Simulating Double Minute Chromosome Evolution using Java

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Abstract

Double minutes are small fragments of circular DNA. Unlike typical chromosomes, they are composed of circular fragments of DNA, up to only a few million base pairs in size and contain no centromere or telomere. They're highly amplified and formed as a byproduct of chromothripsis, or excision and circulation of genomic segments. They are known to harbor oncogenes (genes that are overexpressed) and cause cancer onset when overexpressed. This Java program simulates the evolution of double minutes using recursion, which is the repeated application calling itself. Each double minute shows start and end coordinates and the orientation of the chromosome.

Explanation of Process

The way we attacked the problem of simulating double minutes is having to figure out the best way to represent them. We imagine double minute replication as a phylogenetic tree. A phylogenetic tree is a branching diagram showing that shows the evolutionary relationships among various biological species or other entities based upon similarities and differences in their physical or genetic characteristics. First, we had to create an amplicon. An amplicon is a section of DNA or RNA that has been reinserted elsewhere. To make an amplicon, we need the chromosome of where it is located, start and end coordinates, and the orientation. The chromosomes are represented by a map. A map is a structure composed of a key and a value for each key. The keys in this case are each chromosomes. The values are the amounts of base pairs for each chromosome. The coordinates are randomized and organized where the first coordinate is always less than the second coordinate. The orientation is represented as either true or false. From there we apply recursive calls for it to replicate on its own. We start from a parent amplicon and then the recursive calls will replicate them by 2 each level.
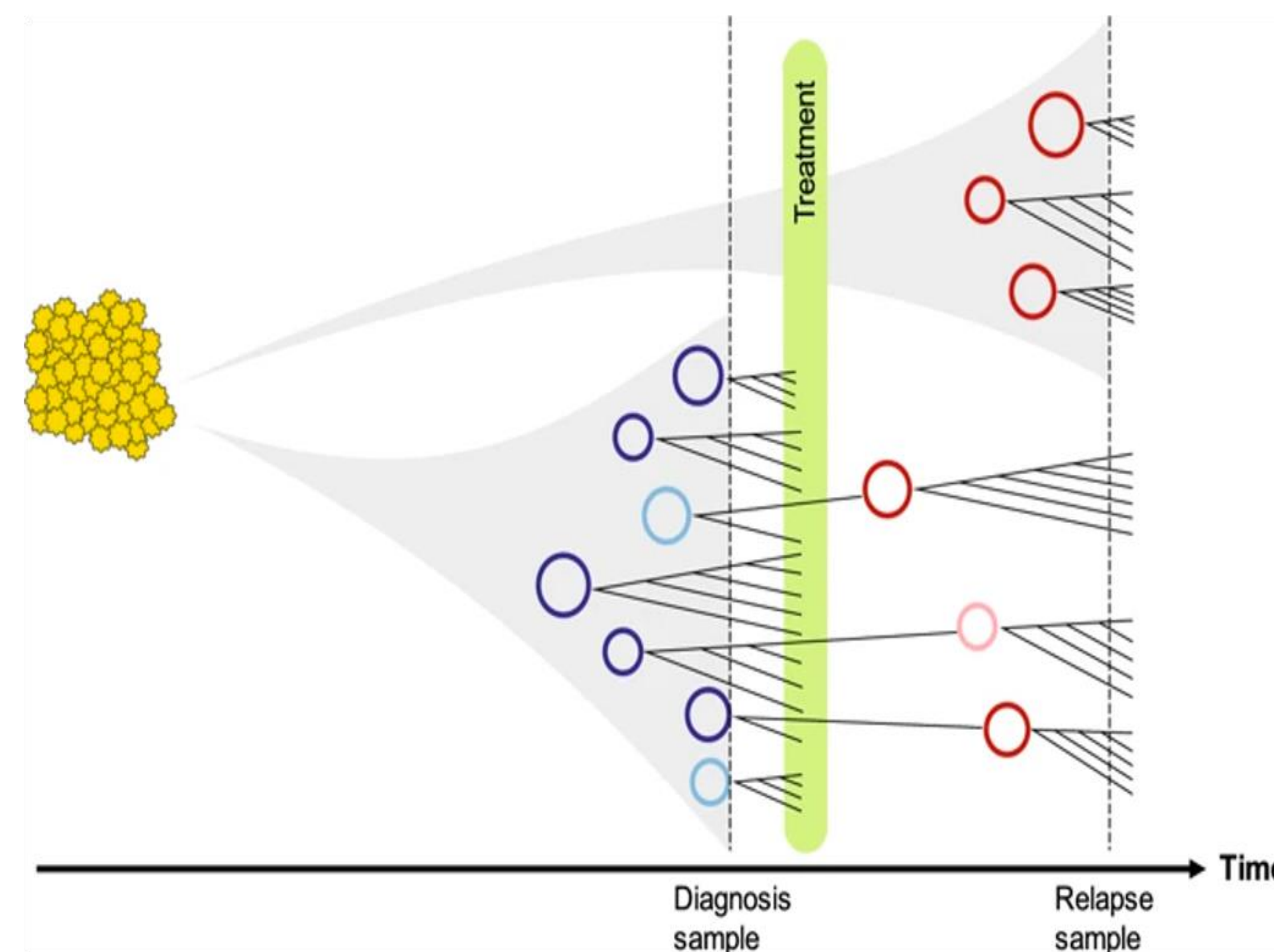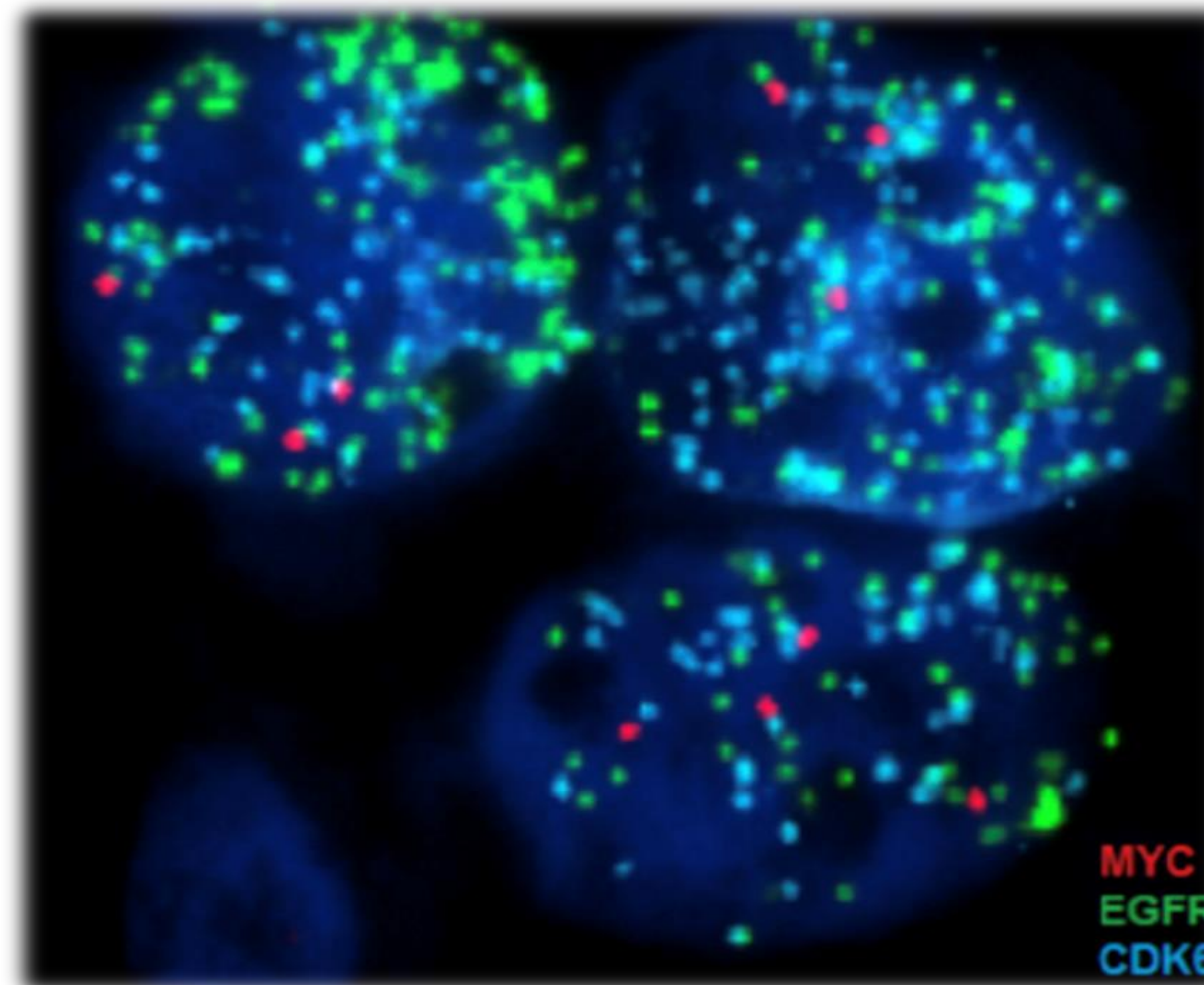
Images of Double Minutes in Cancer Cells

Figure 1: Top: oncogene-carrying double minutes in a cancer cell.
Figure 2: DM evolution before and after treatment.

Goal for DM Evolution and Future Work

Double minute replication in oncogenes is what causes cancer onset. The goal for Double Minute Evolution is to produce ways to stop double minutes from evolving within cells, thus stopping the spread of cancer. The goal of simulating double minute evolution is to simulate FASTQ files and extract the phylogenetic tree from these files. The code I have been simulating shows these phylogenetic trees on display. The double minutes are represented in BED format with the chromosome and coordinates shown. DMs evolve but can be reduced after cancer treatment. Following treatment, DMs that remain are harder to eliminate since their have selective advantages.

Future work includes creating separate methods to simulate double minutes given a user input phylogenetic tree or a random phylogenetic tree. Also, we plan to test the program against actual data to see how well it does to simulate double minutes and create phylogenetic trees.

Acknowledgements and References

[1] Xu, K., Ding, L., Chang, TC. et al. Acta Neuropathol (2019) 137: 123. https://doi.org/10.1007/s00401-018-1912-1
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