What are Genomics and Computational Genomics?

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Genomics

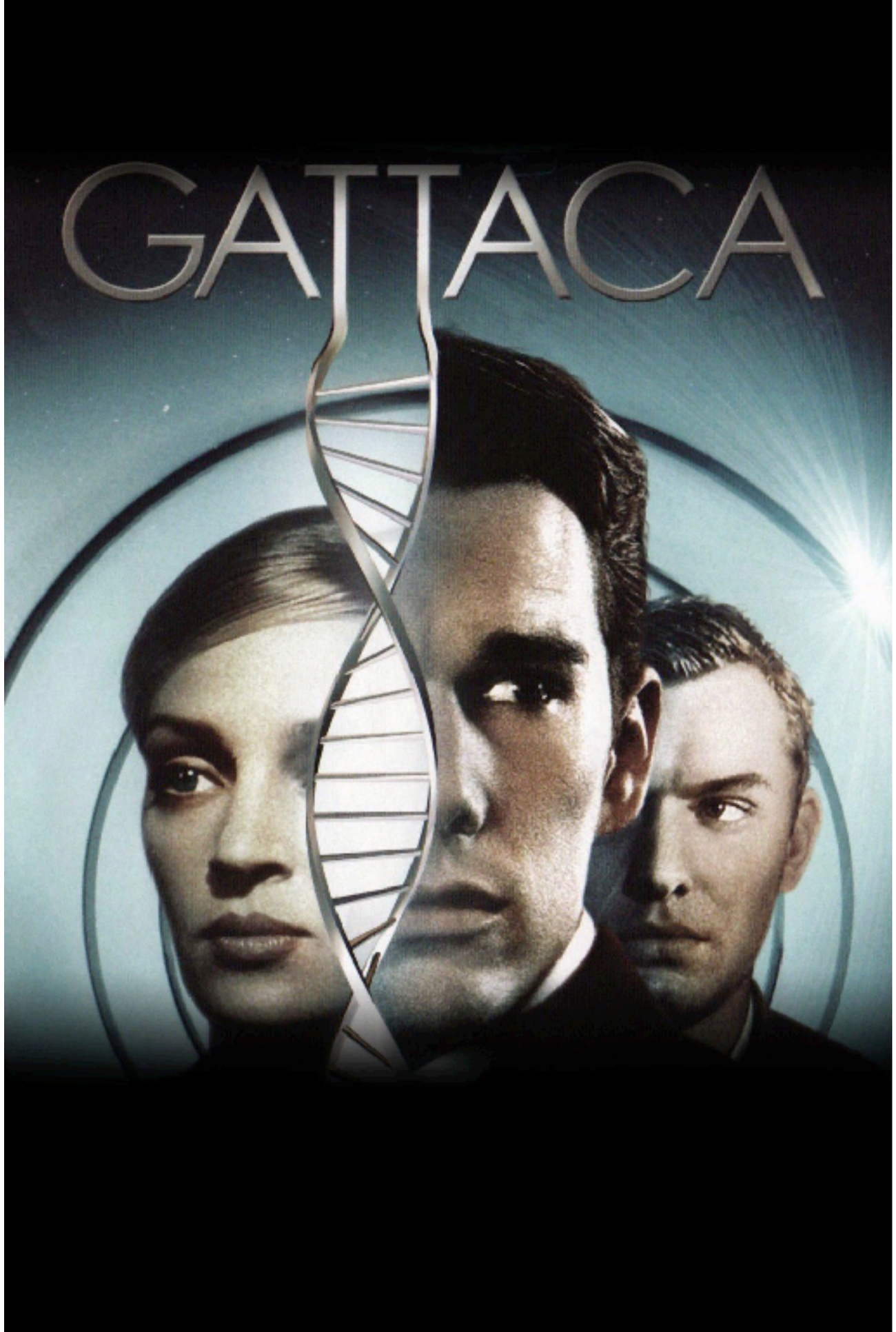
What do you know about genomes and genomics?

Where did you hear about them?

1993

JURASSIC PARK

1997



READING THE BOOK OF LIFE: THE OVERVIEW

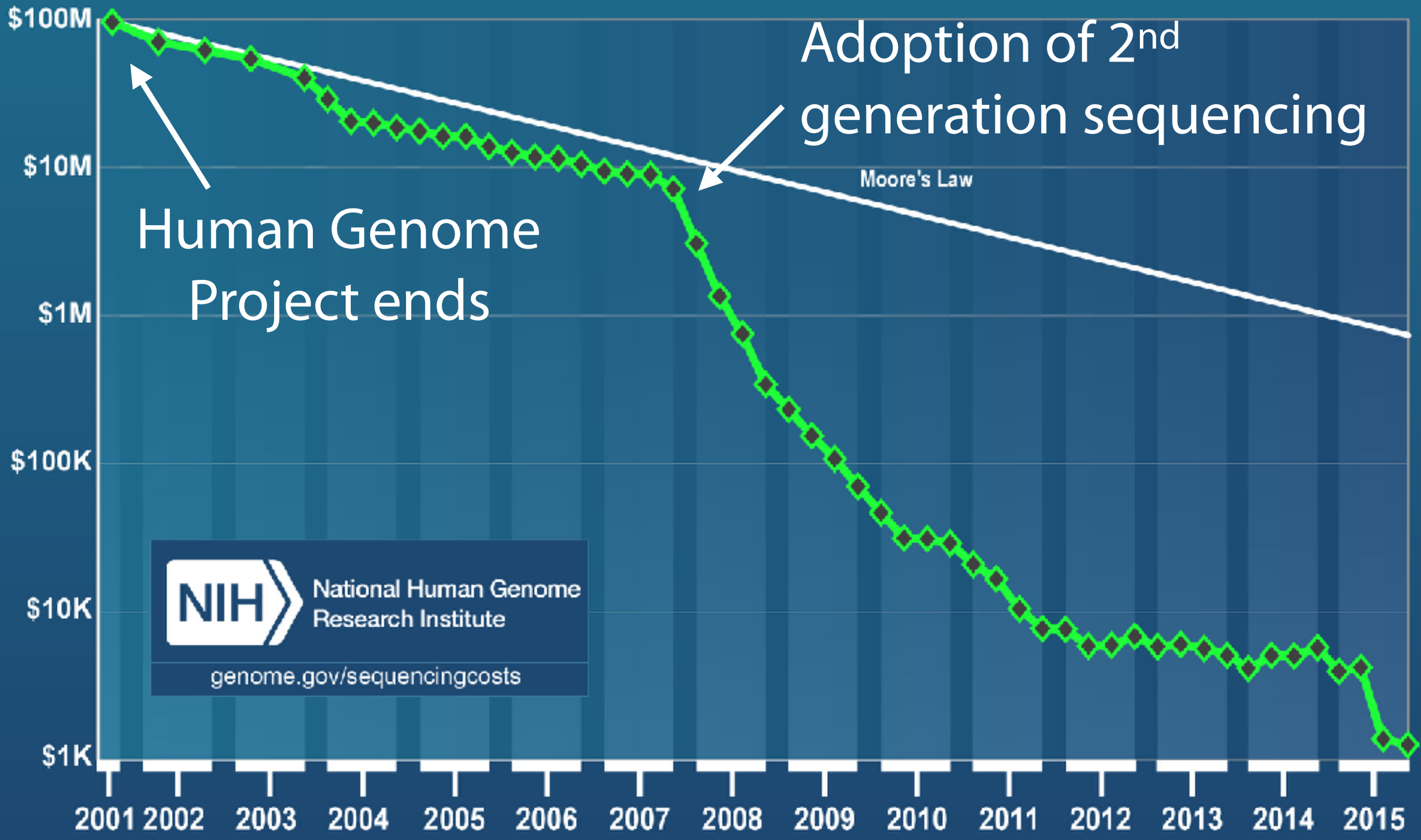
READING THE BOOK OF LIFE: THE OVERVIEW; Genetic Code of Human Life Is Cracked by Scientists

By NICHOLAS WADE
Published: June 27, 2000

Sequencing

When I started graduate school in 2007, sequencing technology was entering a new era...

Cost per Genome



DNA sequencing instruments from Illumina: www.illumina.com

GA II
1.6 billion nt/day
(2008)

GA IIx
5 billion nt/day
(2009)

HiSeq 2000
75 billion nt/day
(2011)

HiSeq 2500
120 billion nt/day
(2012)

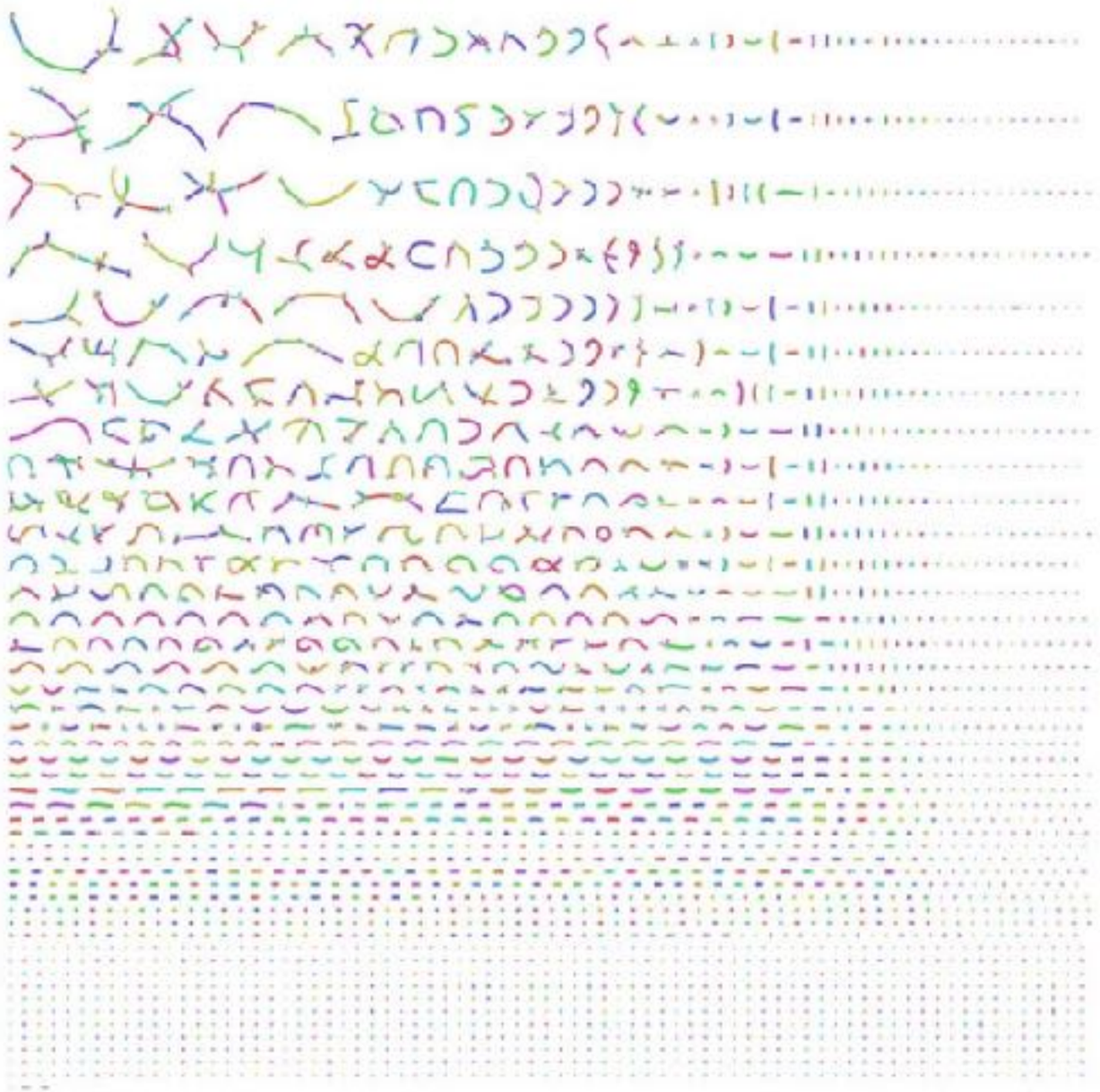
HiSeq 3000/4000
200-400 billion nt/day
(2015)

NovaSeq 5000/6000
1-3 trillion nt/day
(2017)

nt = nucleotide = **A**, **C**, **G** or **T**

Team of Rival Scientists Comes Together to Fight Zika

By **AMY HARMON** MARCH 30, 2016



A visualization of the recently sequenced Aedes aegypti genome. Each of the 3,752 colored lines is a fragment of its three chromosomes that could not be fit together without the additional information that the Aedes Genome Working Group hopes to produce. A 2007 genome map for Aedes aegypti is fragmented into about 10 times as many pieces. Mark Kunitomi

The New York Times

June 27, 2013

Studying Tumors Differently, in Hopes of Outsmarting Them

By CARL ZIMMER

THE NEW YORKER

MEDICAL DISPATCH | JULY 21, 2014 ISSUE

ONE OF A KIND

What do you do if your child has a condition that is new to science?

BY SETH MNOOKIN

The New York Times | http://nyti.ms/1tcvLXq

SCIENCE

Man's Genome From 45,000 Years Ago Is Reconstructed

OCT. 22, 2014

Carl Zimmer

Sequencing

Sequencing is now a common tool for life scientists

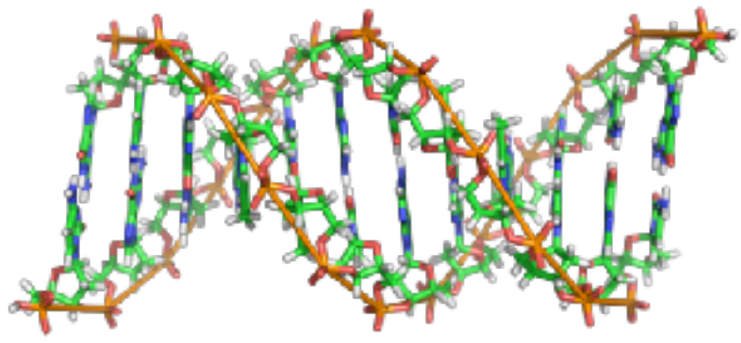
The story echoes that of computing; once computers became fast & cheap, they were adopted everywhere

Genome

"The complete set of genes or genetic material present in a cell or organism."

Oxford dictionaries

"Blueprint" or "recipe" of life



Self-copying store of read-only information about how to develop and maintain an organism

TAGCCCGACTTG

Genomics

Oxford dictionaries

"The branch of molecular biology concerned with the **structure**, **function**, **evolution**, and **mapping** of **genomes**."

where are the genes and other interesting bits?

how do sequences *change* over evolutionary time?

what does all the DNA *do*?

what are the physical shapes of the genome and its products?

Collins English Dictionary

"The branch of molecular genetics concerned with the study of genomes, specifically the identification and sequencing of their constituent genes and the **application** of this knowledge in **medicine**, **pharmacy**, **agriculture**, etc."

Genomics: contrast with biology & genetics*

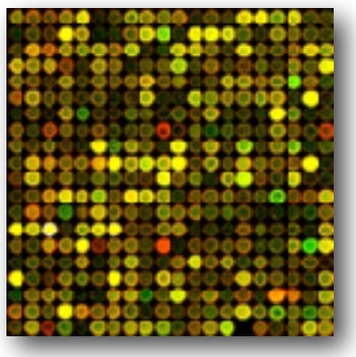
* This slide has gross generalizations

Biology & Genetics		**Genomics**
Targeted studies of one or a few genes	scope	Studies considering all genes in a genome
Targeted, low-throughput experiments	technology	Global, high-throughput experiments
Clever experimental design, painstaking experimentation	hard part	Tons of data, uncertainty, computation

Genomics: shaped by technology

Sanger DNA sequencing

1977-1990s



DNA Microarrays

Since mid-1990s

2nd-generation DNA sequencing

Since ~2007

3rd-generation & single-molecule DNA sequencing

Since ~2010

These provide very high-resolution snapshots of the world of nucleic acids (not just DNA)

Genomics: tool for basic science

"The branch of molecular biology concerned with the **structure**, **function**, **evolution**, and **mapping** of genomes." Oxford dictionaries

Structure / mapping

What is the DNA sequence of the genome?
Where are the genes?
What is the genome's three dimensional shape in the cell?

Function

What does all the DNA in the genome do?
What genes interact with what other genes?
How does the cell know what DNA is on/off?

Evolution

How did history shape our ethnicities and populations?
What big events shaped our current genetics?
Which portions of the genome are conserved by evolution?

Genomics: tool for medicine

"The branch of molecular genetics concerned with the study of genomes, specifically the identification and sequencing of their constituent genes and the **application** of this knowledge in **medicine**, **pharmacy**, **agriculture**, etc."

Collins English Dictionary

How is genotype related to health phenotypes?

What's the difference between DNA in a tumor vs DNA in healthy tissue?

Can genomic data help predict what drugs might be appropriate for:

- a particular cancer patient?
- a particular genetic disorder?

Can genomic data reveal weaknesses in the defenses of pathogens?

Can genomic data help us predict what flu strains will prevail next year?

Computational Genomics

Addresses crucial problems at the intersection of genomics and computer science

The intersection:

Key biological models are straight out of computer science: **circuits** and **networks** for molecular interactions, **trees** for evolution and pedigrees, **strings** for DNA, RNA and proteins

Thanks to sequencers and microarrays, research bottlenecks increasingly hinge on computational issues: **speed**, **scalability**, **energy**, **cost**

With large, noisy, biased high-throughput datasets comes a critical need for **machine learning** and **statistical reasoning**

Computational Genomics: computation

How to efficiently analyze the huge quantities of fragmentary evidence that come from DNA sequencers

How to model biological phenomena and make predictions

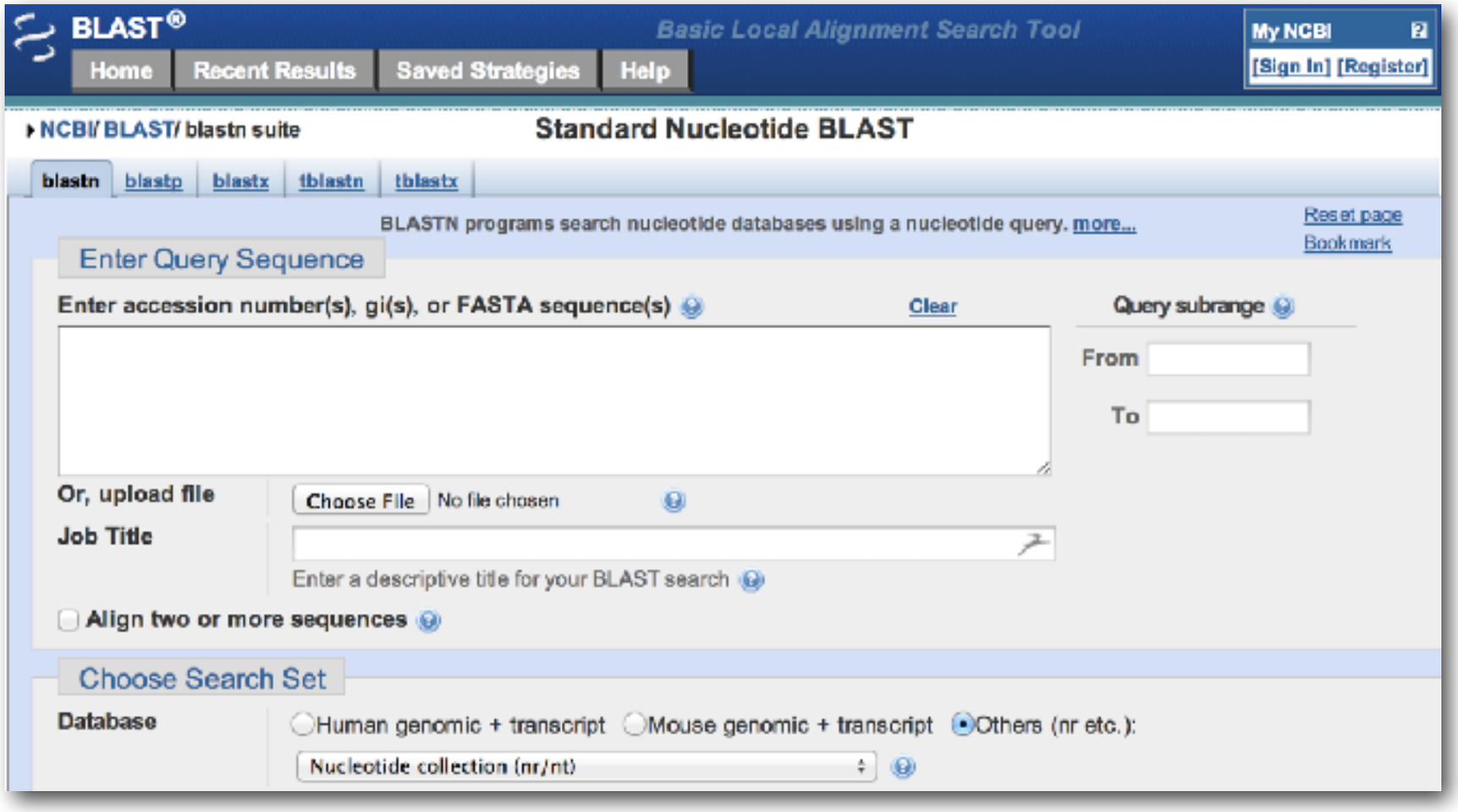
How to combine data from disparate datasets to reach new conclusions in the presence of error and systematic bias

How to store huge quantities of data economically and securely while also allowing it to be queried

How to visualize large, complicated datasets

Draws on: Algorithms, data structures, pattern matching, indexing, compression, information retrieval, distributed and parallel computing, cloud computing, machine learning, ...

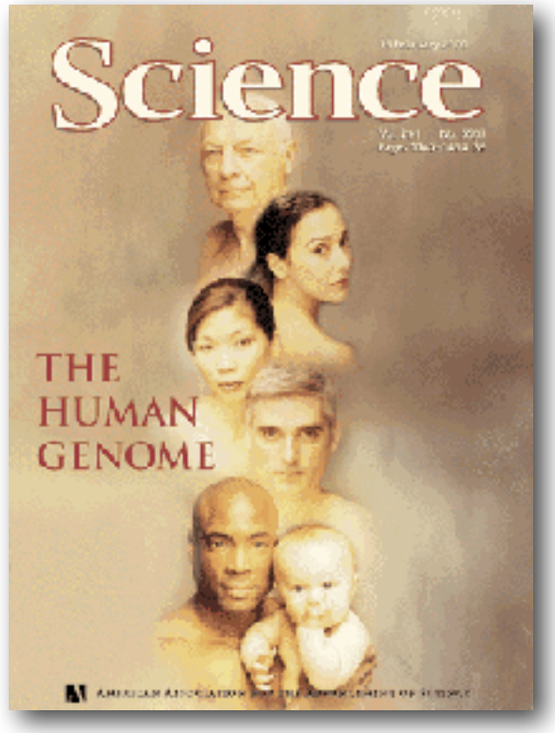
Computational Genomics: success stories



http://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastn&PAGE_TYPE=BlastSearch&LINK_LOC=blasthome

The BLAST sequence alignment program is a hugely successful tool, a fixture of biological analysis and cited over 50,000 times

Computational Genomics: success stories



The Human Genome Project depended crucially on contributions by computer scientists, especially new methods for assembling DNA fragments into chromosomes.

Computational Genomics: success stories


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Whole-Genome Sequencing in a Patient with Charcot–Marie–Tooth Neuropathy

NATURE REVIEWS | GENETICS

APPLICATIONS OF NEXT-GENERATION SEQUENCING

Advances in understanding cancer genomes through second-generation sequencing


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Origin of the Haitian Cholera Outbreak Strain

theguardian

News Science Genetics

Mayo Clinic plans to sequence patients' genomes to personalise care

Project will give doctors the genetic information they need to choose drugs that work best and minimise side effects

The idea of using high-throughput DNA sequencing in medical settings is only possible because of novel, extremely efficient software developed in the years after second-generation sequencers arrived.

Links

Past winners of the (Computational Biology) Overton Prize:
www.iscb.org/iscb-awards/overton-prize

Genomics and sequencing in the popular press:
www.cs.jhu.edu/~langmea/poppress.shtml

The DNA Data Deluge (*behind paywall*):
https://doi.org/10.1109/MSPEC.2013.6545119