm does not necessarily produce the shortest overall path in the number of combined hi, dlad and ld moves, we conjecture that this is the shortest possible number of hi moves.

The Future

Here are some further areas we have to explore:

1. We conjecture that our algorithm minimises the number of hi moves in its reversal path. We have yet to prove this
2. Develop an algorithm to find the shortest possible cilliate operation path.
3. Look at more species in the *Drosophila* genus and see if the correlation between cilliate operation path length and divergence time holds.
4. Produce permutations for each species as the reference, and use the results from those to construct a phylogenetic tree.

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