The Structure of DNA in E. Coli

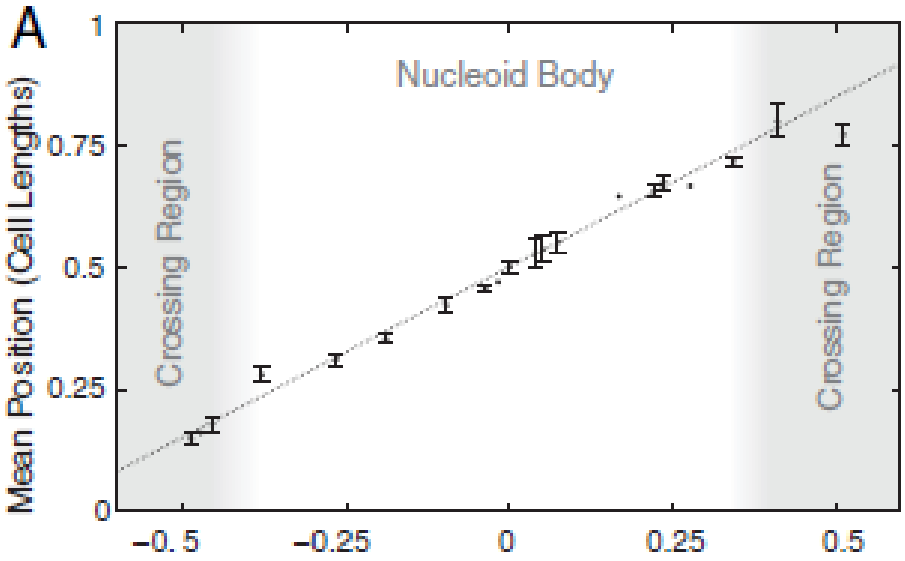
Sylvia Hürlimann
MIT PRIMES
May 21, 2011

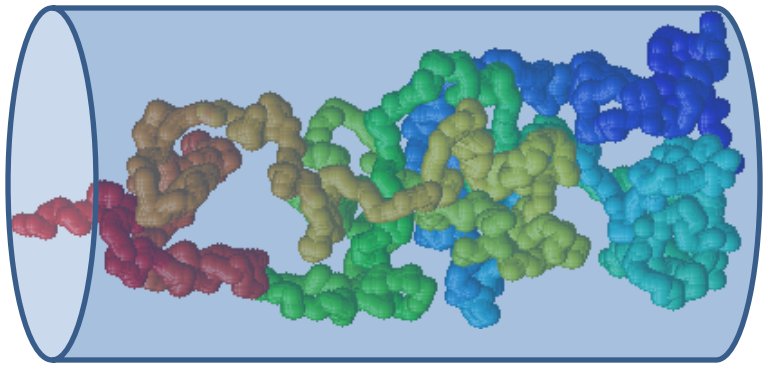
Description of E. Coli and its genome

- E. Coli has a circular genome that is roughly six million base pairs long
- The genome is confined within a section of the cell called the nucleoid, which is roughly shaped like a cylinder.

Experimental Data

- The E. coli nucleoid is experimentally shown to be linearly organized along the axis of the nucleoid





One of our model conformations

Wiggins P A et al. PNAS 2010;107:4991-4995

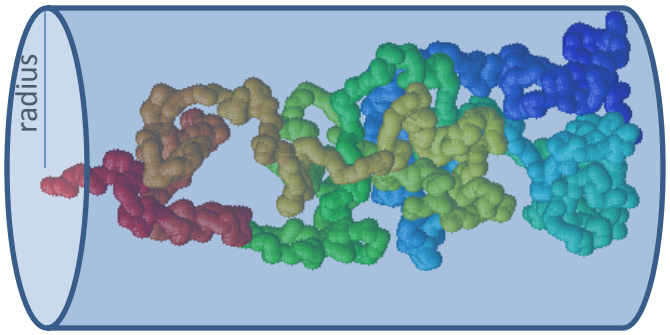
Can a polymer model explain E. coli genomic organization?

- Previous authors have suggested that the genome can be modeled as a polymer
- In this model, the structure of the genome is determined by three factors:
  - intranucleoid interactions (stiffness, volume interactions)
  - confinement of the chromosome within the nucleoid
  - the tethering of the DNA at two ends of the nucleoid
- Previous studies, however, never tested these predictions with a detailed simulation.

Wiggins P A et al. PNAS 2010;107:4991-4995

How can we test a detailed polymer model?

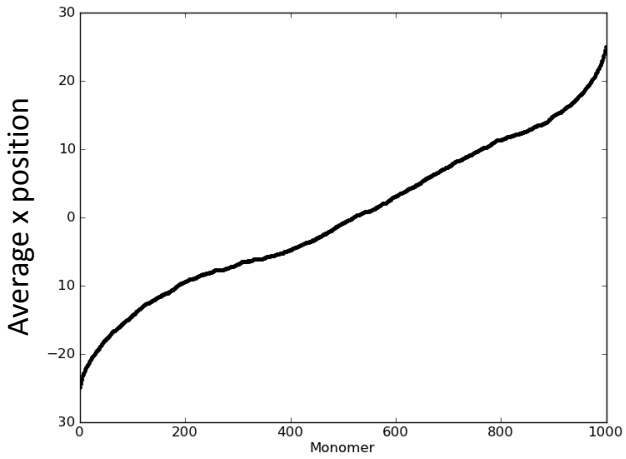
- We place a polymer inside a cylinder and tether the ends of the chain to either end of the cylinder. After running the simulation for many time steps, we calculate the average x position of each monomer
- Vary parameters such as:
  - whether the ends are tethered
  - the size of the cylinder
  - the stiffness (or flexibility) of the chain
  - whether the chain can overlap itself

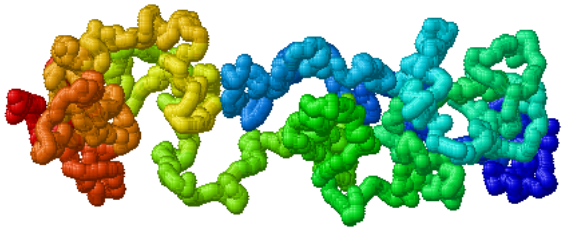


Length or x-axis

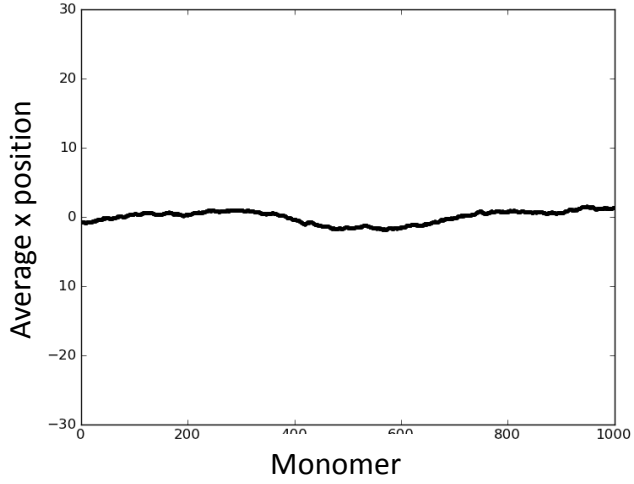
Results: effects of tethering

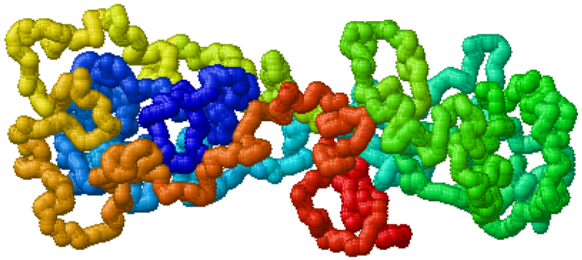
With tethering





Without tethering



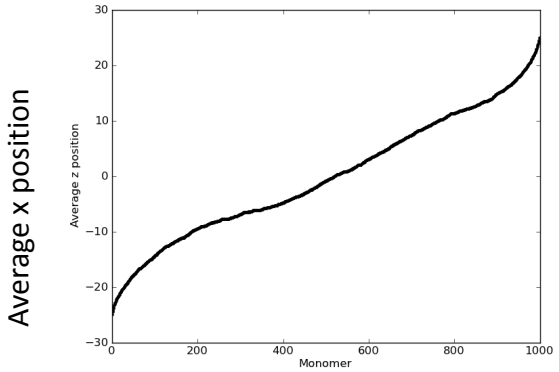


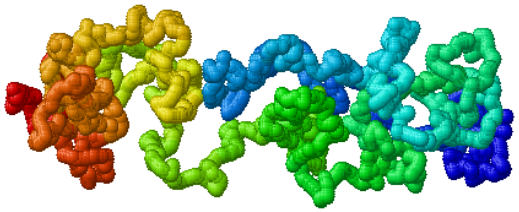
- The genome lacks structure along the axis of the cylinder
- Supports the claim that the tethering of the chain to the ends of the nucleoid is important to structure

Results: varying cylinder size

Cylinder Size

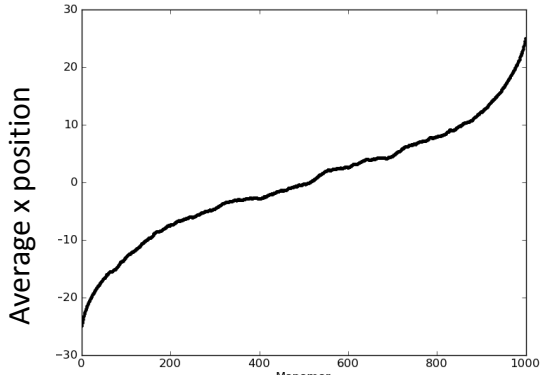
50x20x20

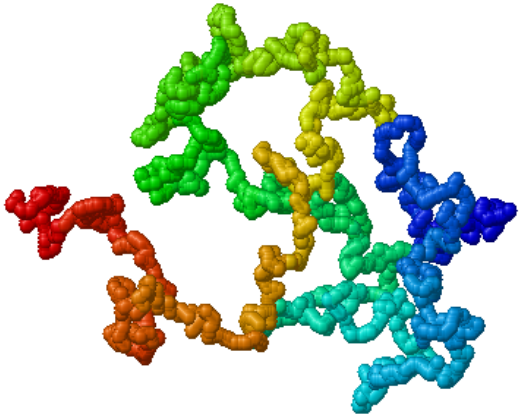




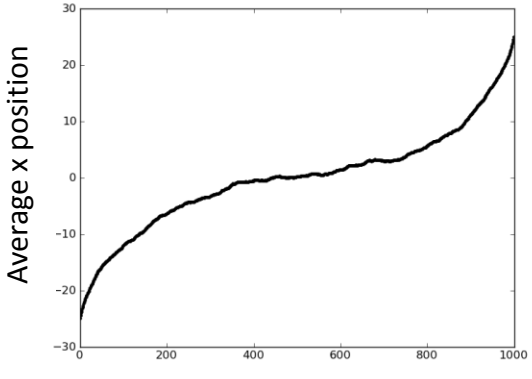
Almost linear

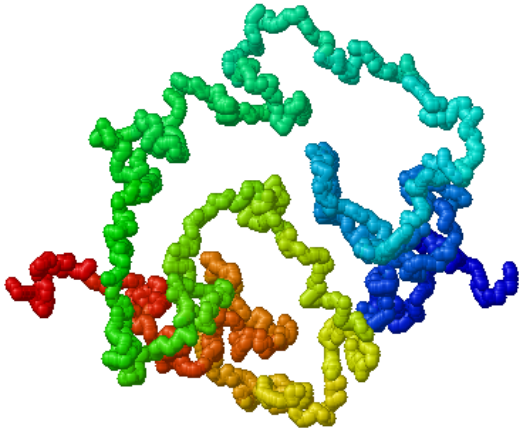
50x40x40





50x60x60





Less structured

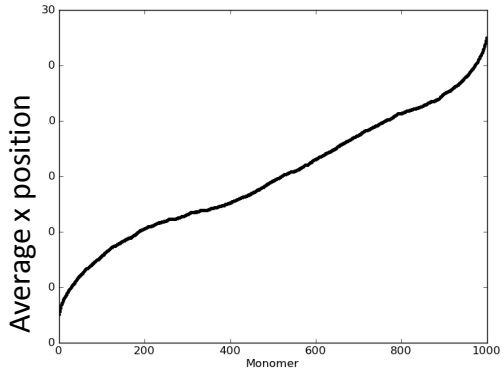
Interpretation

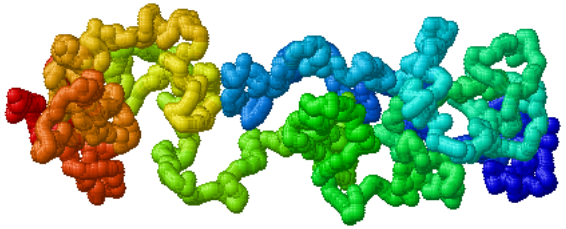
- As the diameter of the cylinder increases, the DNA becomes gradually less linearly organized similarly to what happened when the stiffness of the chain increased
- Supports the argument that confinement of the DNA is an important factor in its structure

Simulation results: varying stiffness

Stiffness of the chain

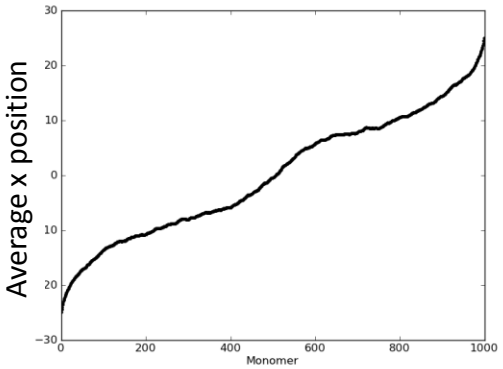
0*kbond

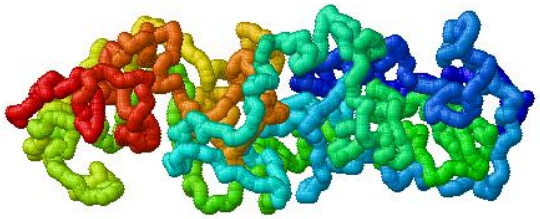




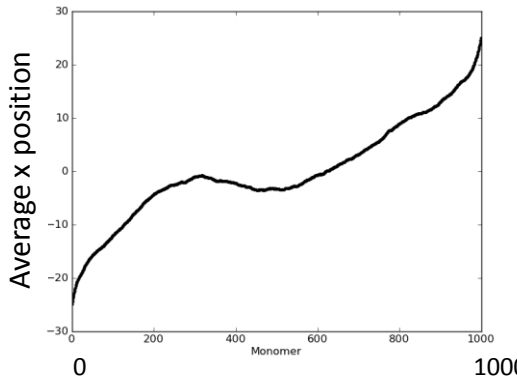
Almost linear

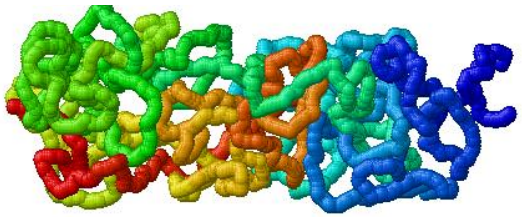
0.25*kbond





0.50*kbond



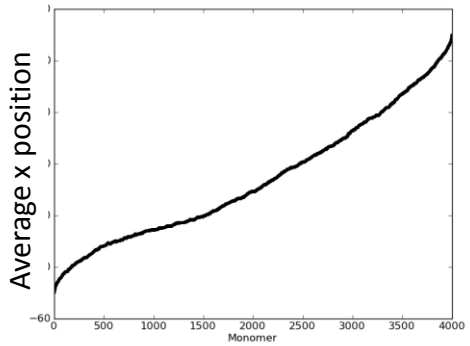


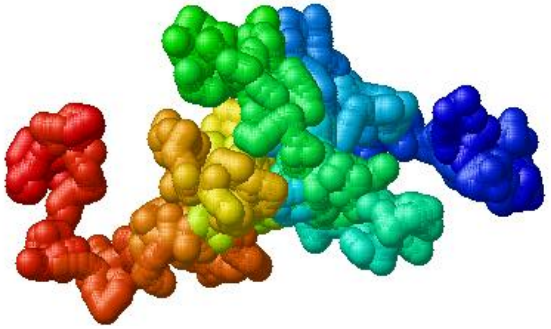
Less structured

Simulation results: varying stiffness (without volume interactions)

Stiffness of the chain

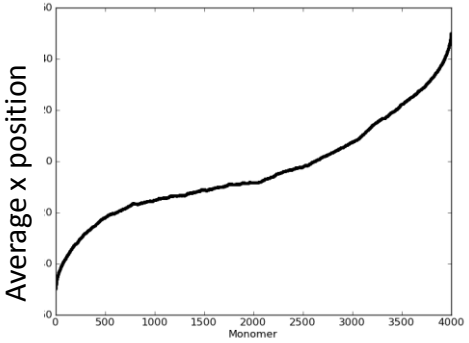
0*kbond

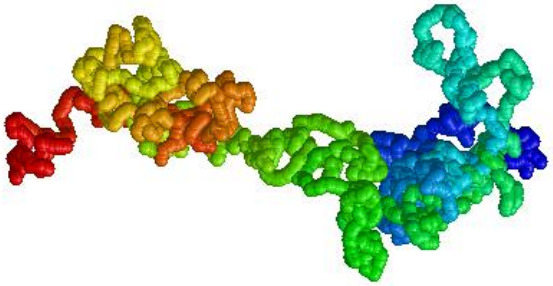




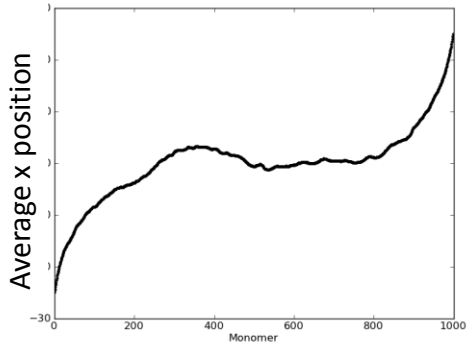
Almost linear

0.25*kbond





0.50*kbond



Less structured

0 1000

Monomer

Interpretation

- Results with and without volume interactions show the same general trend but stiffness has a greater affect when there are no volume interactions
- This implies that volume interactions do not play a large role in the organization of the chain

Future directions

- How does the shape and size of the cylinder affect the structure?
- How does the density of the chain affect the structure?
- Do these results still hold for longer chains?

And many thanks to my mentors
Geoffrey Fudenberg and Maxim Imakaev
as well as to Leonid Mirny