CATEGORY: LIFE & MATERIAL SCIENCE - LS02
POSTER P5137
CONTACT NAME Adrian Sanborn: asanborn@stanford.edu

GPU TECHNOLOGY CONFERENCE

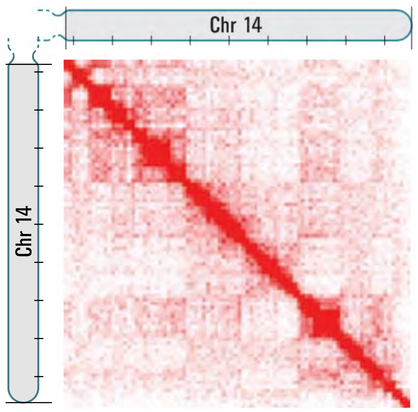
GPU-accelerated modeling of folded human DNA

Adrian Sanborn
Center for Genome Architecture, Houston, TX
Department of Computer Science, Stanford University, CA

Genome Folding

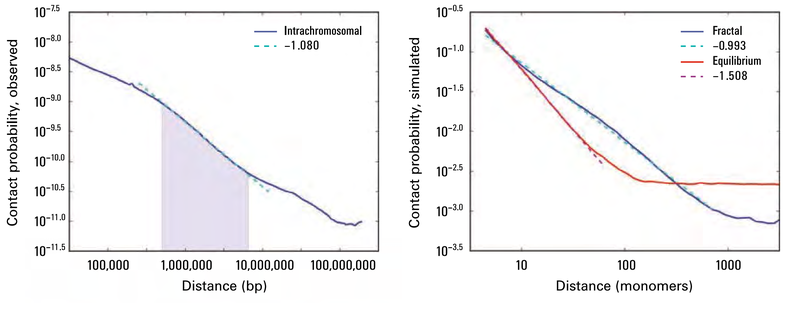
The human genome is over 2 meters long, yet it must fold inside a nucleus just a few microns wide. The manner in which DNA folds is linked to cellular functions such as gene expression.

New experiments have generated large **maps of self-contacts** formed by human DNA in its folded state, giving clues to its physical conformation.

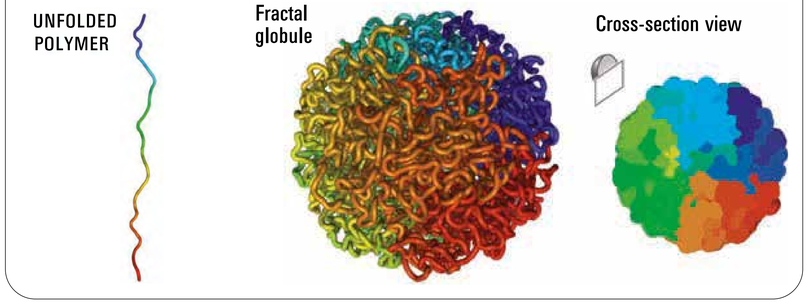


Fractal Globule Model

Measurements of **contact probability** as a function of distance separating two loci exhibits a **power-law** scaling between distances of 500kb and 7Mb.



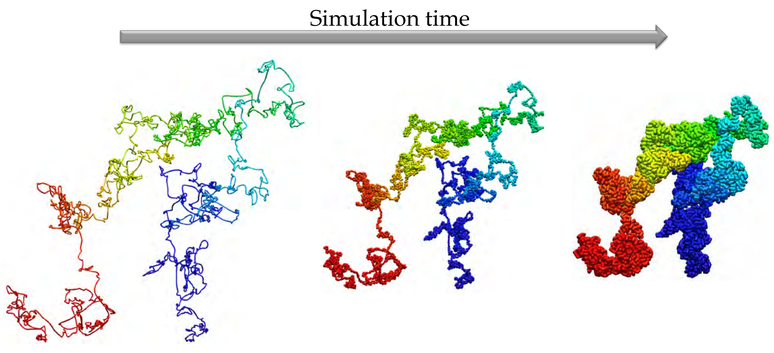
This is consistent with a non-equilibrium state known as the **fractal globule.**

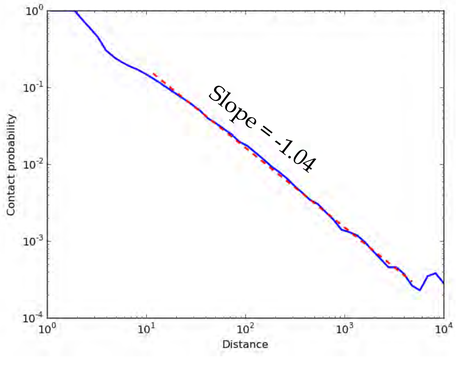


Molecular Simulations

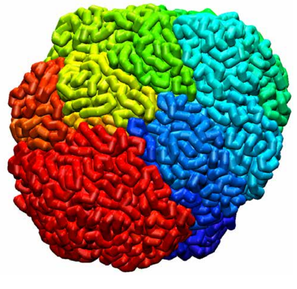
Initial models of the fractal globule were created using Monte Carlo simulations requiring some physically unrealistic transformations. We wondered whether fractal globules could be simulated in more realistic conditions using molecular dynamics.

Fractal globules are characterized by scale-free, isotropic compaction. Thus, our simulations implement a **global crushing force** that draw monomers to a central spatial position. We initialize the polymer in a self-avoiding walk.





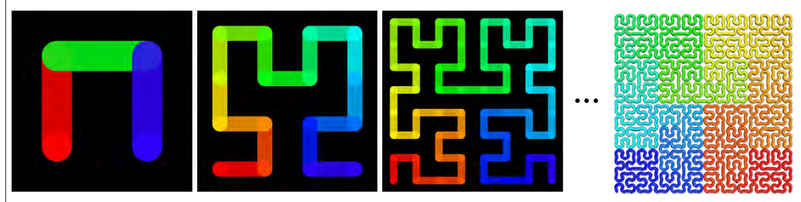
Collapsed state



By taking advantage of **GPU acceleration**, we are able to run hundreds of replicate simulations with polymers length up to 50,000 within a several days. When we compute contact probability aggregated over all replicates, we obtain a power law with exponent -1.04, consistent with previous results.

Mathematical Fractal Models

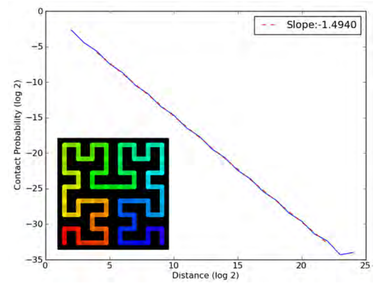
We analyzed the contact patterns of the fractal globule, a scale-free structure, in the context of general scale-free curves. We studied **self-similar curves** which were constructed through an iterative process, such as the Hilbert curve:



When we plot contact probability for these curves, we consistently observe a power law with exponent equal to

dim(*boundary*) / dim(*curve*) - 2.

For example, the Hilbert curve has contact probability exponent equal to 1 / 2 – 2 = - 1.5



In fact, by using a **combinatorial description**, we can rigorously derive the contact probability exponent of the Hilbert curve from first principles.

Collaborators: Andrew Jewett; also Suhas Rao, Miriam Huntley, and Erez Lieberman Aiden.

Support: NIH New Innovator Award (DP2-OD008540-02), Cancer Prevention Research Institute of Texas Recruitment Grant (R1304).

References:

E. Lieberman-Aiden *et al.*, Comprehensive mapping of long-range interactions reveals folding principles of the human genome, *Science* **326**, 289–93 (2009).
S. Rao, M. Huntley *et al.*, A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping, *Cell* **159**, 1665-80 (2014).