Introduction:
3D genome architecture

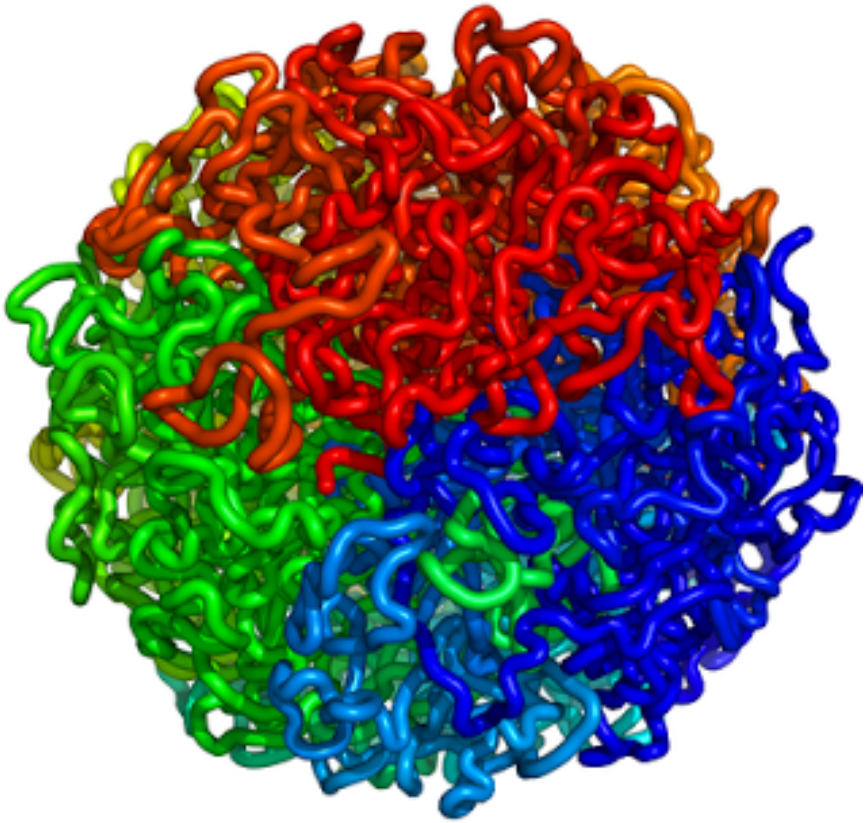
CS/CME/Biophys/BMI 371

Feb. 27, 2018

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

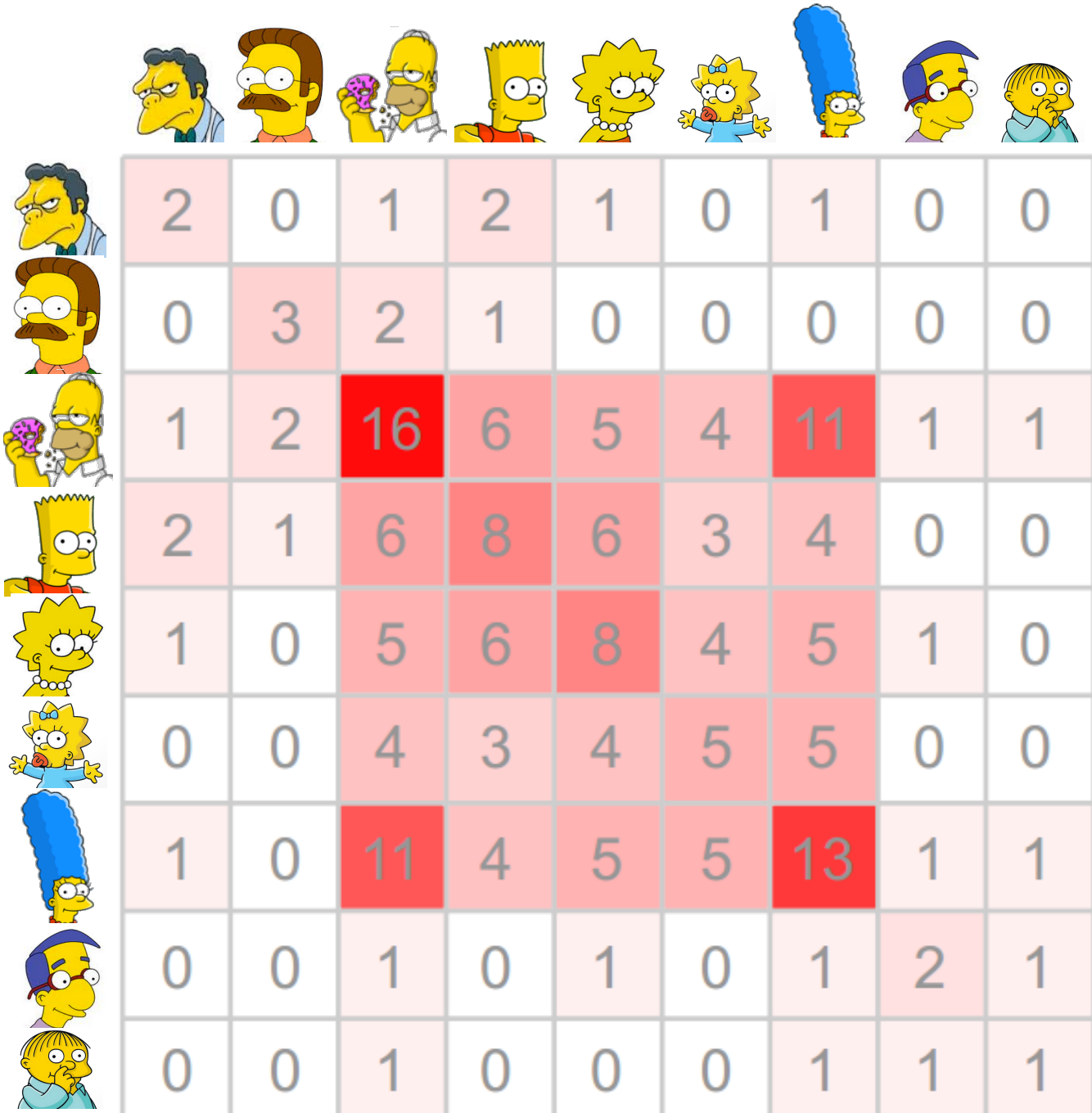
How can we study 3D genomic architecture?

- 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 proximal 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

Chromosome conformation capture techniques identify frequencies of contacts between one part of a DNA strand and another. These contact frequencies can be used to infer structural features of chromatin, such as domains and loops.

SIMPSONS
CONTACT MAP

Number of pictures together



From Erez Lieberman-Aiden

Papers for Thursday

- To think about: how much information does each paper give about the actual structure of the genome in each individual cell?
- Rao et al., *Cell* 2014
  - Large amount of population-level Hi-C data
  - Analyze organization of genome, but no 3D modeling of individual genome structures
- Tjong et al., *PNAS* 2016
  - 3D modeling based on population-level data
  - Infer likely ensemble of individual structures
- Stevens et al., *Nature* 2017
  - 3D modeling based on single-cell data

Background material

- Slides on genome organization from CS/CME/BioE/ Biophys/BMI 279 (Adrian Sanborn):
  - http://web.stanford.edu/class/cs279/lectures/lecture7.pdf
- Review paper
  - "Organization and function of the 3D genome" (Nature Reviews Genetics, 2016)
  - http://www.nature.com/nrg/journal/v17/n11/full/nrg.2016.112.html
- 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

Mid-quarter feedback

- Thank you!
- Critique feedback
  - We just got out feedback for another 25 critiques, and will do the rest soon
- Option for more, shorter critiques
  - Reminder: If you prefer, you can substitute two one-page critiques (on two different papers) for one “regular” critique.
- I will try to give slightly more extensive introductions
  - Please make an extra effort to keep presentations from being too long
  - You need to rehearse with a stopwatch