Introduction:
3D genome architecture

CS/CME/Biophys/BMI 371
Feb. 27, 2017
Ron Dror
“3D genome architecture”

- Each human cell contains about 2 meters of DNA
- How is it packed into the nucleus?

http://www.erez.com/Science
Why should we care?

• Every cell in your body contains the same DNA (i.e., the same genes)
• Yet the cells are very different from one another, because the genes are expressed differently (i.e., different quantities of protein get made from each gene)
• These expression differences are probably linked, in part, to the physical organization of the DNA
  – They’re also related to chemical modifications of DNA (post-translational modifications)
How can we study 3D genomic architecture?

• One can use microscopy to observe actual physical locations of labels attached to the chromosomes, but resolution is relatively low

• Most of the available information comes from chromosome conformation capture techniques (e.g., Hi-C and TCC)
  – These techniques find DNA “contacts” (i.e., places where one DNA strand touches another)
  – To do this, they introduce chemical links between spatially proximate DNA strands, and then use DNA sequencing techniques to find out which parts of the chromosomes were linked

• Computational problem: reconstruct structure (and dynamics) from this partial information
  – Remember that chromosomal structure varies over time and from cell to cell
Background material

• Review paper
  – “Organization and function of the 3D genome” (Nature Reviews Genetics, 2016)

• Original Hi-C paper
  – “Comprehensive Mapping of Long-Range Interactions Reveals Folding Principles of the Human Genome” (Science, 2009)
    – http://science.sciencemag.org/content/326/5950/289