

# DNAV: A WebGL based tool for visualizing the twists and turns in the human genome

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## Summary

The human genome is tightly folded to fit within the restricted space of the nucleus. One of the key goals in understanding the folding principles of DNA is to unravel the mysteries of how functional elements that are separated from each other are brought together. Long-range interactions between folded segments of chromosomes form complex three-dimensional networks and are fundamental in controlling gene expression. These long-range interactions have been observed using chromosome conformation capture (3C). This Hi-C data contains a wealth of information on the nearest-neighbor influence on the deviation of the DNA axis that can be modeled theoretically. We have developed a tool using WebGL to visualize the modeled structures.

## Data

The data is obtained from the Hi-C data generated to map the organization of the human genome by Lieberman-Aiden et al. Briefly, to map long-range contacts using Hi-C, the DNA fragments are cross-linked chemically. This creates covalent links between spatially separated DNA segments. DNA is then cut using a molecular scissor called restriction enzyme and filled with biotinylated nucleotides. DNA segments are then joined together, purified and sequenced using the paired-end method (see figure 1A). This reveals the alphabets of regions that are in spatial proximity but would otherwise be far apart in linear DNA molecule. While the Hi-C analysis of the human genome has revealed the folding principle of the genome at a macro level, the data generated by the method can be exploited to understand the landscape interactions in the human genome.

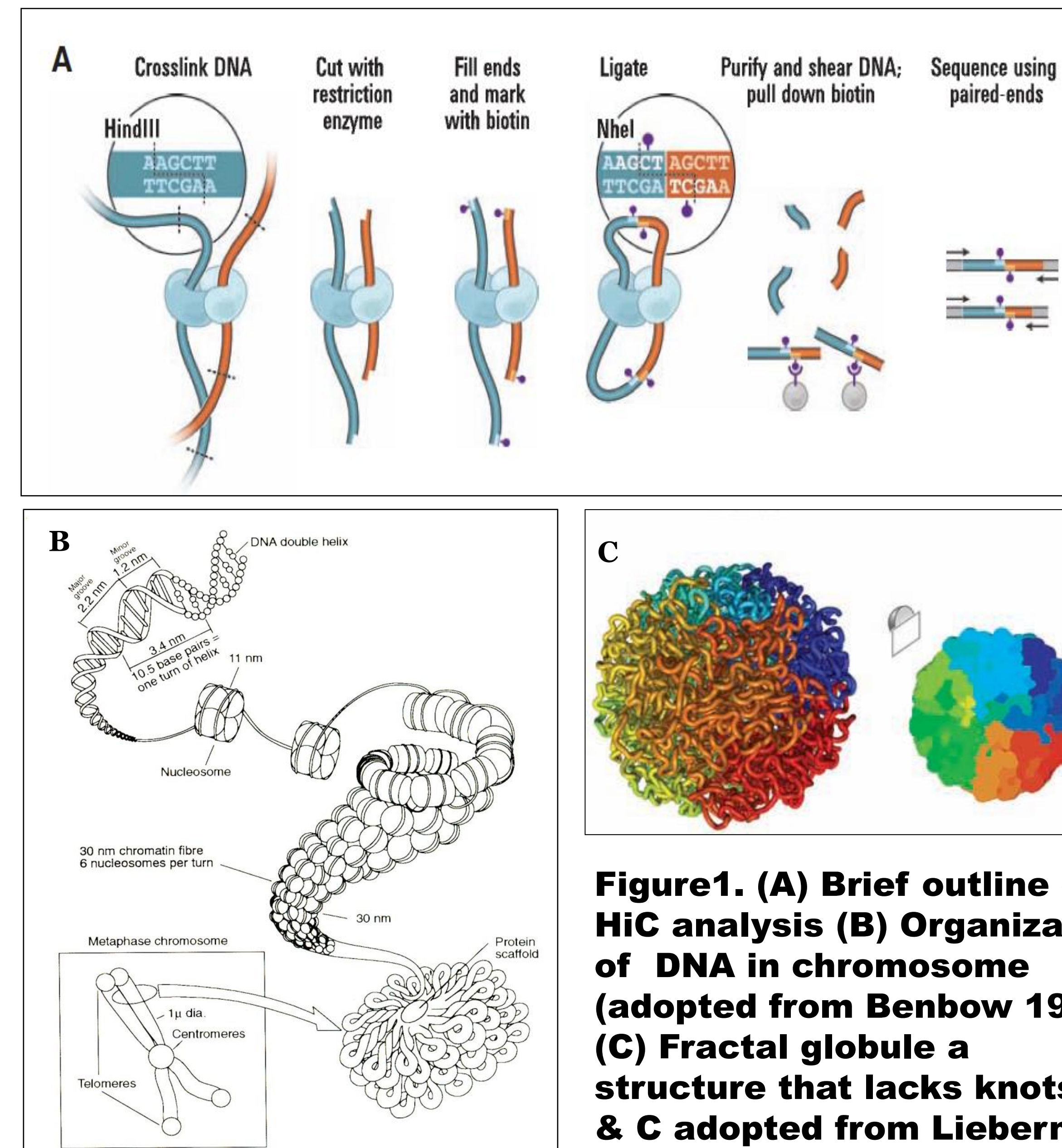
## Using WebGL to create a tool to visualize 3D models of DNA

- WebGL is a JavaScript application for rendering graphics. It is growing popularity and increasing support among web developers, made it an ideal choice for the development of a web based tool. It is also backed by Google and due to the nature of applications it is becoming very popular in an academic setting. WebGL is being used by many research departments as a quick and easy way to create visualizations based on the data that their research has collected.

- WebGL allows site users to not have to download any additional libraries and is instead a graphical library that runs directly from your browser.

- WebGL is a JavaScript library which allows for 3D graphics rendering within the JavaScript/html environment. This creates a tremendous amount of versatility and allows for extremely dynamic web pages with minimal external applications.

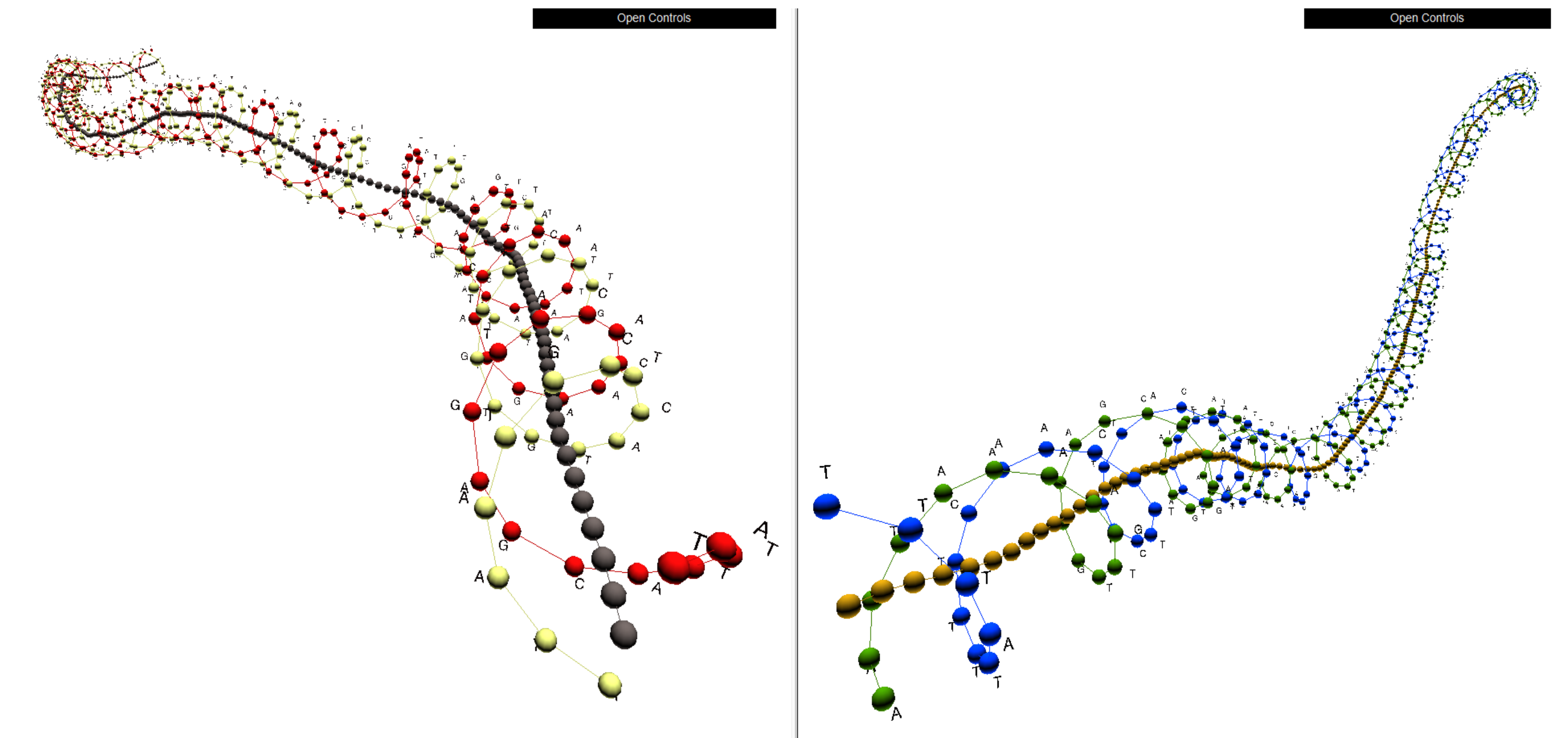
- We chose WebGL over other rendering libraries due to its ease of use and the fact that it allows users to see the rendering directly in their browser, which means that from any computer that is using one of many popular browsers you can go to the website and use DNAV.



**Figure 1. (A) Brief outline of HiC analysis (B) Organization of DNA in chromosome (adopted from Benbow 1992) (C) Fractal globule a structure that lacks knots (A & C adopted from Lieberman et al 2009).**

## DNAV web Tool

- DNAV connects to a remote server and retrieves coordinates that are then plotted in a 3-Dimensional environment which allow for the user to move inside, around, up or down to achieve the desired viewing angle of the DNA strand.
- We also added a color coding tool which the user can use to determine the color of different parts of the DNA strand enabling them to choose color schemes which might better suit their needs.
- Adding a screenshot feature creates an easy way for the user to capture certain points along the DNA strand and save that information for use in future projects.
- The ability to show or remove the helix around the center of the DNA added a visual functionality to better see the curvature of the DNA spine.
- The DNA sequence is also visible from any angle while viewing the DNA strand



**Figure 2. Graphical rendering of the DNA structure created using DNAV**


## The Next Step

- Creating a directory which will allow users to pull up annotations for certain parts of the DNA and clearly mark which sections and sequences are being referenced
- Create a smoother interaction between web page and server allowing for a more seamless query of the SQL database
- Adding a search and query application to allow the user to search through different sets of DNA and show them to be compared
- Increase rendering efficiency for faster load times and smoother viewing control
- Improve the control scheme for more fluid and intuitive interaction between the user and tool.
- From a biological perspective, the long-range maps can also be used to understand how genome rearrangements often seen in tumor genomes may affect spatial organization in genomes

## References

Lieberman-Aiden et al., (2009) Comprehensive mapping of long-range interactions reveals folding principles of the human genome, *Science* 326, 289-293..

Benbow, R. M. (1992) Chromosome structures, *Sci Prog* 76, 425-450.

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