Arts and Ideas

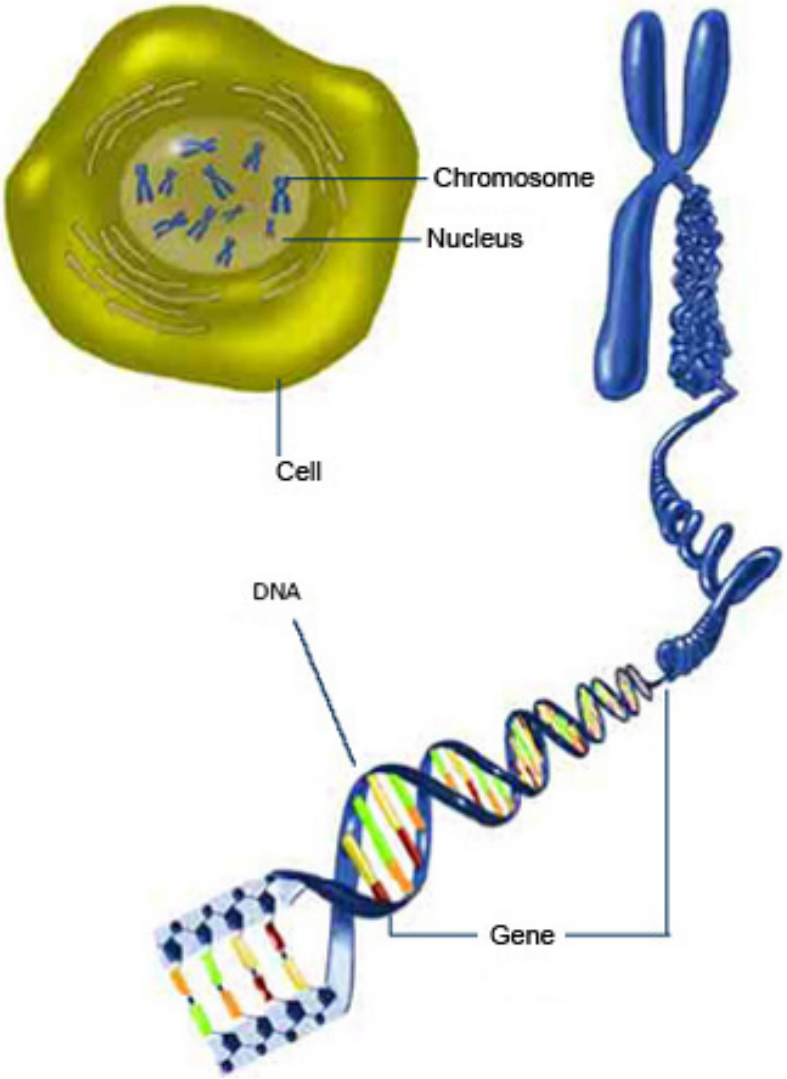
Where DNA and CPU Meet

a presentation on how computer science
and biology inform each other

Dr. Ray Klump
Chair, Mathematics & Computer Science

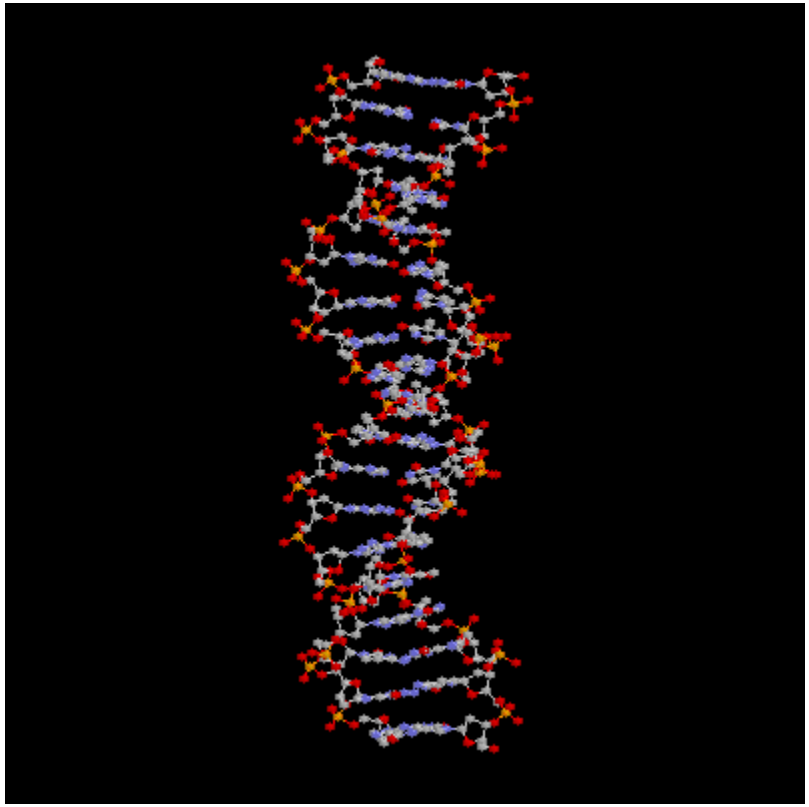
What is the human genome?

DNA is the **blueprint of life.**

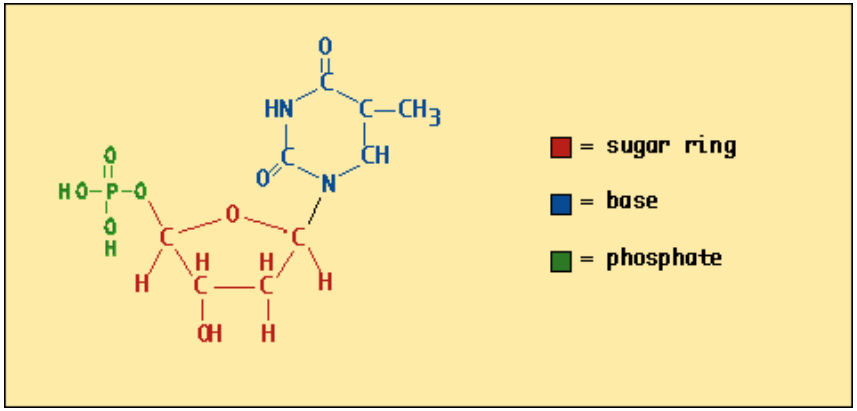

Chromosome
Nucleus
Cell
DNA
Gene

Sequencing involves mapping out the **order of molecules** within DNA.

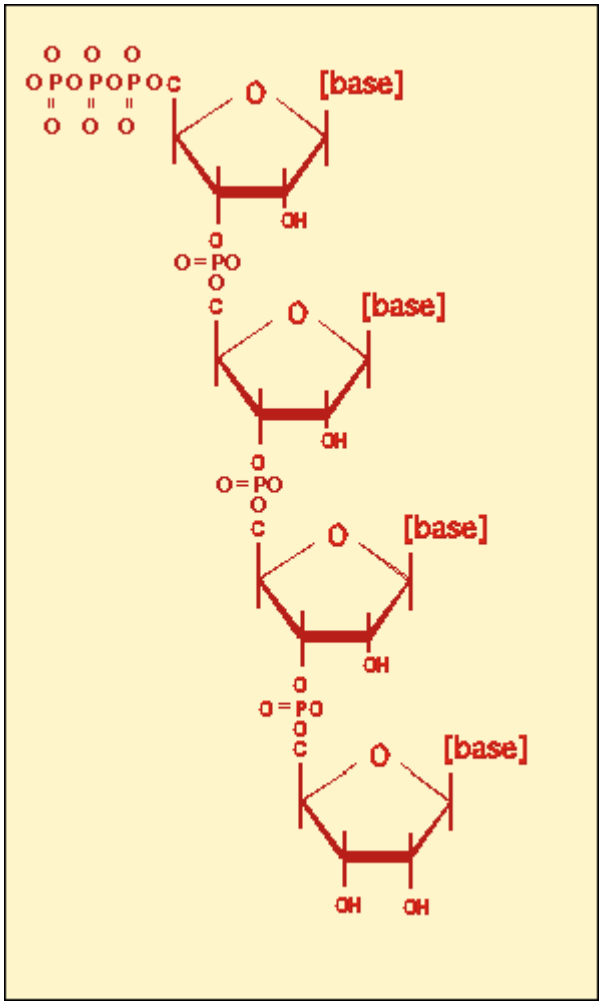
DNA is a molecule consisting of a **long chain of nucleotides** labeled A, G, C, and T.



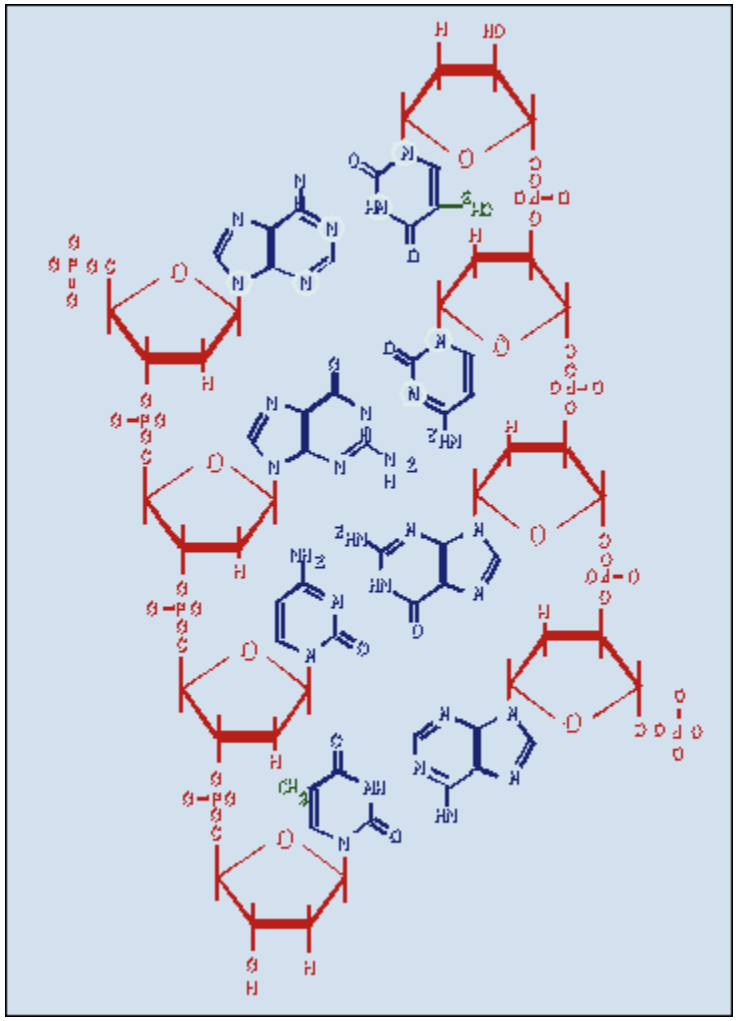
Each nucleotide has a carbon ring as well as another ring of carbon, nitrogen, and oxygen called the **base**.



DNA chains are made by connecting these molecules together at their phosphates.



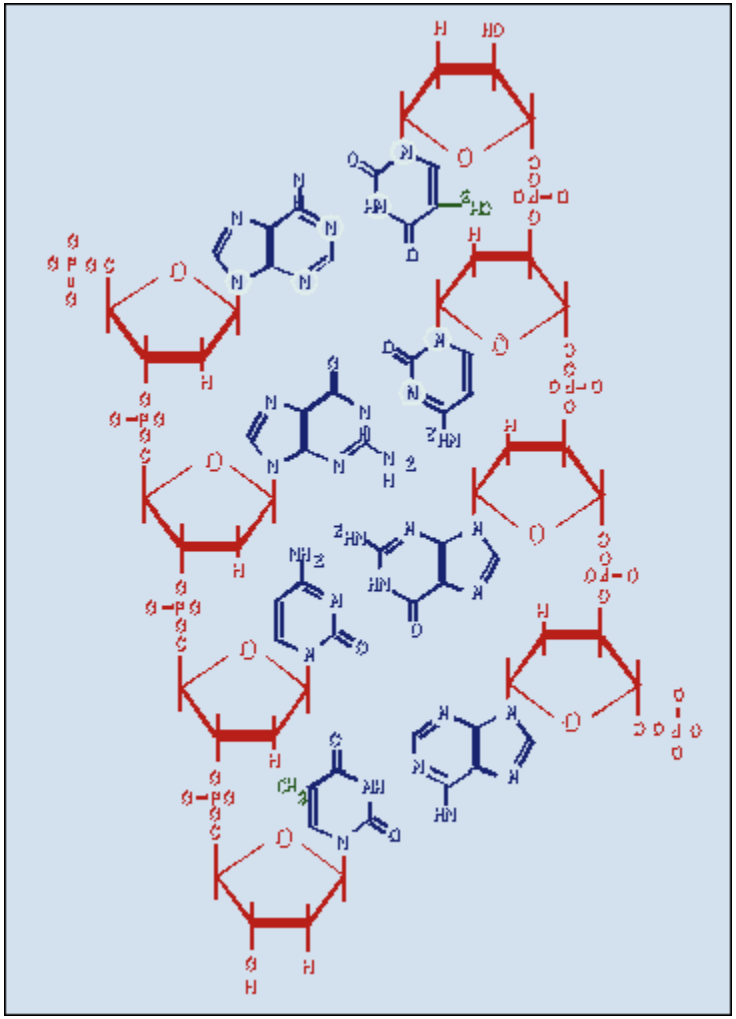
Double-stranded DNA forms when two single strands **line up at their bases**.

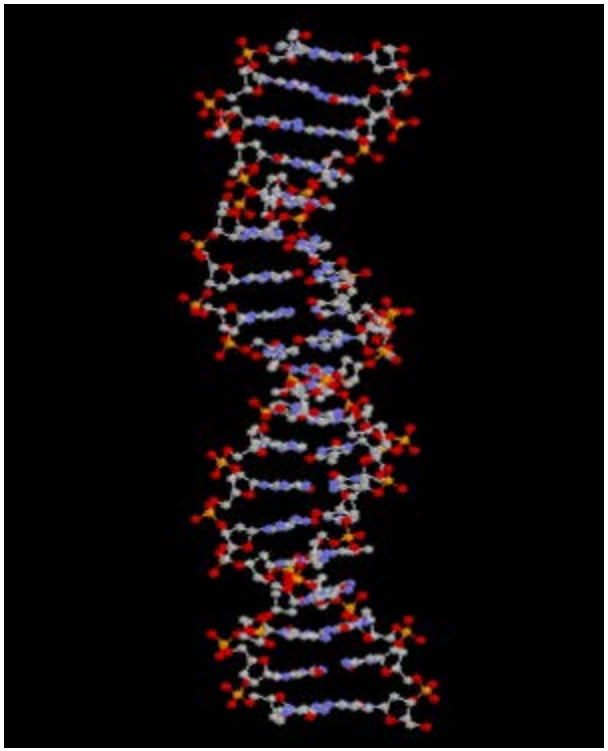


The strands line up predictably:

A ←→ T

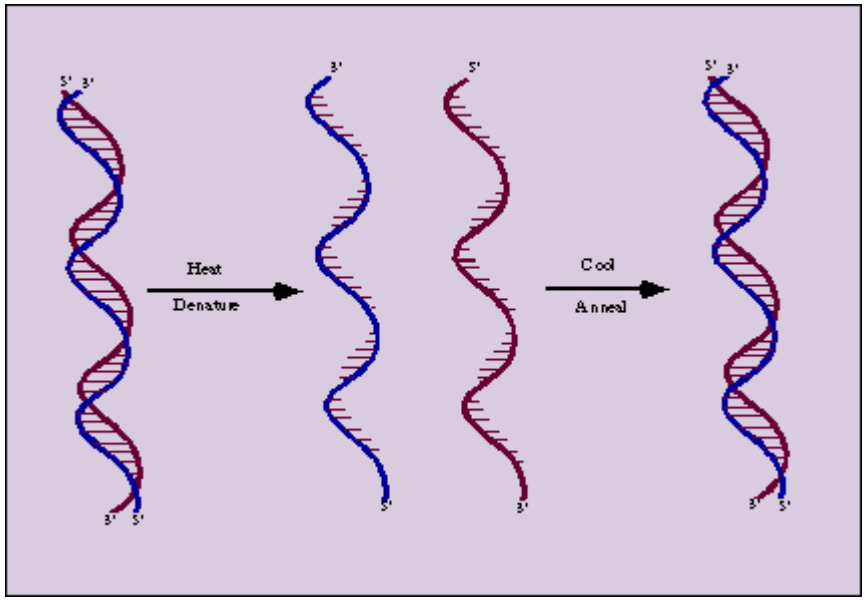
G ←→ C

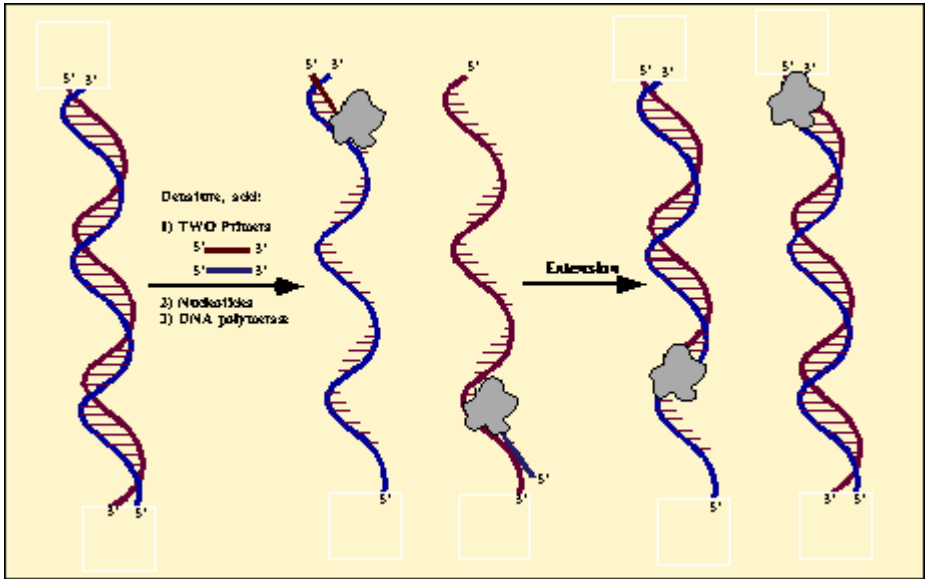




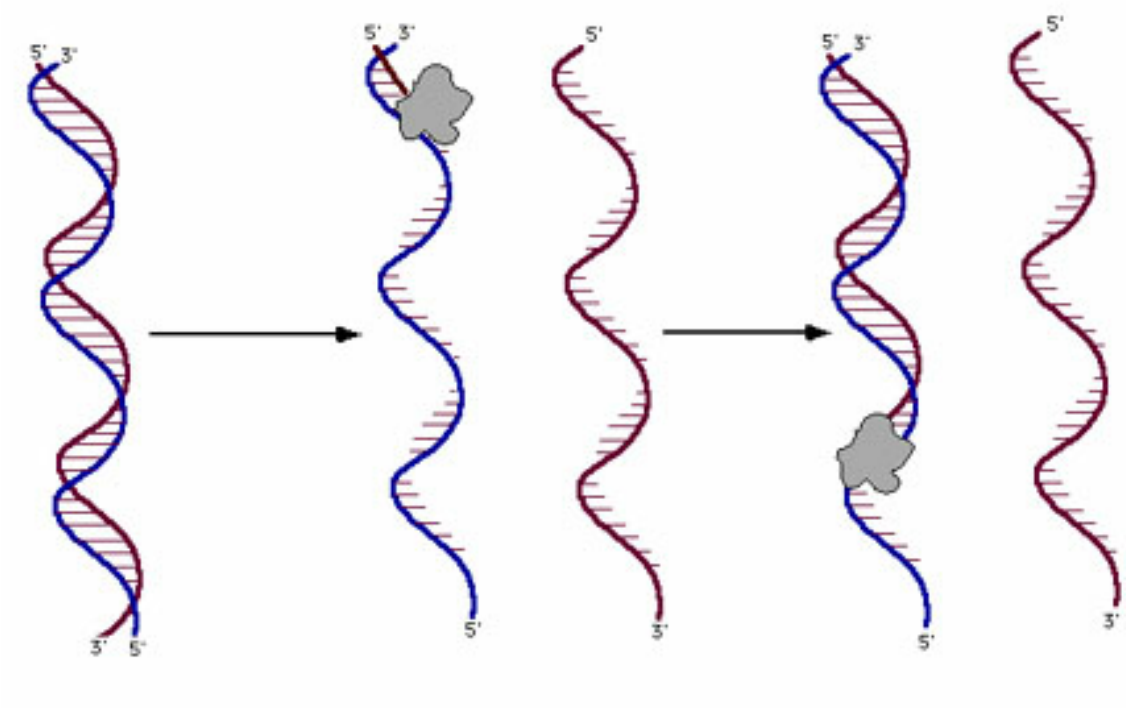
The blue middle are the rungs of **bases** that make the **double helix**.

The “**pickiness**” of the nucleotides helps us **build DNA** from existing strands through **denaturation**, **annealing**, and **replication**.

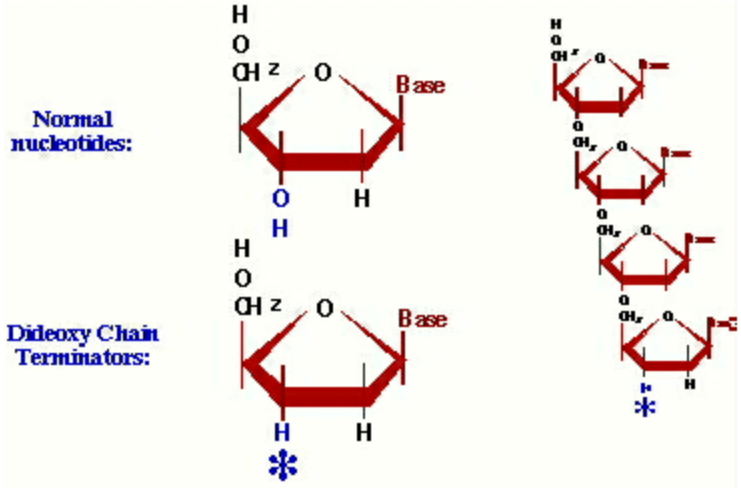




DNA sequencing reactions are similar.



For sequencing, however, the reactions are run in the presence of **dideoxynucleotides**. These **terminate the chains** on specific bases.



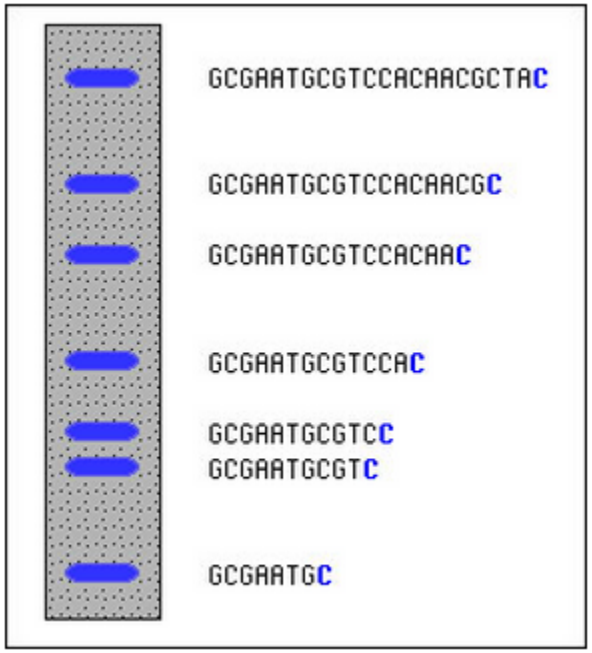
DNA Polymerase reads the template strand and synthesizes a new second strand to match:

5' - TACGCGGTAACGGTATGTTCGACCGTTTAGCTACCGAT
3' - ATGCGCCATTGCCATACAAGCTGGCAAATCGATGGCTAGAGATCCAA - 5'

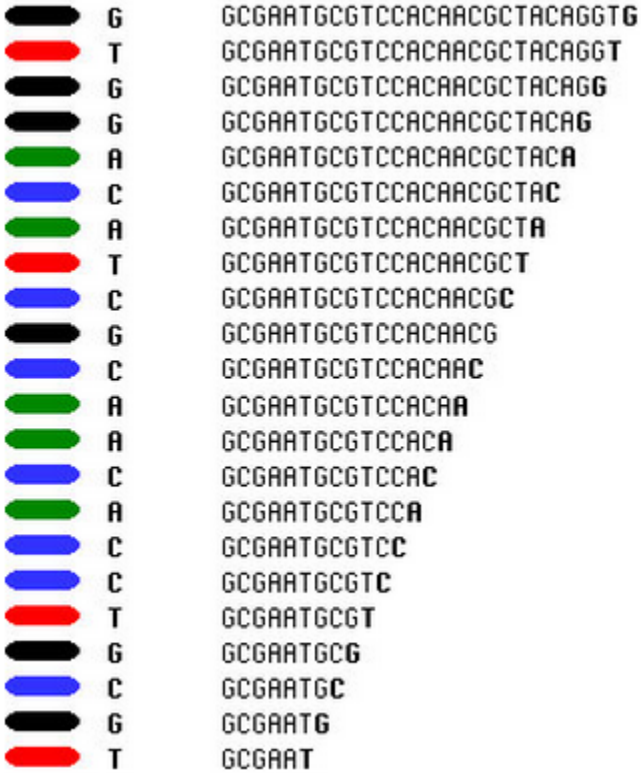
IF 5% of the T nucleotides are actually dideoxy T, then each strand will terminate when it gets a ddT on its growing end:

5' - TACGCGGTAACGGTATGTTCGACCGTTTAGCTACCGAT•
5' - TACGCGGTAACGGTATGTTCGACCGTTTAGCT•
5' - TACGCGGTAACGGTATGTTCGACCGTTT•
5' - TACGCGGTAACGGTATGTTCGACCGTT•
5' - TACGCGGTAACGGTATGTTCGACCGT•
5' - TACGCGGTAACGGTATGTT•
5' - TACGCGGTAACGGTATGT•
5' - TACGCGGTAACGGTAT•
5' - TACGCGGTAACGGT•
5' - TACGCGGT•

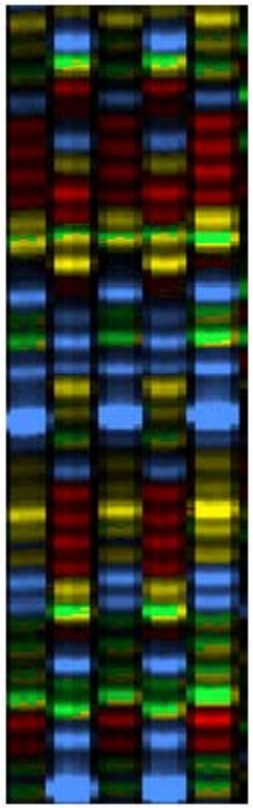
If dideoxy-C is used …

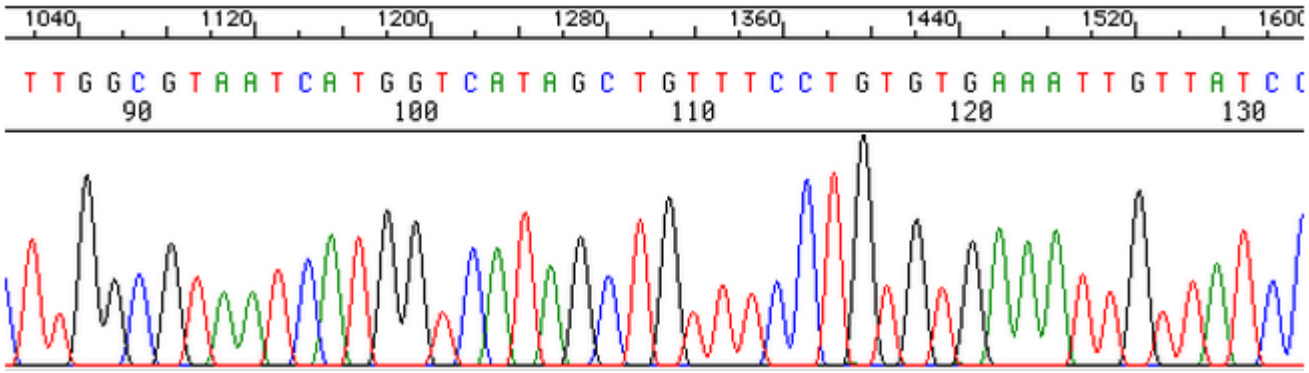


If all four dideoxy's are used



Electrophoresis automates this





Scaling this process to the size of the **human genome** requires **sophisticated computer algorithms**.

3 billion bases!

Today's **computer technology** has made interpreting sequence data possible.

The **US Human Genome Project** uses huge libraries of large human DNA strands to sequence the genome.

The **US Human Genome Project** took 13 years and $3 billion.

The **project identified** all of the nearly **25,000 genes** in human DNA, and it determined the sequences of the **3 billion base pairs** that comprise it.

It is estimated that the
Human Genome Project returned
$140 for every dollar invested.

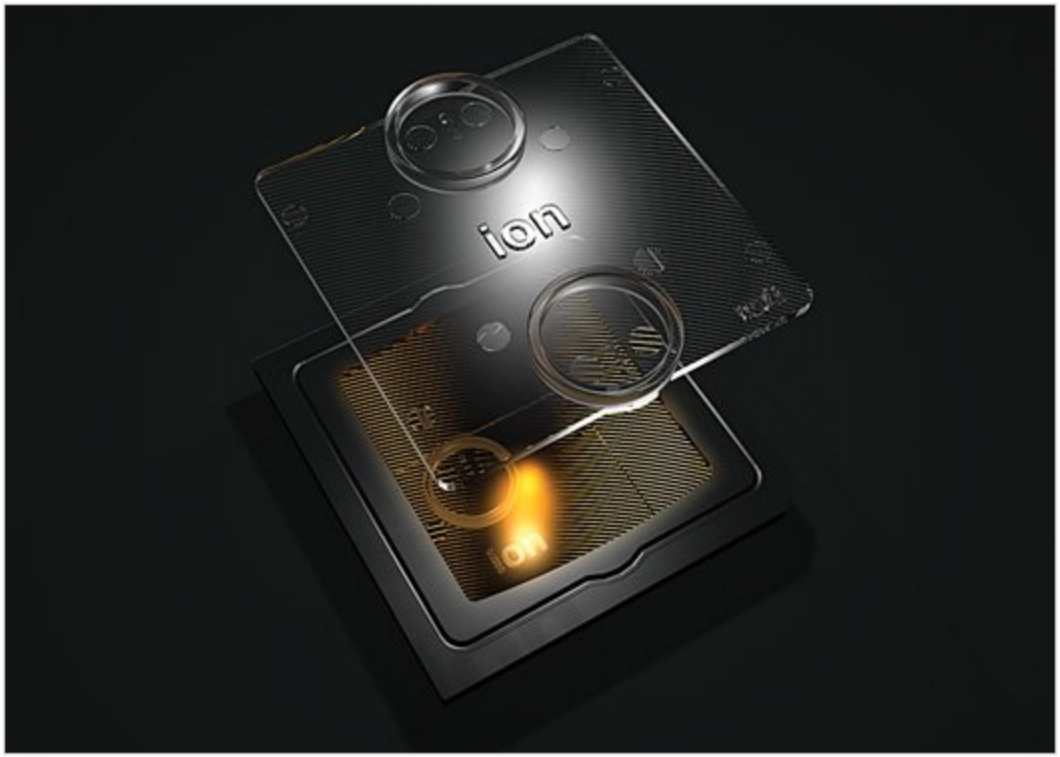
Today, this same sequencing can be done by a stand-alone laboratory in **one day** for several thousand dollars.

The $1,000 Genome, and the New Problem of Having Too Much Information

The next sequence is even cheaper

By Jennifer Abbasi Posted 02.27.2012 at 11:19 am 5 Comments

FEATURE



Packed Chip The Ion Proton I can sequence much of a human genome for just $1,000. Sequencing will become even cheaper *Courtesy Life Technologies*

DNA Sequencer Plugs Right Into Your USB Port, Analyzes Your Genome

By Rebecca Boyle Posted 02.22.2012 at 3:21 pm 5 Comments

MinION Sequencer MinION is a disposable device that contains a sensor chip, ASIC and the fluidics system needed to perform a complete single-molecule sensing experiment. *Oxford Nanopore Technologies Ltd.*

"This technology promises to deliver a complete human genome in 15 minutes."

Moore's Law has been good news for this work. A new version will make **two-hour, full-genome sequencing** possible.

3.2 GB worth of data per person.

Research consortia are using advances in **DNA sequencing** technology to **unlock the mysteries** surrounding diseases and disorders.

Understanding each individual's DNA sequence carries the **promise of personalized medicine**.

Example:

Mendellian Disorders

Example:

Cancer Genetics

and the

Cancer Genome Atlas

ACM Member News

DAVID PATTERSON'S 'BIG DATA' PROJECT TAKES AIM AT A CANCER CURE

David Patterson and his team have been working for over a year on what he describes as an odd sort of project for a computer scientist—building a software pipeline for cancer genomics that is faster, cheaper, and more accurate than ones that already exist.

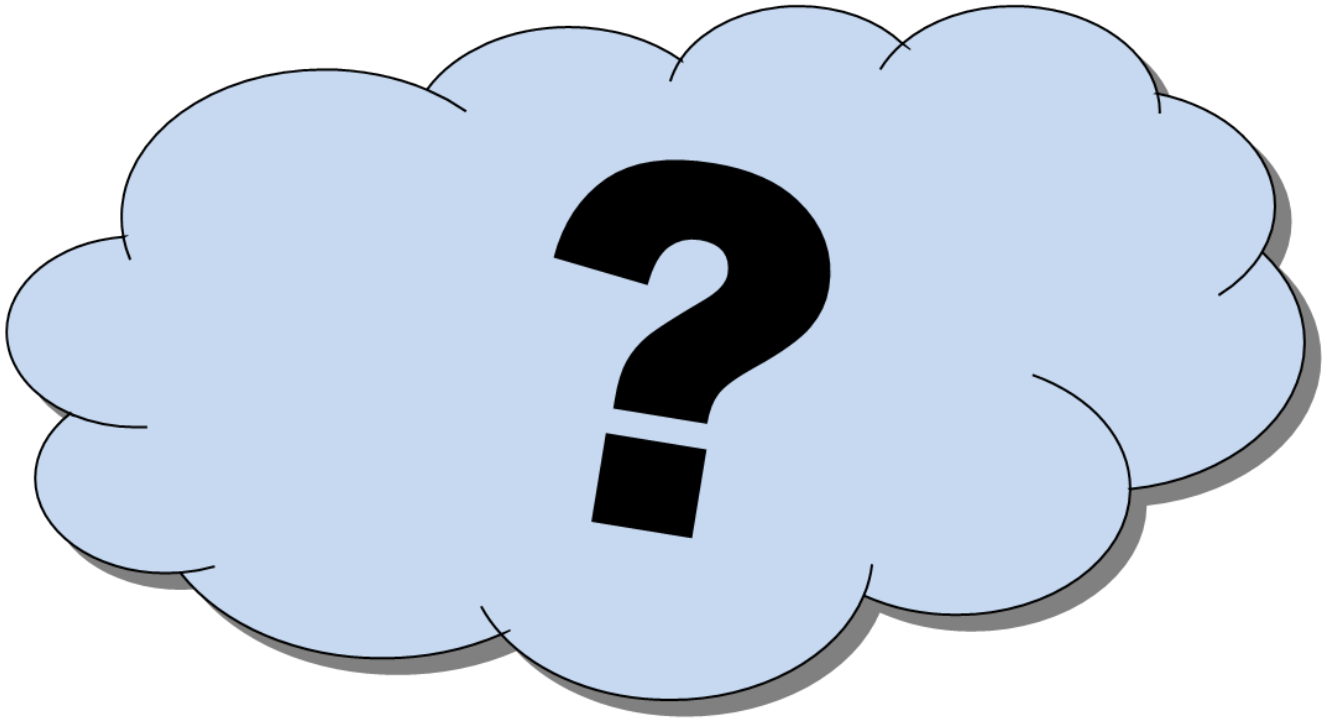
Patterson, a former ACM president who has been a computer science professor at the University of California Berkeley since 1977, recalls an application was needed for the university's new AMPLab, which integrates Algorithms, Machines, and People to make sense of "big data."

Example:

St. Jude Children's Hospital

When **genome sequencing** begins reaching millions of patients, it will **help address the most common problems in medicine**.

Of course, **how do you store** all that data and retrieve it quickly?



Companies have been created that **host genomes on the cloud** for scientists and doctors to access.

Doctors will need to be trained to apply genomic information to standard medical practice.

But there’s more!

In addition to genome sequencing, **Computer Science** is being used for a lot of other **biological research** today.

Data mining has been used to determine dangerous drug interactions.

The FDA maintains a **database** called AERS that lists 4 million negative reactions since 1969, but this data alone doesn’t capture the **full complexity** of drug interaction.

Other data sources include international side effects databases, social network data, warning labels, electronic medical records, and the drugs' biological targets.

Data mining alone can’t prove that particular drugs cause particular side effects, but **it can provide clues**

Predicting side effects can be done even **before the drug hits the market**.

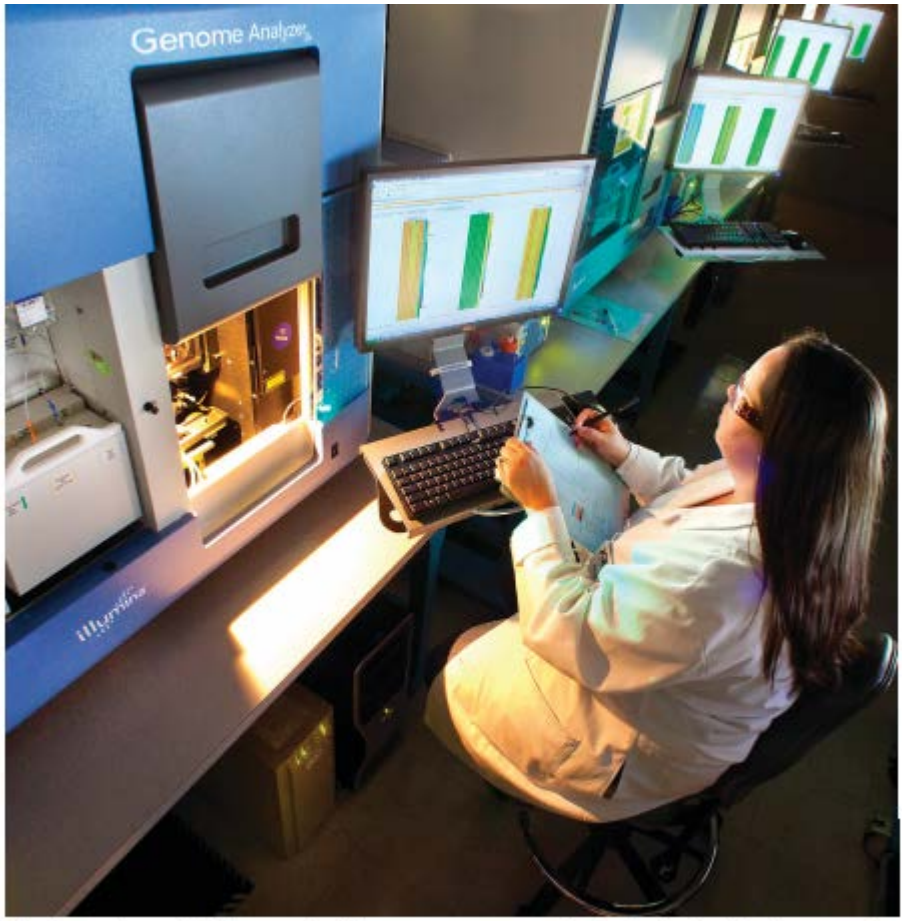
The Similarity Ensemble Approach (SEA) looks for **similarities in the targeted proteins**.

For example, a recent study looked at **656 drugs** to detect similarities with molecules that bind with **73 different proteins** associated with side effects.

They discovered nearly
1,200 new interactions.

Software has been written to model **the spread of disease**.

Computer Science has also been used extensively to **simulate cells, organs, and organisms**.



The huge volume of data generated from genome sequencing technologies, like those used as part of the DOE's Joint Genome Institute, has inspired computer scientists worldwide to create software that can take that data and build computational models simulating the behavior of biological systems.

The **first comprehensive computational model of a living organism** is of Mycoplasma genitalium.

Other projects have concentrated on **modeling a specific organ**.

President Obama pitches $100 million investment in human brain research

The President first mentioned his plan to invest in brain research in his State of the Union address. He wants the research to involve private institutions as well as government agencies.

Comments (34)

THE ASSOCIATED PRESS

TUESDAY, APRIL 2, 2013, 8:17 AM

CHARLES DHARAPAK/AP

President Obama said the so-called BRAIN Initiative may eventually help find cures for disorders like Alzheimer's, epilepsy and traumatic injuries.

Such models, when combined with genome information, could allow doctors to prescribe the best treatment based on an **individual's personal genome and history**.

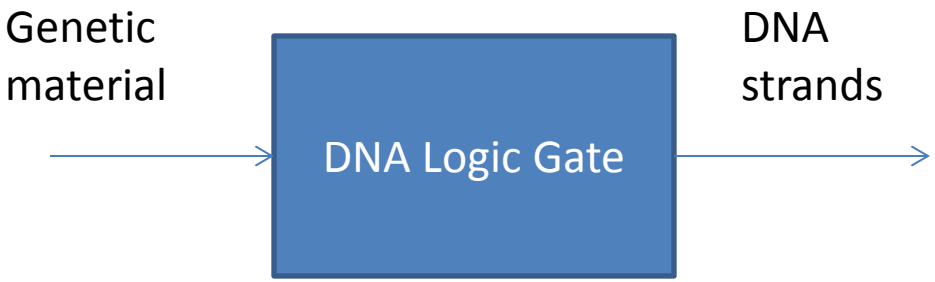
This is the idea of

truly personalized medicine!

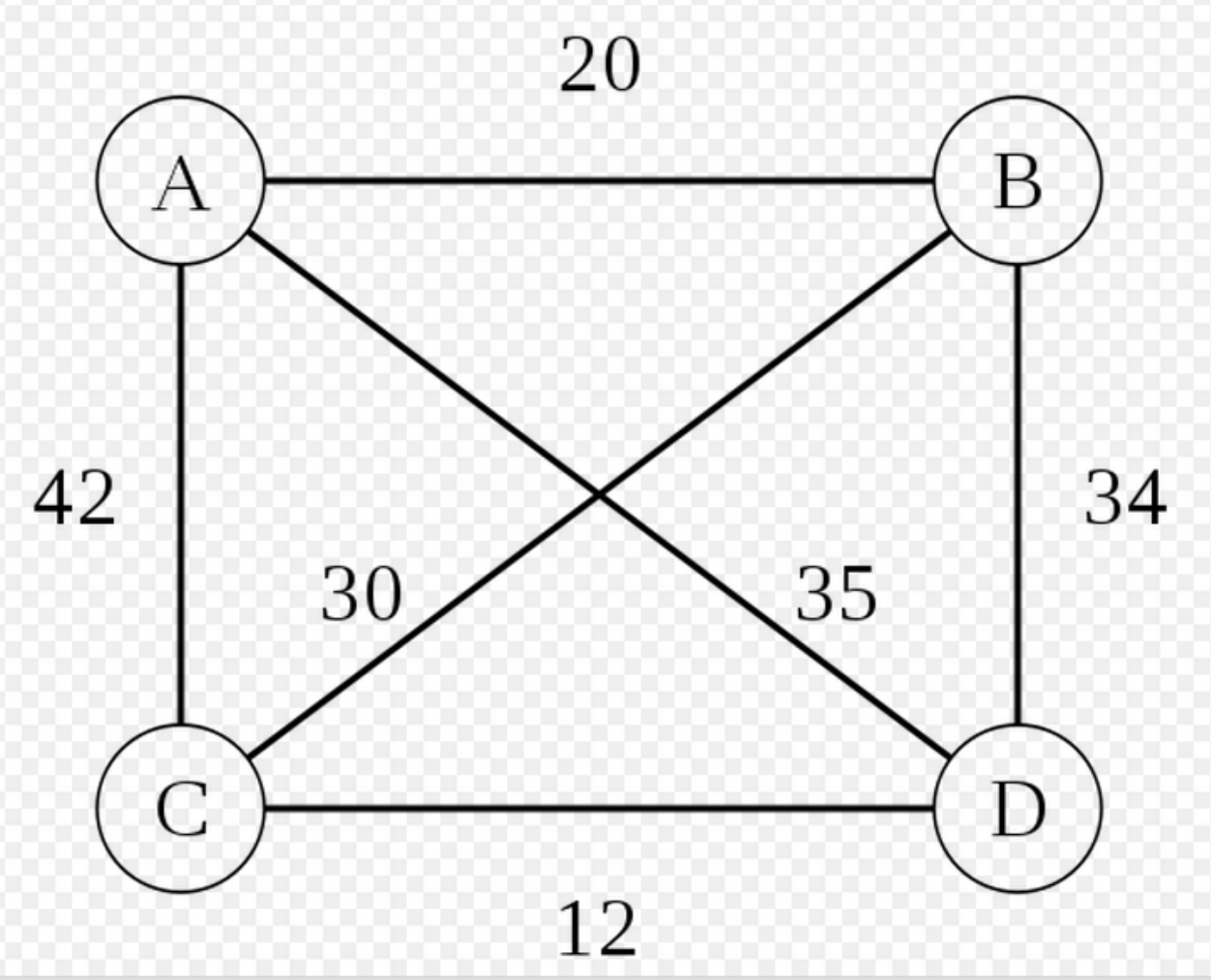
Biology is also transforming Computer Science.

DNA computers will be capable of storing billions of times more data than your personal computer.

DNA logic gates have been created to make more general-purpose computers.



The Traveling Salesman Problem



DNA computing was used by Leonard Adleman in 1994 to solve this.

1. Strands of DNA represent the seven cities. In genes, genetic coding is represented by the letters A, T, C and G. Some sequence of these four letters represented each city and possible flight path.

2. These molecules are then mixed in a test tube, with some of these DNA strands sticking together. A chain of these strands represents a possible answer.

3. Within a few seconds, all of the possible combinations of DNA strands, which represent answers, are created in the test tube.

4. Adleman eliminates the wrong molecules through chemical reactions, which leaves behind only the flight paths that connect all seven cities.

Why DNA computing?

Cheaper, smaller, more environmentally friendly computers.

Conclusion

Computer Science and Biology are transforming each other in exciting ways, **much of which is related to DNA**.