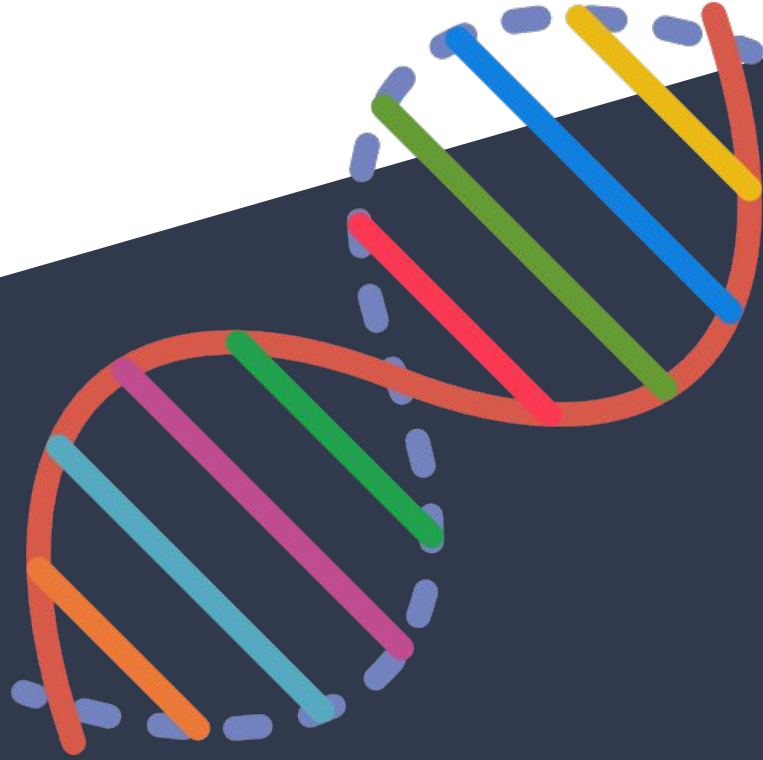
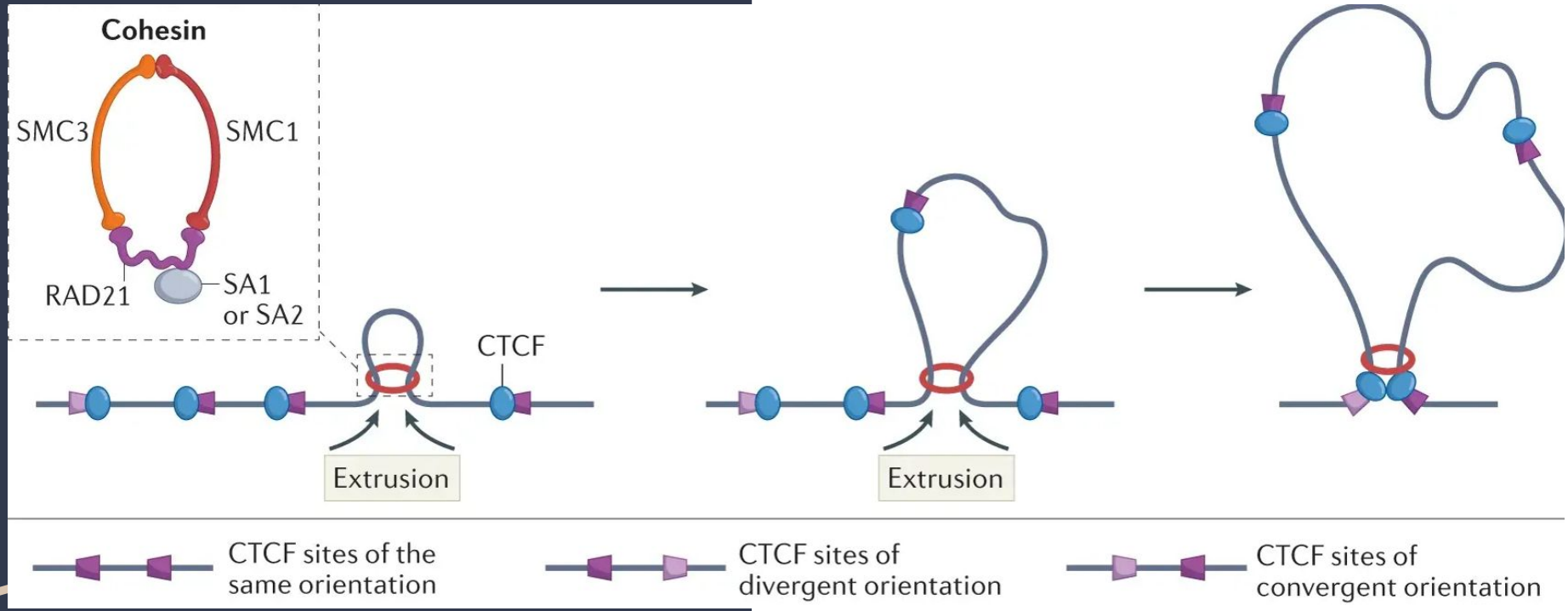
Utilizing Machine Learning to Identify Time Asymmetry of DNA Loop Extrusion

Anna Du



Loop Extrusion

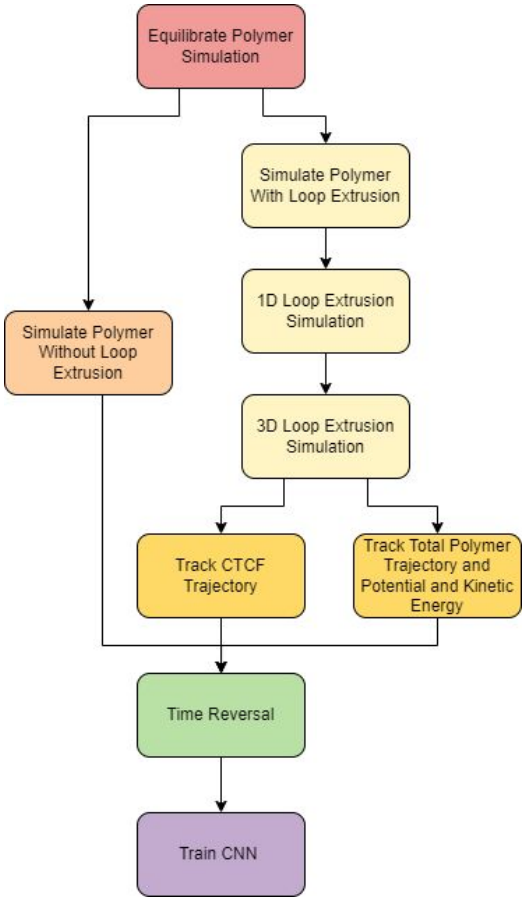


(Zhang, 2022)

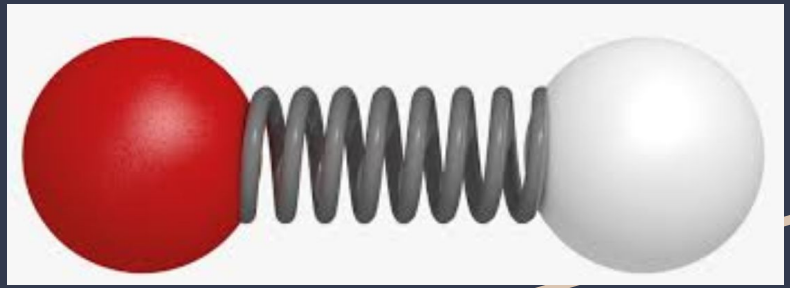
Goal

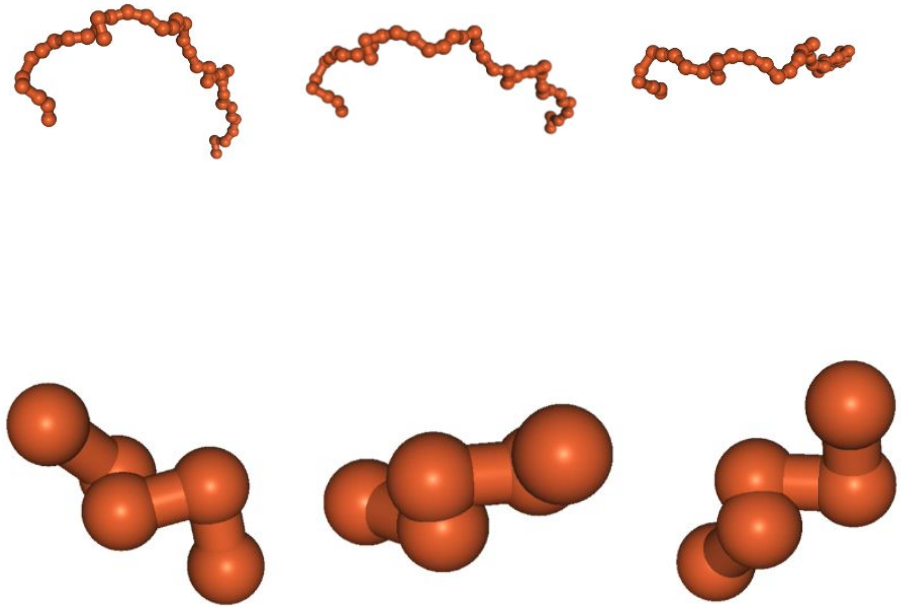
Detect loop extrusion in living systems by comparing “movies" of DNA with loop extrusion that are played forward and backward in time.

Workflow

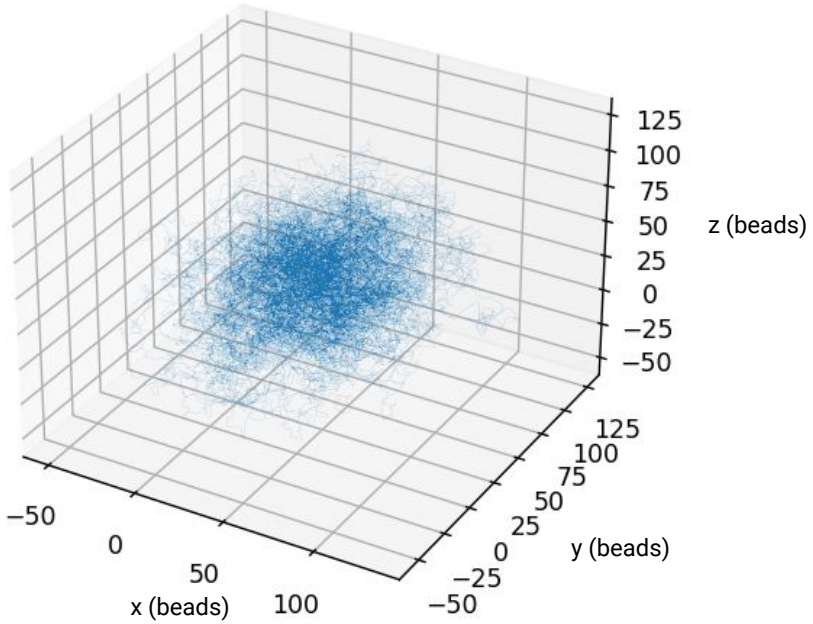


Polychrom Synthetic Dataset



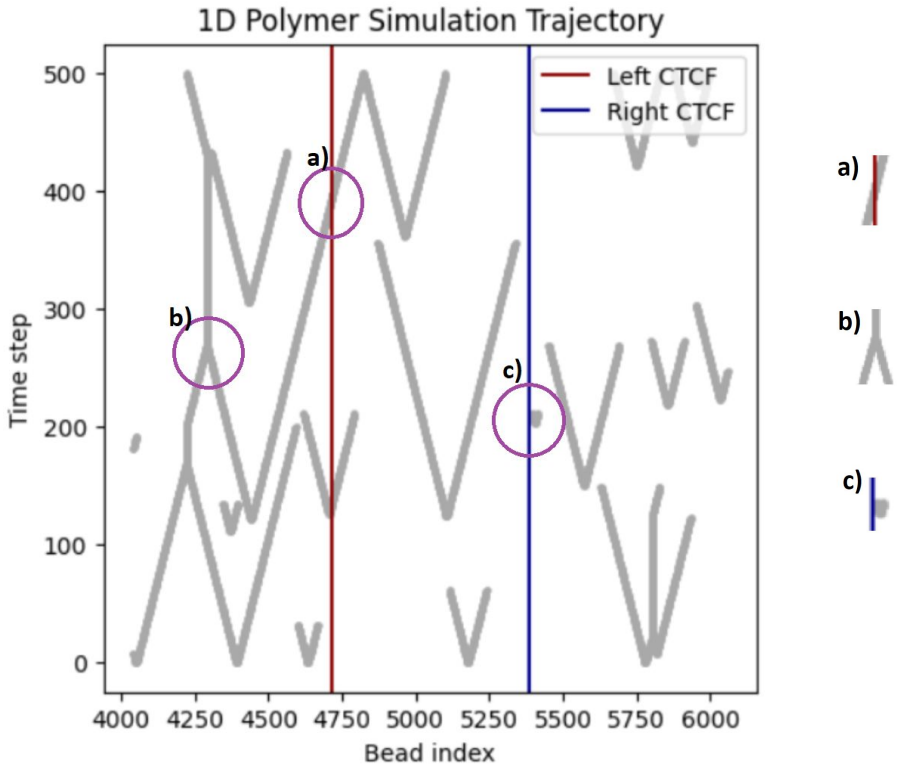


Equilibrated Polychrom Simulations

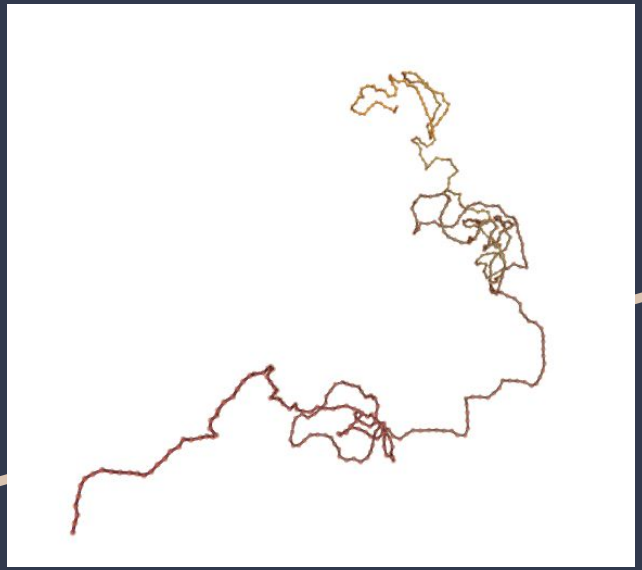


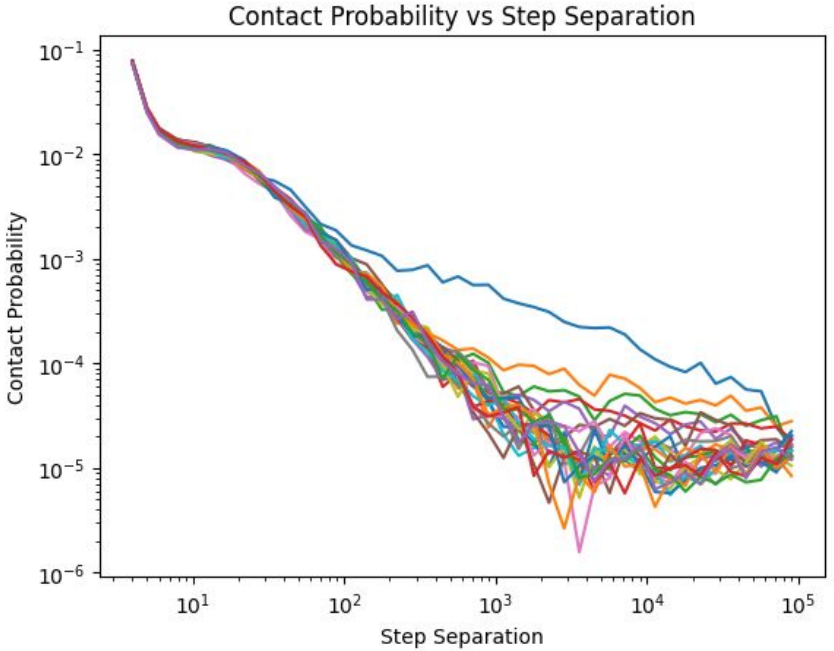
Representation of the Polychrom generated polymer using MatPlotLib

1D Loop Extrusion Simulations

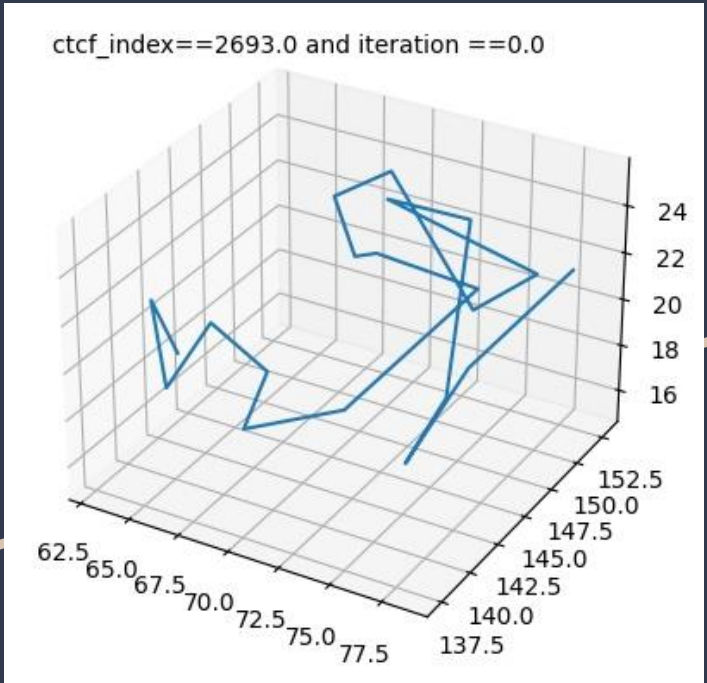


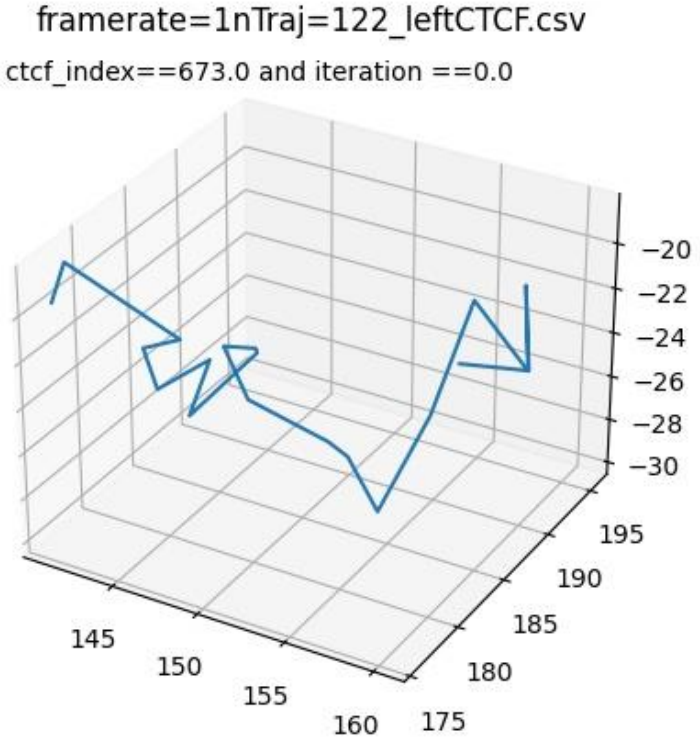
3D Loop Extrusion Simulations





CTCF Location Tracking

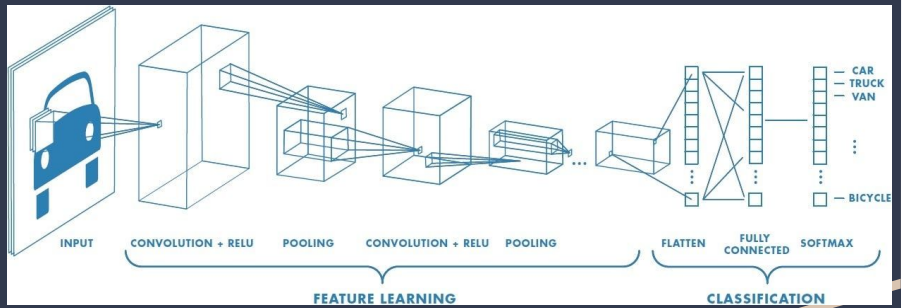




Time Reversal

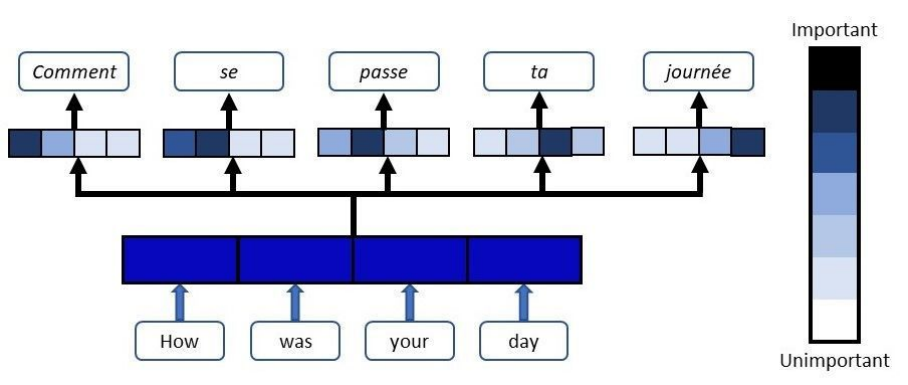
- Create a synthetic dataset for assessing the potential for loop extrusion detection
- DNA motion movies exhibit distinct behaviors when played forward compared to when played backward due to the influence of loop extrusion
- Quantitative method to distinguish between reversed and non-reversed DNA movement.

CNN



- Time-dependence relates to forward and backward propagation in neural networks.
- Create more efficient pathways to generate numerical training data both time dependent and multi-variant.
- Seek correlations both forward and backward through time.
- Help observe changes in genetic systems that can form a potential mutation event, which could form cancer, diabetes, or other diseases.

Alternative Strategies



- Transformers can be used as an alternative model to run simulations
  - Utilizes attention to focus on the entire sequence as a whole
  - Requires fewer training data to form a more efficient and accurate model
  - Handle sequences of variable lengths

Current Applications

- Used as an alternative to live imaging cells on the sub-nuclear level
- Understand the fundamental nature of the structure of sub-nuclear arrangements of genetic material
- Identify targeted therapies for cancers and diseases, based on driver and passenger mutation

Acknowledgement

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References

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Thank You!