Biomedical Data Science: An Introduction

M Gerstein

Slides freely downloadable from
Lectures.GersteinLab.org

Twitter meeting hashtag:
#CBDS7Feb

Historical Perspective on Data Sci. – Jim Gray

#3 - Simulation

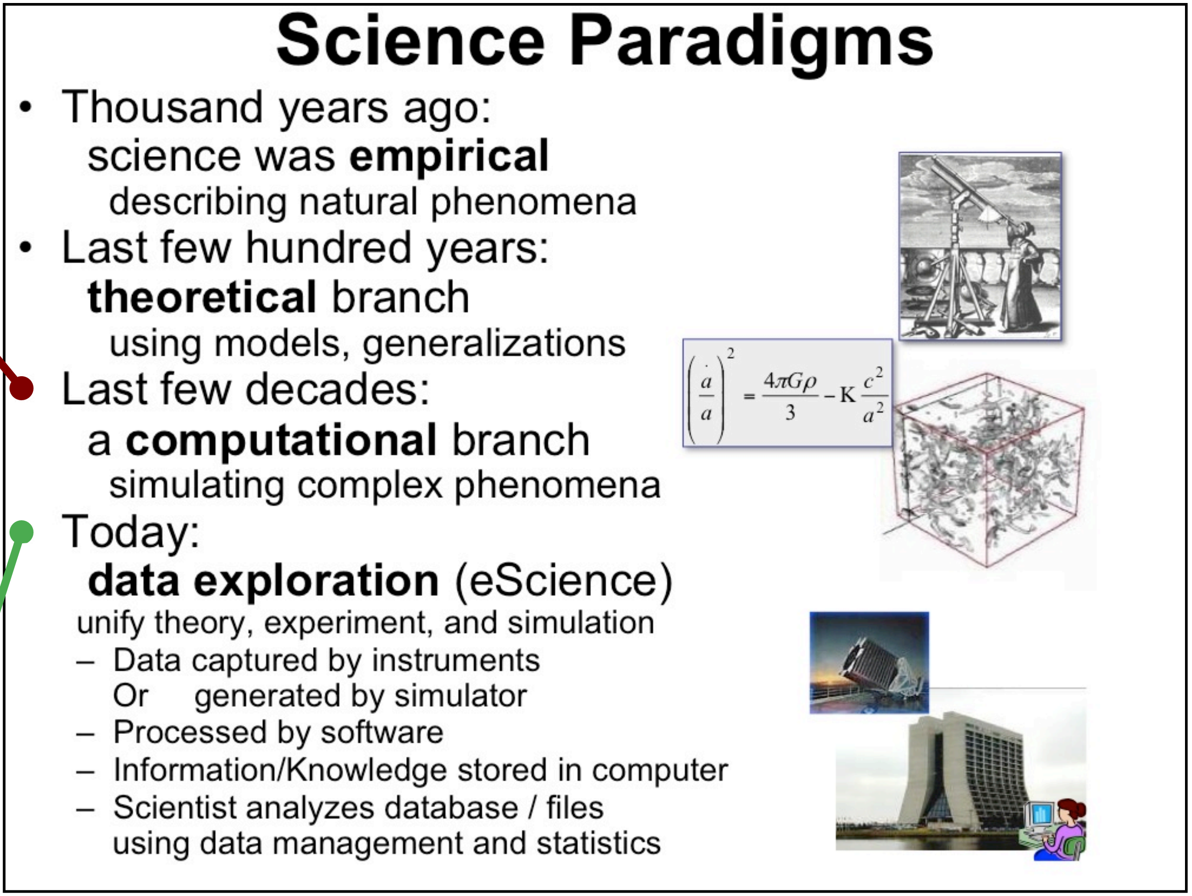
Prediction based on physical principles (eg Exact Determination of Rocket Traj.)

Emphasis: Supercomputers

#4 - Data Mining

Classifying information & discovering unexpected relationships

Emphasis: DB emphasis

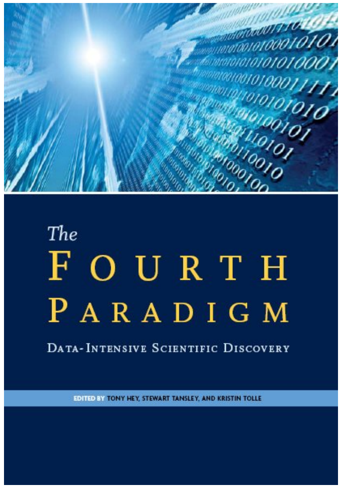


Science Paradigms

- Thousand years ago:
  science was **empirical**
  describing natural phenomena
- Last few hundred years:
  theoretical branch
  using models, generalizations
- Last few decades:
  a **computational** branch
  simulating complex phenomena
- Today:
  data exploration (eScience)
  unify theory, experiment, and simulation
  - Data captured by instruments
    Or generated by simulator
  - Processed by software
  - Information/Knowledge stored in computer
  - Scientist analyzes database / files
    using data management and statistics

$$\left(\frac{\dot{a}}{a}\right)^2 = \frac{4\pi G\rho}{3} - K\frac{c^2}{a^2}$$

Gray died in ’07.
Book about came out in ’09...


The
FOURTH
PARADIGM
DATA-INTENSIVE SCIENTIFIC DISCOVERY
EDITED BY TONY HEY, STEWART TANSLEY, AND KRISTIN TOLLE

[Slide from :
http://research.microsoft.com/en-us/um/people/gray/talks/stanford%2520symbolic%2520systems%2520seminar.ppt]

What is Data Science, Today?

- Data Science encompasses the study of the entire **lifecycle of data**
  - Understanding of how data are **gathered**
    - Knowledge of what data sources are available & how they may be synthesized
  - The **storage**, access, annotation, management, & transformation of data
- Data Science encompasses many aspects of primary **data analysis**
  - Statistical inference, machine learning, & the design of algorithms and computing systems that enable **data mining**
  - Connecting this mining where possible with analytic **modeling**
  - The presentation & intuitive **visualization** of analysis results
  - The use of data analysis to make **practical decisions**
- Consideration of secondary aspects of data (eg the **data exhaust**)
  - **Creative secondary uses**, not related to intent at collection
    - EG Science of science
  - The appropriate protection of **privacy**

Tukey, J. W. (1962). The Future of Data Analysis. *The Annals of Mathematical Statistics*, *33*(1), 1–67. http://doi.org/10.2307/2237638

Cleveland, W. S. (2001). Data Science: an Action Plan for Expanding the Technical Areas of the Field of Statistics. *International Statistical Review*, *69*(1), 21–26. http://doi.org/10.1111/j.1751-5823.2001.tb00477.x

Donoho, D. (2017). 50 Years of Data Science. *Journal of Computational and Graphical Statistics*,*26*(4), 745–766. http://doi.org/10.1080/10618600.2017.1384734

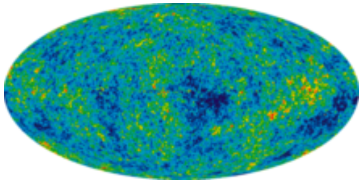
- Commercial Data
  - Social activity generated
  - Ads, supply optimization, &c
  - Integral to success of GOOG, AMZN,FB, WMT…

- Scientific Data
  - Pre-dated commercial mining
  - Large sets generated by special instruments
  - Often created by large teams - not to address single hypothesis but to be mined broadly

Data Science in Traditional Science v business world

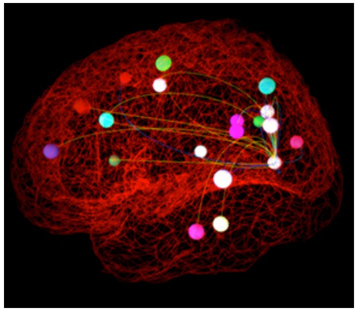
High energy physics - LHC

Genomics - DNA sequencer



Astronomy - Sloan Digital Sky survey

Ecology & Earth Sci. - Fluxnet



Neuroscience - Connectome Project

Coupling of Scientific Data to Models & Experiments

- Scientific data often coupled to a physical/biological model
- Lauffenburger's Sys. Biol. **4Ms:**
  Measurement, Mining, Modeling & Manipulation
  (Ideker et al.'06. Annals of Biomed. Eng.)
- Weather forecasting as an exemplar
  - Physical models & simulation useful but not sufficient ("butterfly" effect)
  - Success via coupling to large-scale sensor data collection

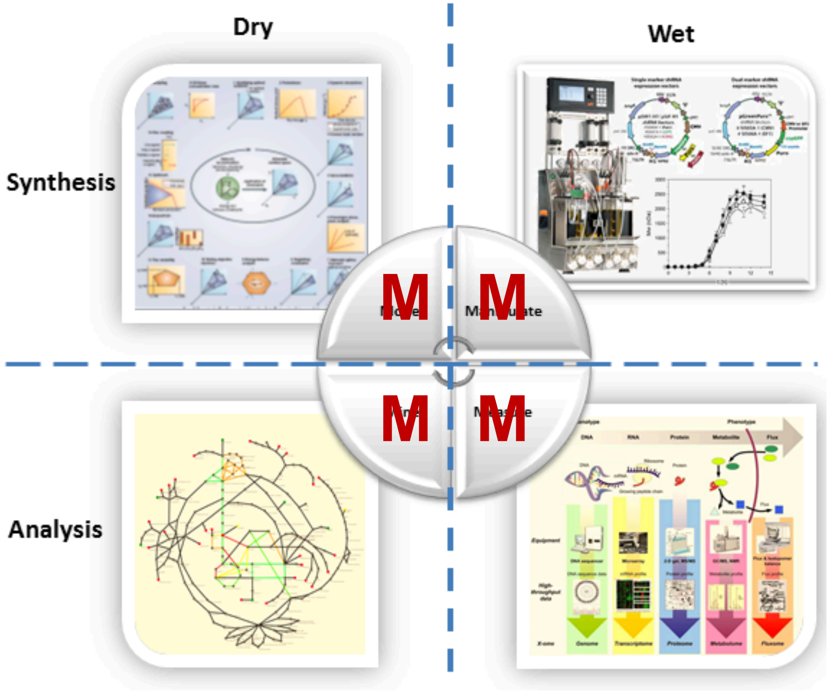
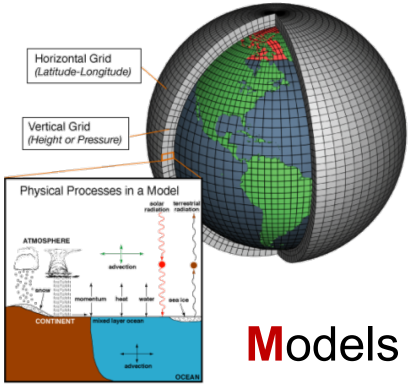
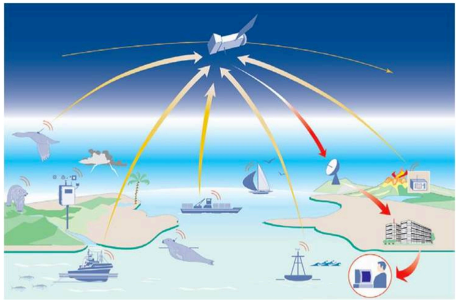


Image from http://web.aibn.uq.edu.au/cssb/ResearchProjects.htm

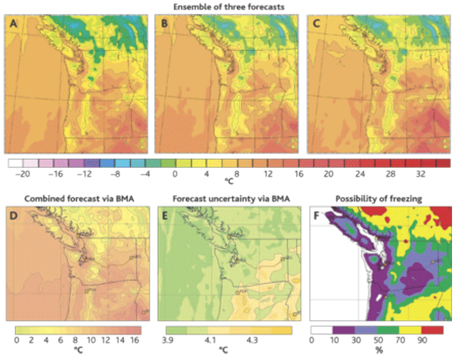




Models + Data Mining

↓

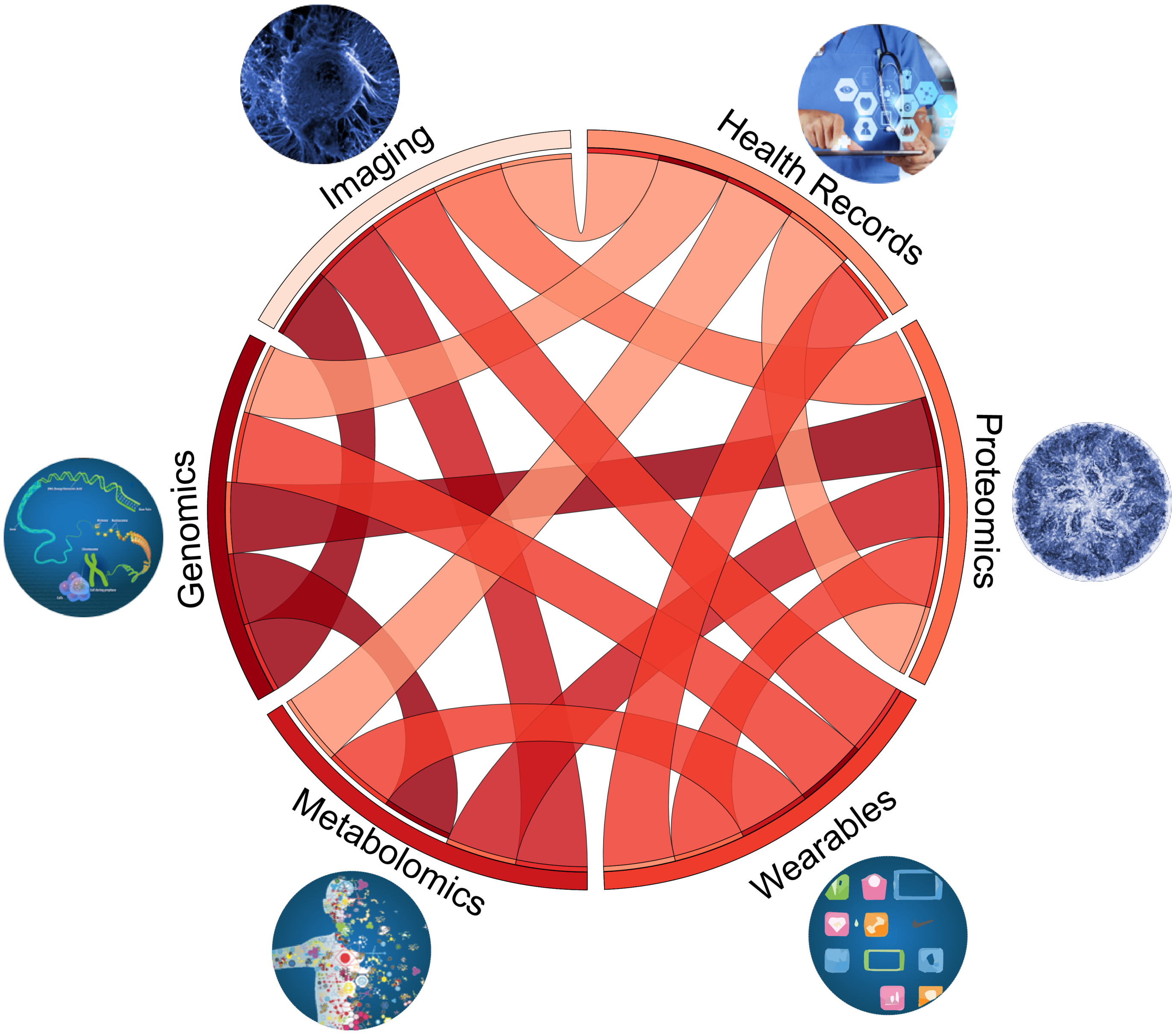
Forecasts



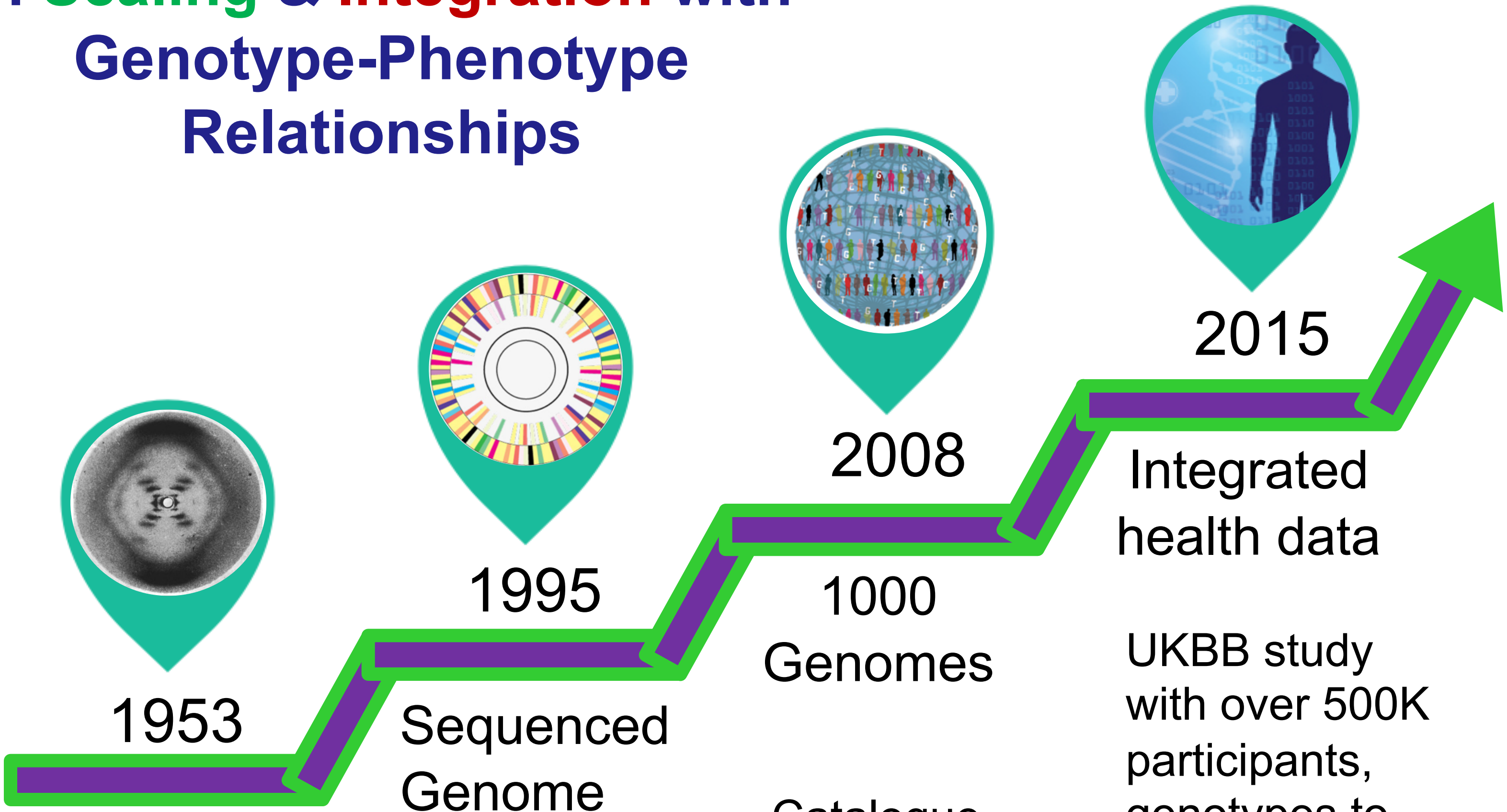
NOAA

Drivers of Biomedical Data Science

- **Integration** across data types
- **Scaling** of individual data types



Case Study: Amazing Progress in Scaling & Integration with Genotype-Phenotype Relationships



1953

Double Helix

Watson & Crick

1995

Sequenced Genome

H. influenzae

2008

1000 Genomes

Catalogue of human variation

2015

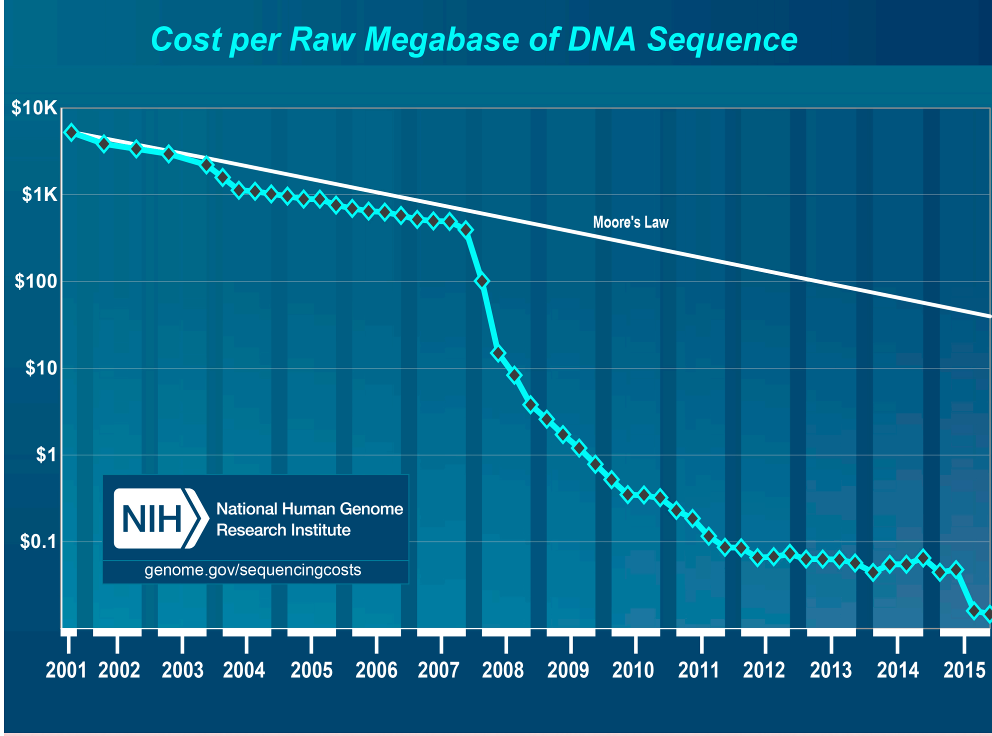
Integrated health data

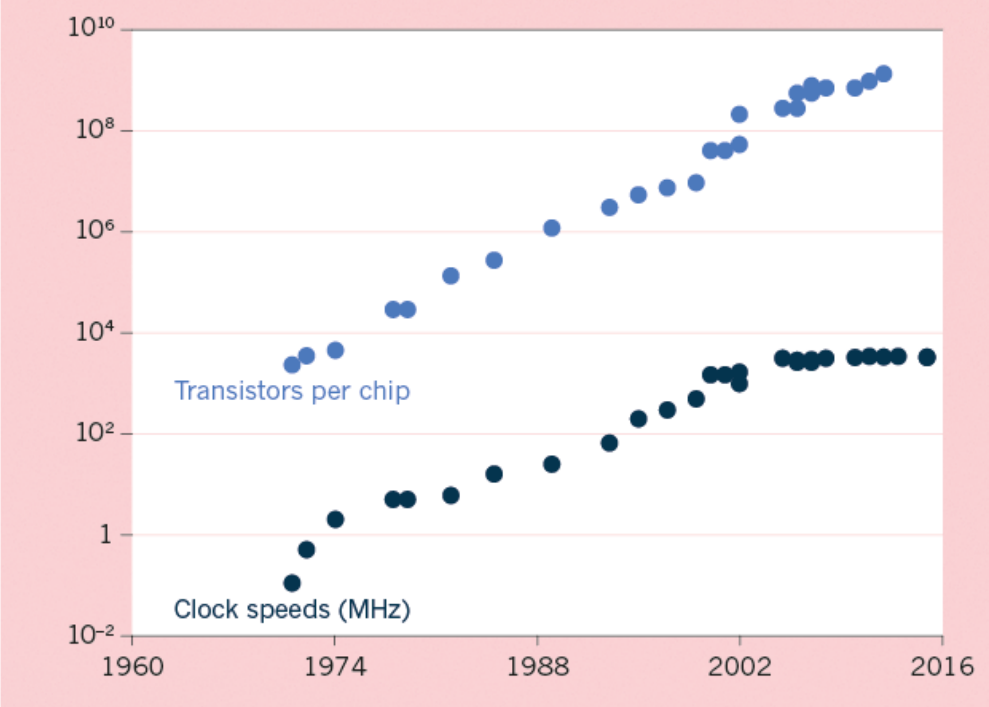
UKBB study with over 500K participants, genotypes to phenotypic details & clinical information

The Scaling of Genomic Data Science:

Powered by exponential increases in data & computing

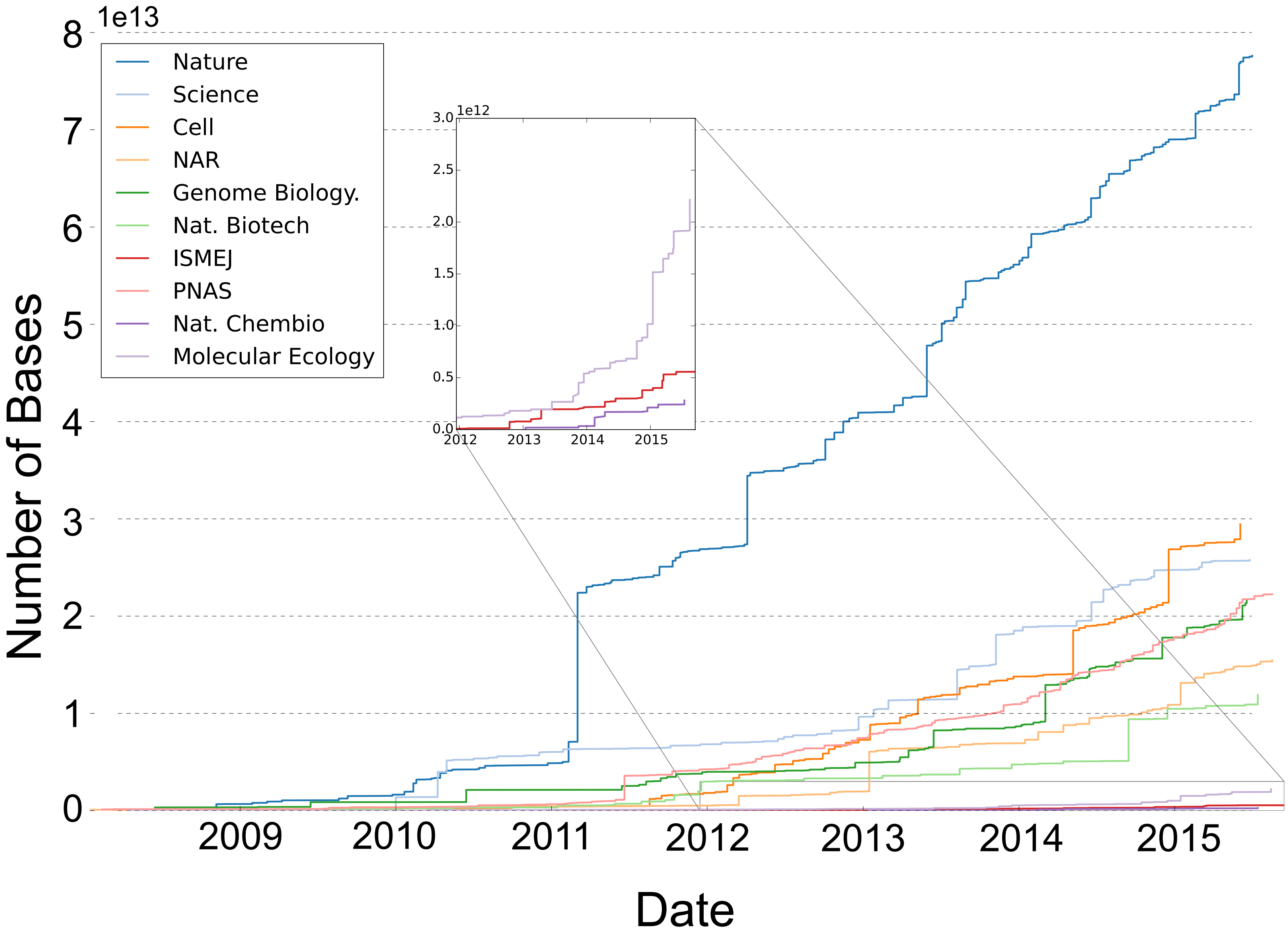
(Moore's Law)





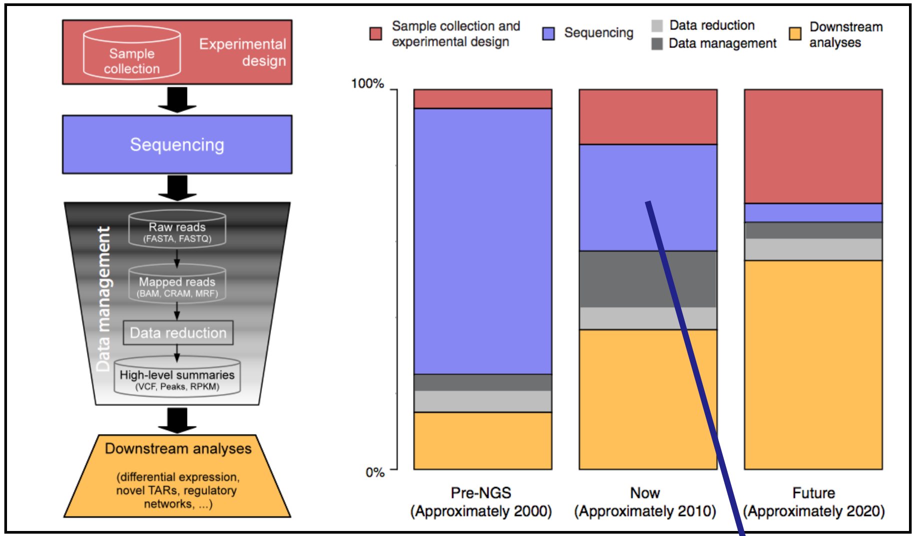
[NHGRI website + Waldrop ('15) Nature]

Exponential Scaling Changes Fields Using Genomic Data



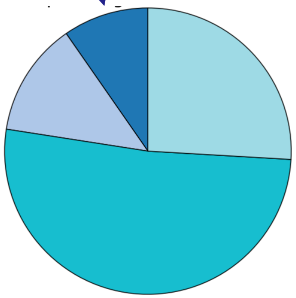
[Muir et al. ('15) GenomeBiol.]

Exponential Scaling changes Genomics Itself



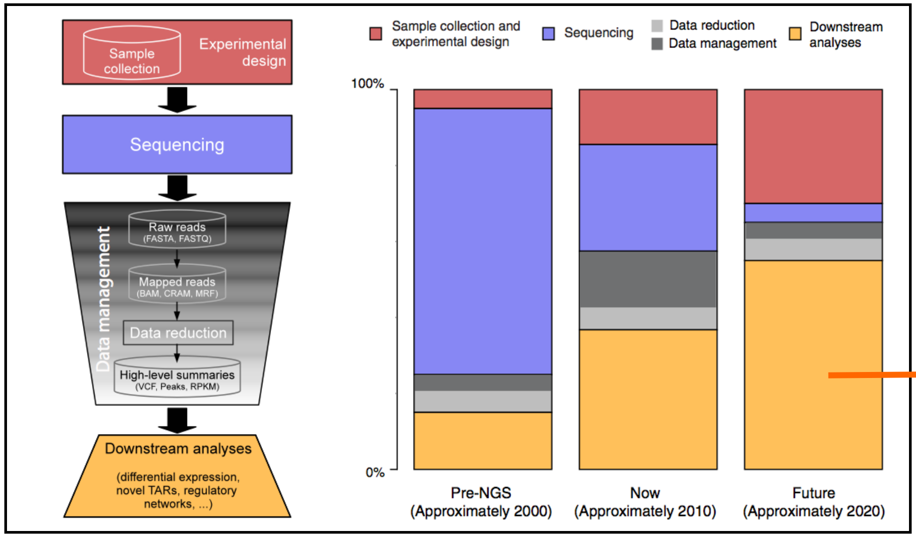
From ‘00 to ~’ 20,
cost of DNA sequencing expt. shifts from the actual seq. to sample collection & analysis

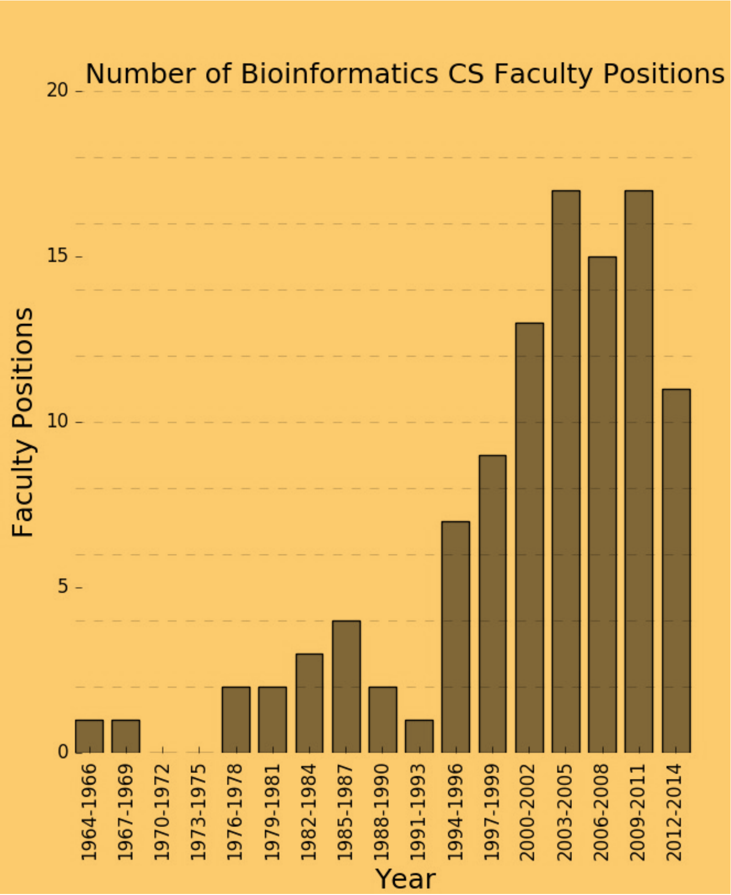
- 🟦 Labor
- 🟦 Instrument depreciation and maintenance
- 🟦 Reagents and supplies
- 🟦 Indirect costs



[Sboner et al. (‘11), Muir et al. (‘15) Genome Biology]

Exponential Scaling changes Genomics Itself



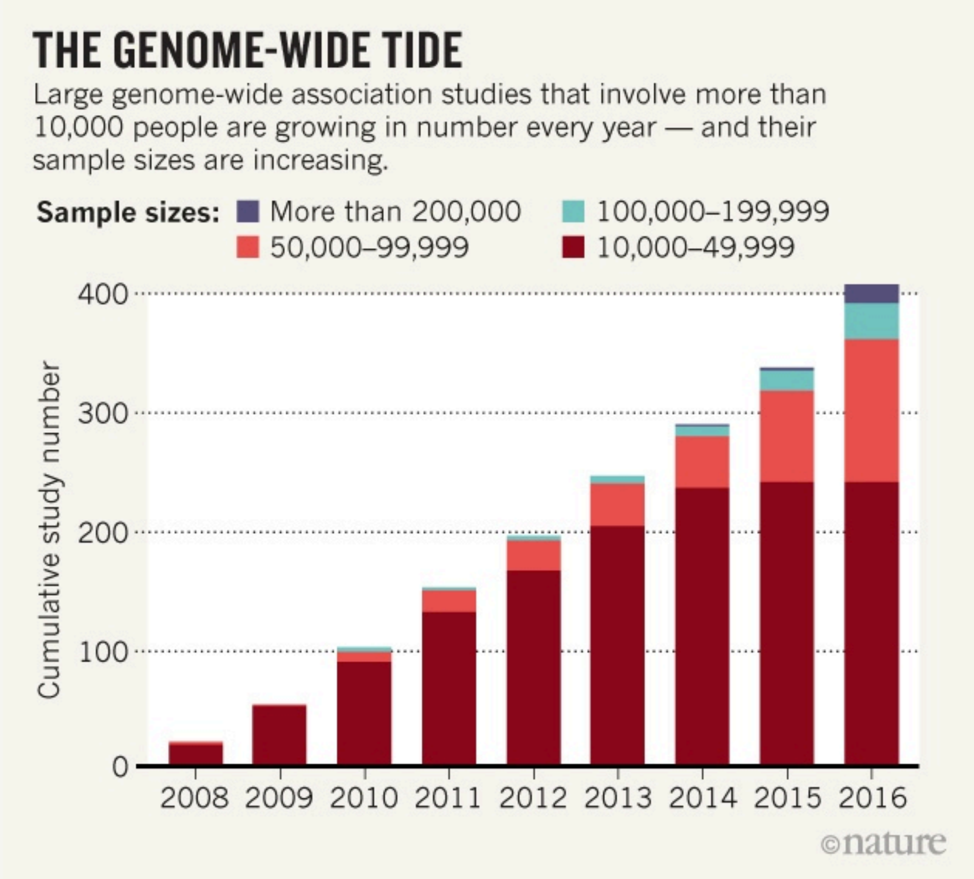


From ‘00 to ~’ 20,
cost of DNA sequencing expt. shifts from the actual seq. to sample collection & analysis

Comparison w/ photography

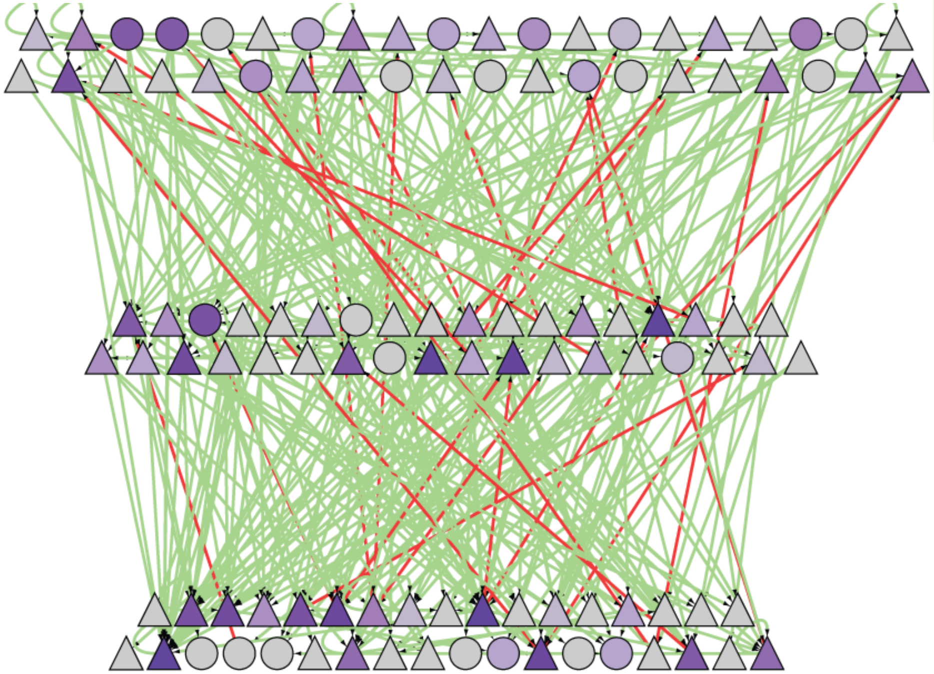
[Sboner et al. (‘11), Muir et al. (‘15) Genome Biology]

A Success of Scale & Integration: Many GWAS variants found, most not in genes, but affecting regulatory network



THE GENOME-WIDE TIDE

Large genome-wide association studies that involve more than 10,000 people are growing in number every year — and their sample sizes are increasing.



- A 1st GWAS done at Yale, for AMD: (Klein et al. 05, Science)
- Many since then
- Most SNVs fall into non-coding regulatory regions
  (major contributions by Yale groups to this ENCODE annotation effort)

[*Nature* 489: 91]

Basic Science to Medicine

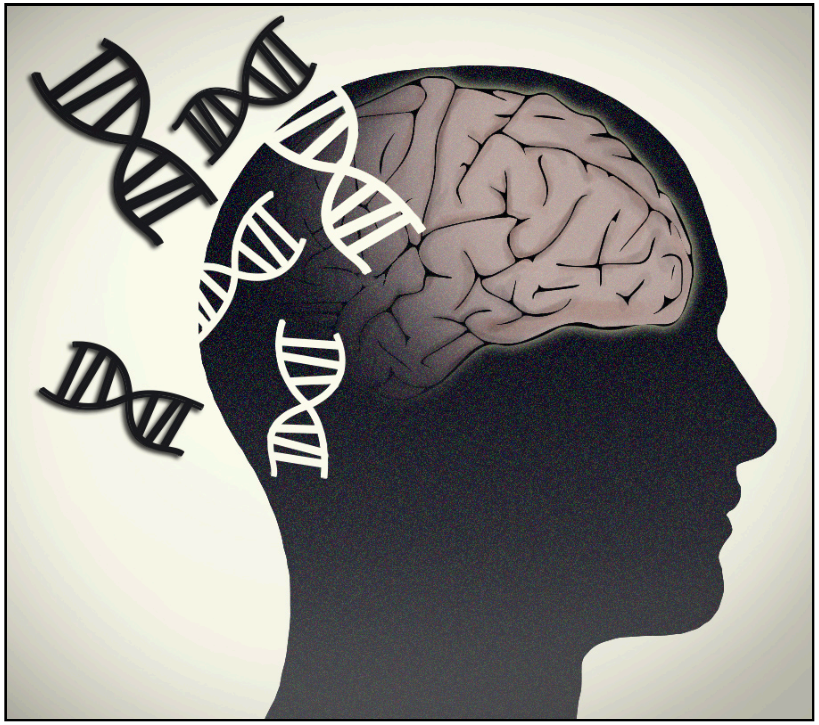
INITIATIVES
AGTC
MVP
biobank uk
TCGA
Genomics england
PCAWG PanCancer Analysis of WHOLE GENOMES
THE PRECISION MEDICINE INITIATIVE
STARTUPS
color
23andMe
Veritas The Genome Company
FOUNDATION MEDICINE®

- Large-scale ‘omics data as an anchor to organize phenotypic data – EMRs, wearables…
- 1st [‘05-]: Exomes & chips of disease-focused cohorts – init. GWAS, TCGA, PGC
- 2nd [‘15-]: Integration of full WGS with rich & diverse phenotypes - UKBiobank, TopMed, Genomics England, PCAWG, All of Us

Medical Big Data: Promise and Challenges (Lee and Yoon , *Kidney Res. Clin. Pract.*, 2017)

EX of ’omics research on focused patient cohorts: Yale Research in Human Neurogenomics

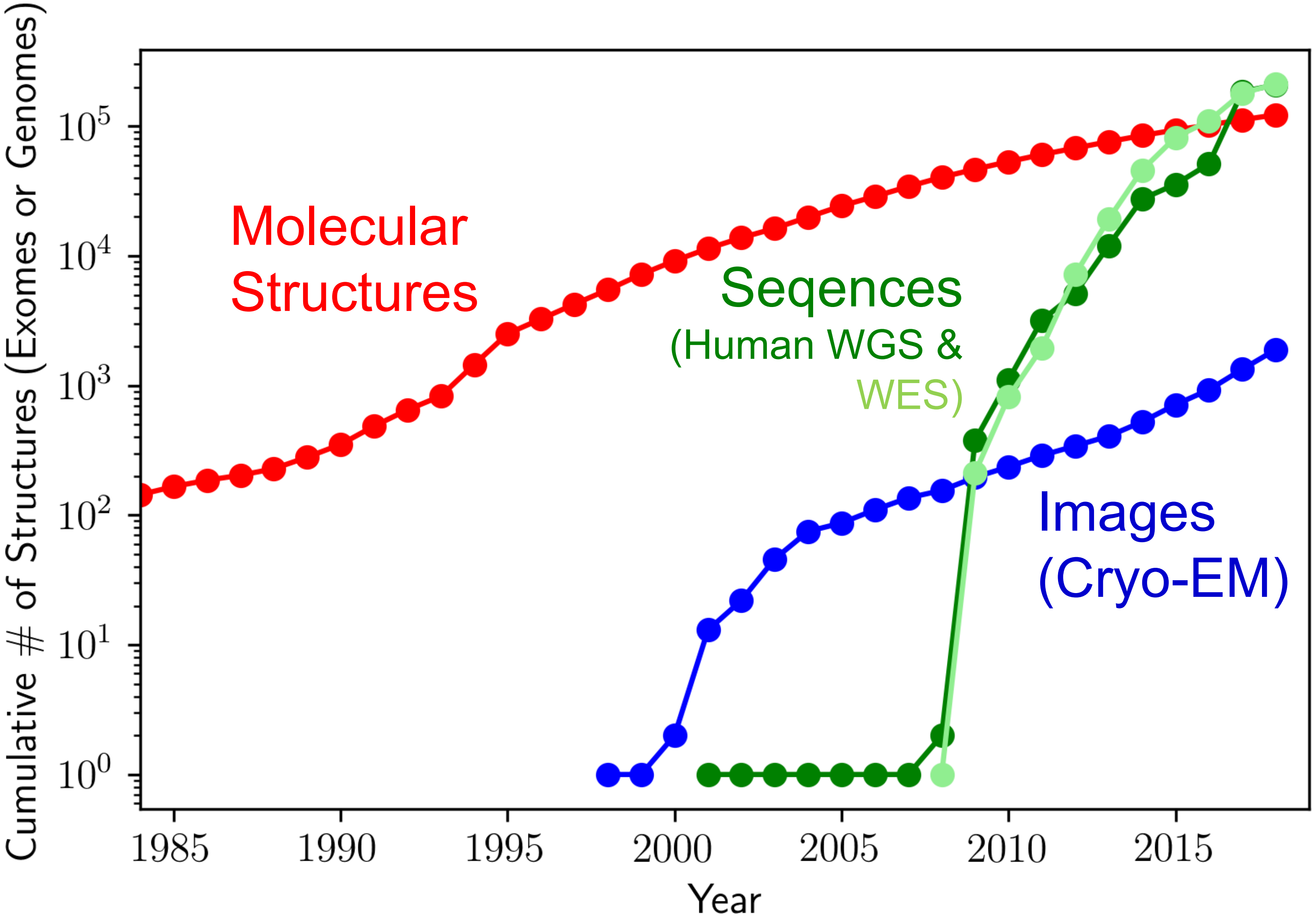
- **Representative Nat’l Initiatives**: CMG, BrainSpan, psychENCODE, BSMN, SFARI, MVP/PTSD, PGC, NIDA Neuroproteomics



- DNA variants, altered protein & RNA levels in brains in development & various diseases (eg TS, ASD, SCZ)

https://geneticliteracyproject.org/2016/09/13/neurons-surprising-amount-genomic-diversity/

How will the Data Scaling Continue? The Past, Present & Future Ecosystem of Large-scale Biomolecular Data



Center for Biomedical Data Science

Yale SCHOOL OF MEDICINE

Yale School of Medicine
Chairs' Lunch
November 4, 2016

Carolyn
Slayman

Center for Biomedical Data Science