# A Chemistry Lab in Your Pocket?

## It's closer than you think

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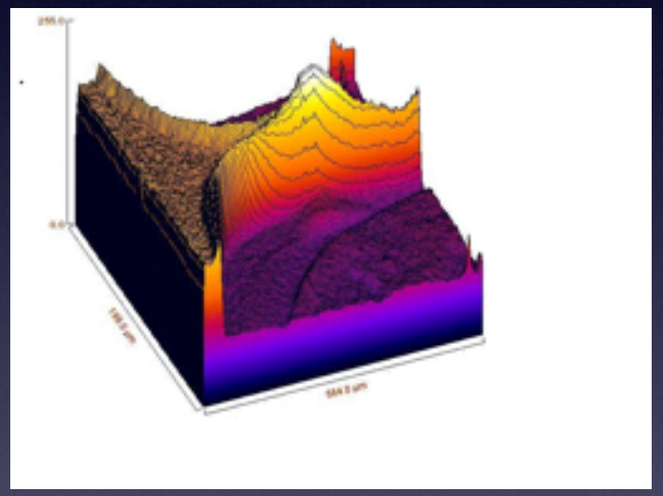
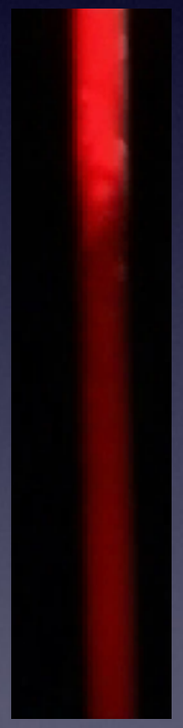
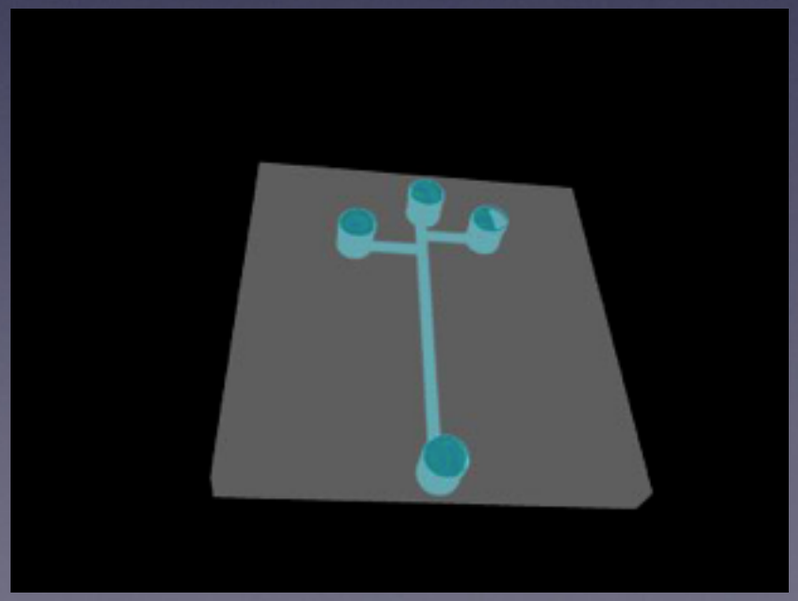
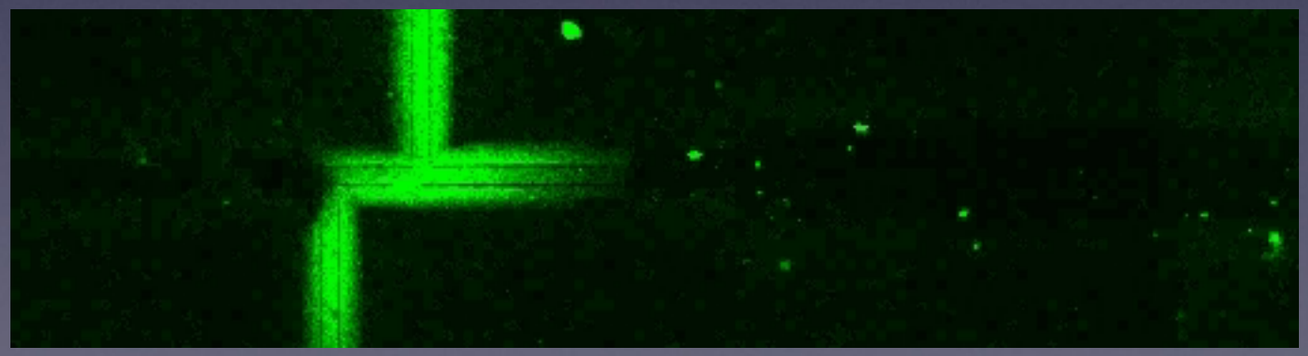
Material Measurement Laboratory
National Institute of Standards & Technology
~~21 October 2014~~ 12 November 2014









NIST
National Institute of Standards and Technology
U.S. Department of Commerce

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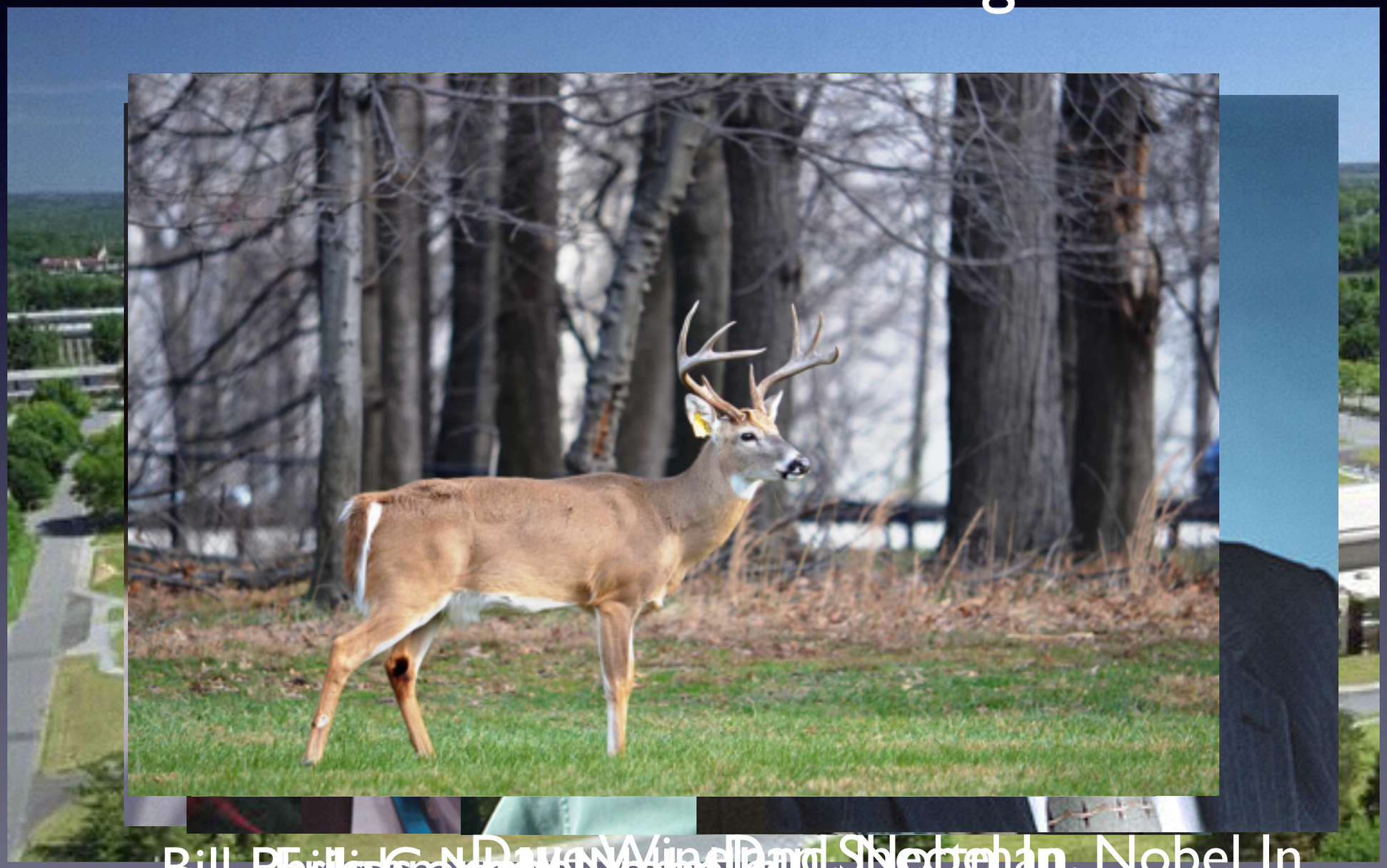
# A Brief Intro:

The news from NIST; nice little place where all the geese are strong, all the deer are good looking, and all the scientists are above average.



Bill Phillips, Nobel In Physics 1997

Eric Cornell, Nobel In Physics 2001

Dave Wineland, Nobel In Physics 2012

Serge Haroche, Nobel In Physics 2012

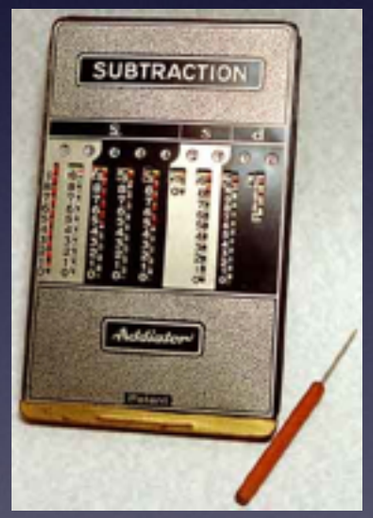
Dan Shechtman, Nobel In Chemistry 2011

John Cahn, Kyoto Prize 2011

# The Last Technology Revolution - Electronics

Calculators of the last four generations, What was state of the art? (an anecdotal vignette)

For my grandfather (born 1925)
All "calculators" were mechanical




Addiator, available in various forms from 1920 to 1970

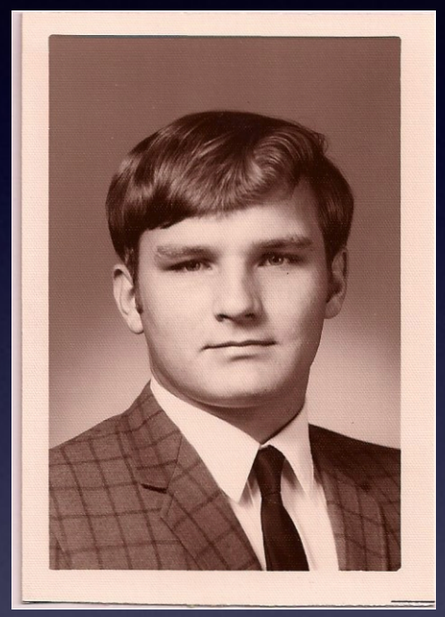
Curta, Introduced in 1948, $1250

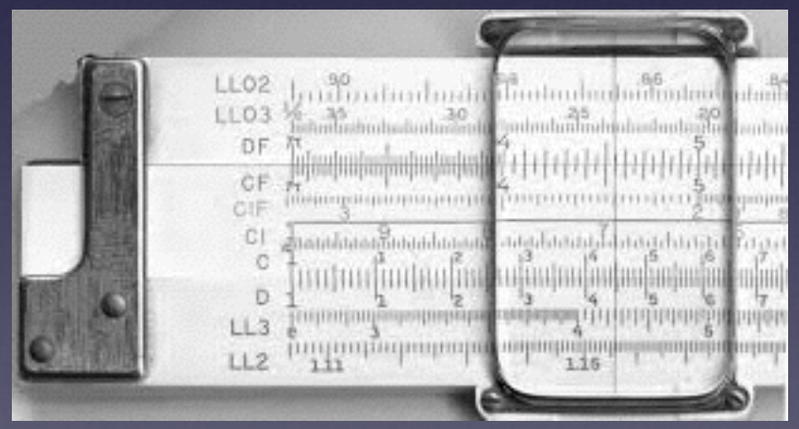
N.B. The Great Depression and WWII strongly curtailed commercial development

# The Last Technology Revolution - Electronics

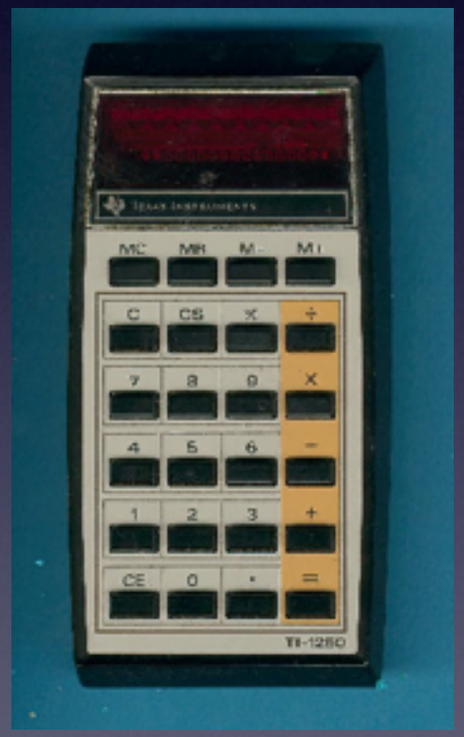
Calculators of the last four generations, What was state of the art?

For my father (born 1951)
First electric calculators available






In the mid 1960's, the slide rule was the calculator

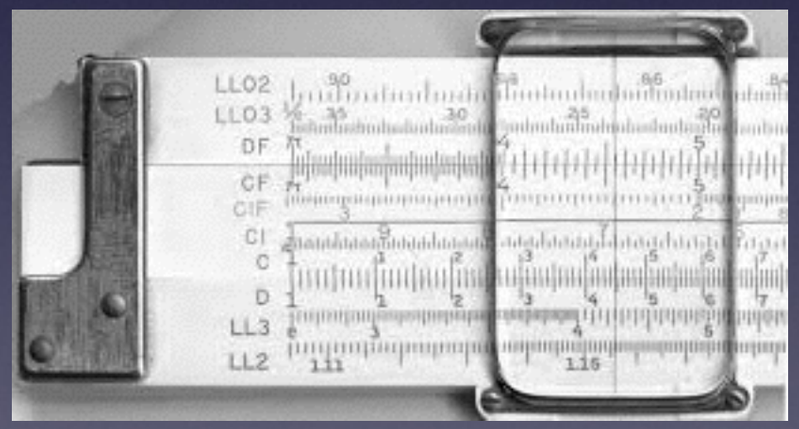



TI-line introduced, available in early 1970's, ~ $150.00

# The Last Technology Revolution - Electronics

Calculators of the last four generations, What was state of the art?

For me (born in1975)
I never used a mechanical calculator




My father tried to teach me how to use a slide rule

In high school, I used a TI-85

# The Last Technology Revolution - Electronics

Calculators of the last four generations, What was state of the art?

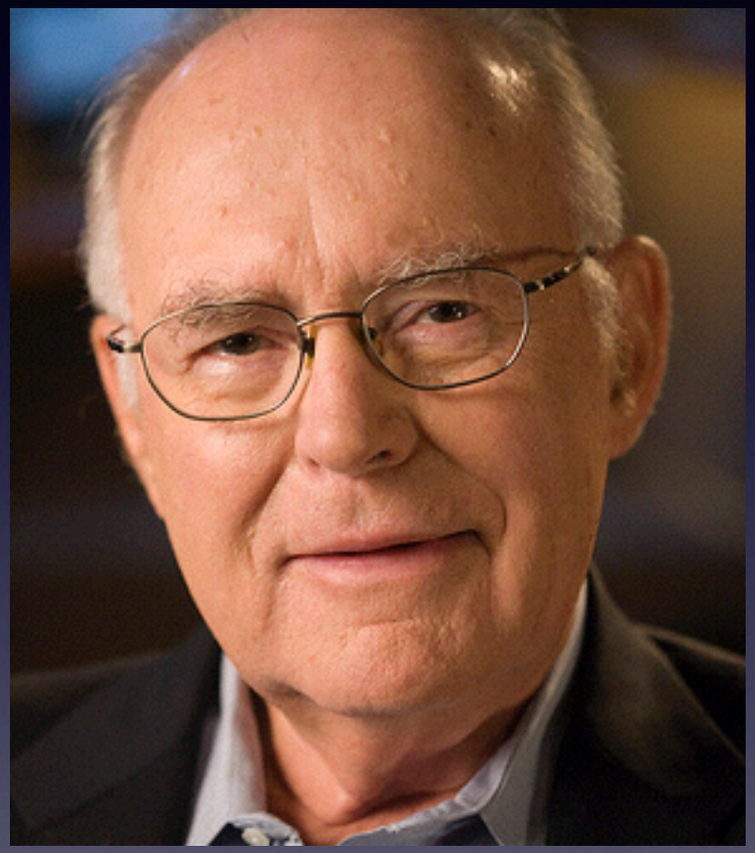
For my nephew (born in 1996)
He has never used a calculator

His friends call phones with “buttons”…

The concept of “physical” buttons is awkward to him

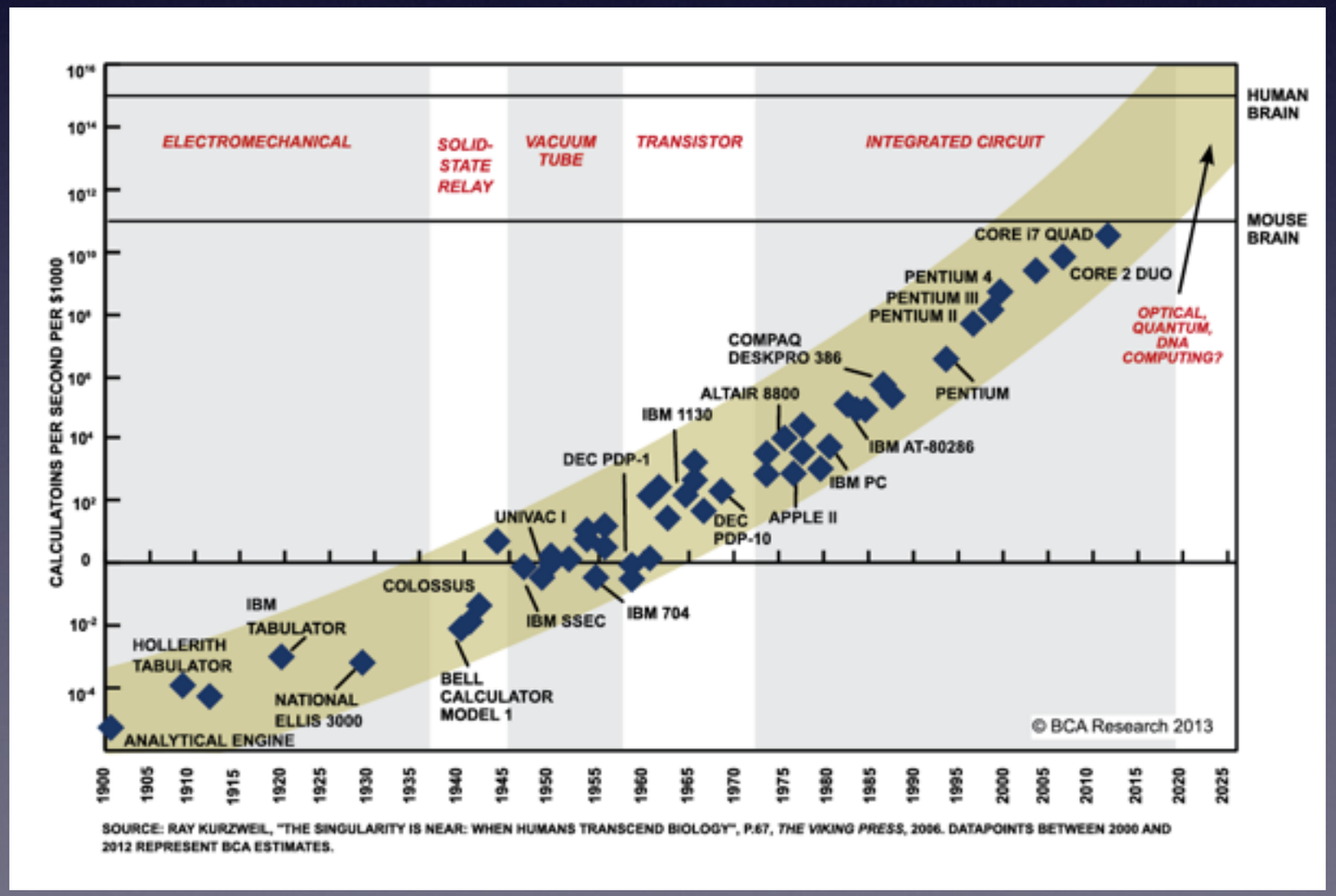
# The Last Technology Revolution - Electronics

## What the co-founder of Intel noticed in 1965…



Gordon Moore, co-founder Intel Corp

Every two years, the "power" of computers available doubles.



# The Last Technology Revolution - Electronics

An example of Moore's law's; a physical manifestation.

Currently available on amazon.com

128GB for $13.99 & FREE SHIPPING

What would it be like to build this in 1940?

# The Last Technology Revolution - Electronics

An example of Moore's law's; a physical manifestation.

To build a 126GB electronic storage device we would need:

1.1 Trillion Vacuum Tubes

2,500 square miles, or the state of Delaware

$4.7 Trillion, or the US military budget for ~6 years

76.8 Gigawatts or power,

slightly more than the power consumption of Germany

# The Last Technology Revolution - Electronics

An example of Moore's law's; a physical manifestation.

Put that in perspective…

Fit the state of Delaware

into a piece of candy

Fund the US Military for 6 years at the cost of a

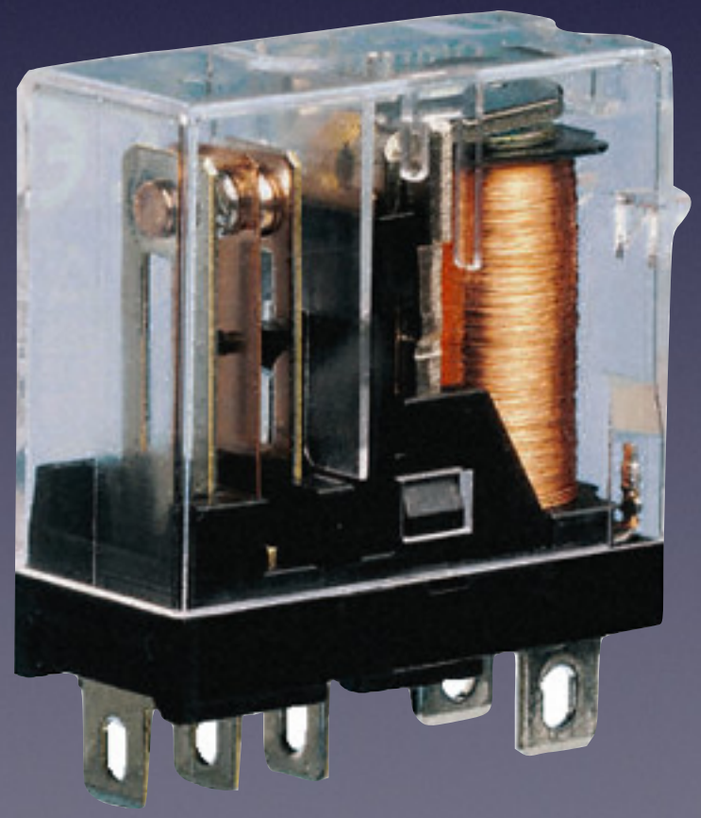

Power the country of Germany with 3X

# The Last Technology Revolution - Electronics

Ok, out of the clouds, how has this happened?

A series of *disruptive technologies*
that *changed* what was *possible* by *eliminating limits*

before 1940, electromechanical relays



- Large physical size
- Heat generation
- Moving parts
- High electricity requirements
- Slow switching
- Short life / High failure rate
- Integration with other parts

# The Last Technology Revolution - Electronics

Ok, out of the clouds, how has this happened?

A series of *disruptive technologies*
that *changed* what was *possible* by *eliminating limits*

1940's to late 1950's, vacuum tubes

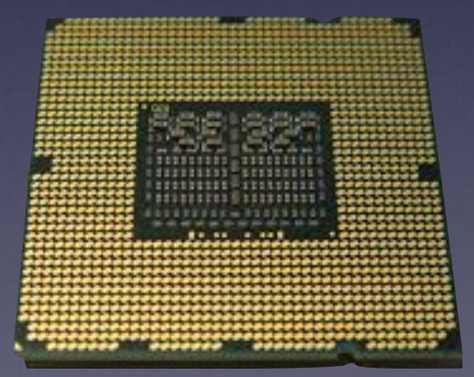
- Large physical size
- Heat generation
- ~~Moving parts~~
- High electricity requirements
- Slow switching
- ~~Short life / High failure rate~~
- Integration with other parts

# The Last Technology Revolution - Electronics

Ok, out of the clouds, how has this happened?

A series of *disruptive technologies*
that *changed* what was *possible* by *eliminating limits*

1970's to present, integrated circuits or "microchips"



- ~~Large physical size~~
- ~~Heat generation~~
- ~~Moving parts~~
- ~~High electricity requirements~~
- ~~Slow switching~~
- ~~Short life / High failure rate~~
- ~~Integration with other parts~~

# The Last Technology Revolution - Electronics

Chemistry & biology has started a similar path starting in the 1980's, but we are just getting started

Computers have moved from snail's pace to 250 thousands times faster than the space shuttle at reentry

250,000 X

*N.B.* CHEMISTRY AND BIOLOGY WILL BE USED INTERCHANGEABLY FOR THE REST OF THIS DOCUMENT; THE READER SHOULD APPRECIATE THE BLURRING DIFFERENCE BETWEEN ASPECTS OF CHEMISTRY AND BIOLOGY AT THEIR INTERFACES

# The Next Technology Revolution

Chemistry & biology has started a similar path starting in the 1980's, but we are just getting started

Chemistry Lab, Harvard, 1902

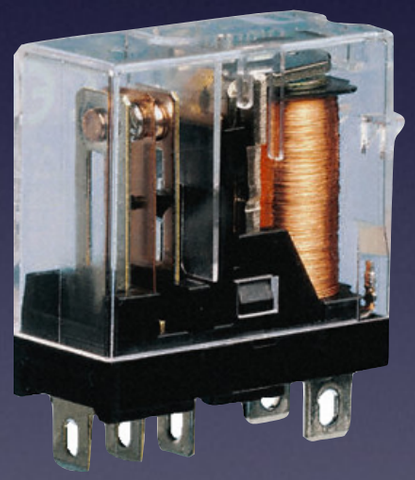
Chemistry Lab, USC, 2006

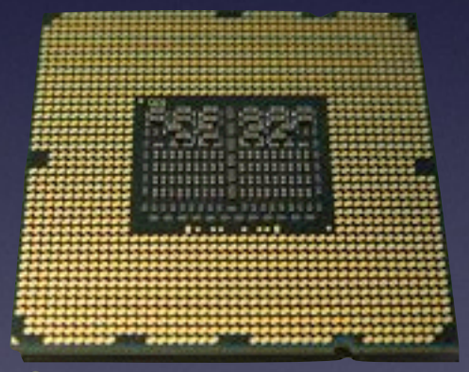
Still operating in the same paradigm

# The Next Technology Revolution

What can we learn from the computer industry to advance chemistry and biology?

Electronics involve the movement and interaction of electrons with various components.





Computers basically are sophisticated machines that control the flow of electrons — to AMAZING results to process information

# The Next Technology Revolution

What can we learn from the computer industry to advance chemistry and biology?

Chemistry involves the interaction of fluid elements & molecules with each other

How can we make sophisticated machines to control the interaction of fluids and molecules to learn about and control chemistry

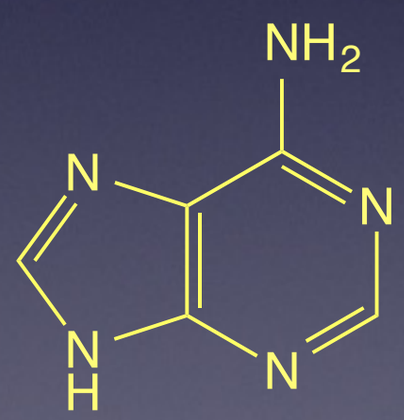
# The Beginning of the New "Chemistry"

## Lets look at the development DNA Sequencing

A brief primer:

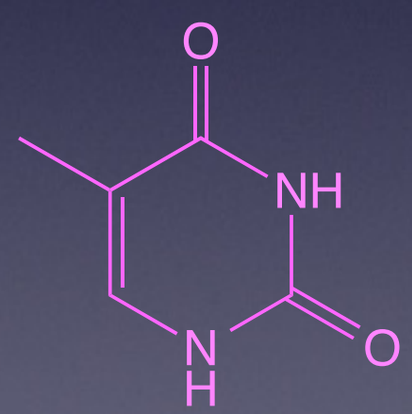
- DNA is the "blue-print" molecule of life; it largely determines how each organism develops
- Its "alphabet" consists (mostly) of 4 letters

They are:



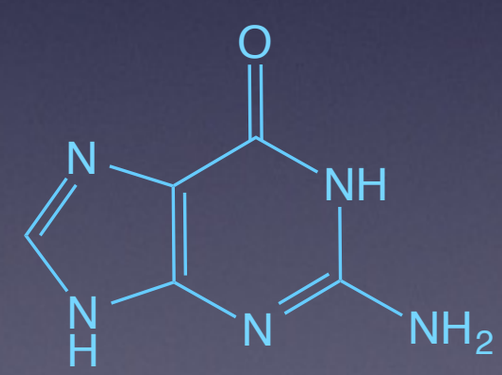

Adenine

A



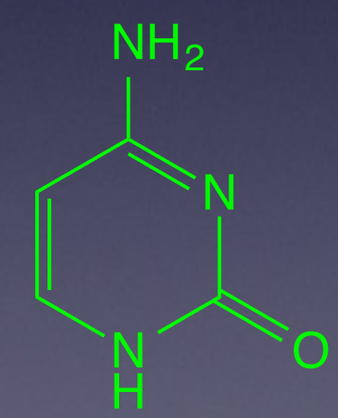

Thymine

T




Guanine

G




Cytosine

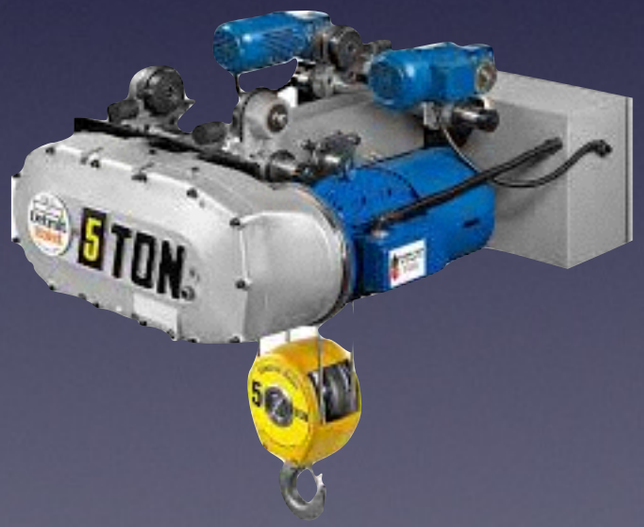
C

# The Beginning of the New "Chemistry"

## Lets look at the development DNA Sequencing

A brief primer:

- The order of these "letters" in the DNA molecule are the "instructions"
  - Tie your shoes
  - Rouse ye hoist



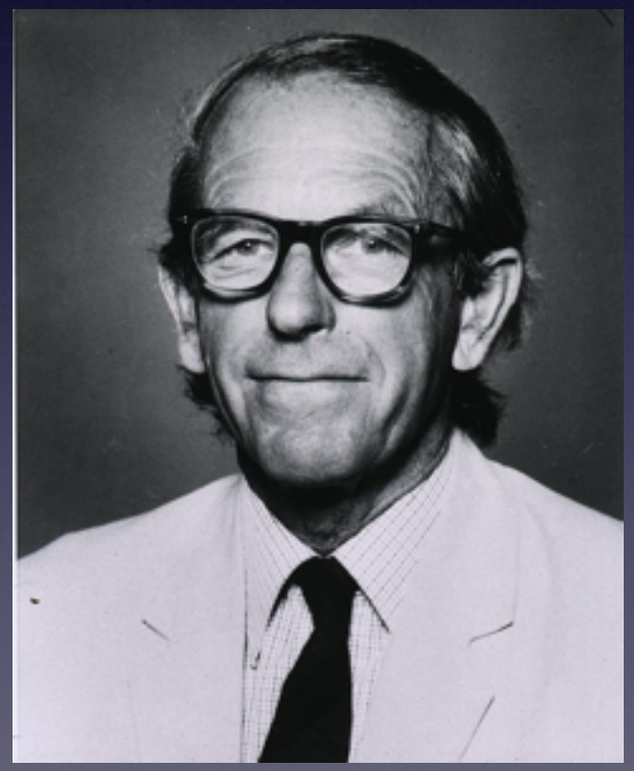

Same letters, different order
Different meaning

# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing

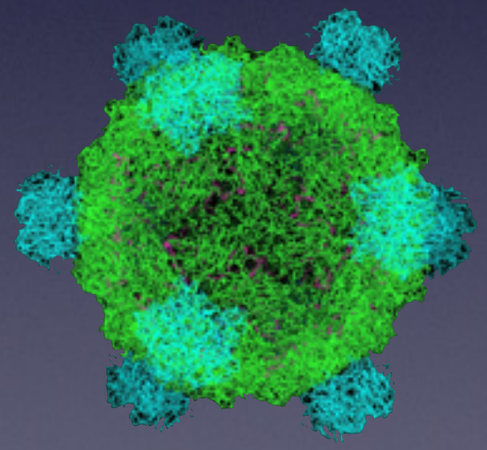
How to "read' these instructions?

First demonstrated in 1975 by Frederick Sanger



Frederick Sanger
1918 - 2013

Sequenced the genome of phiX-174



5368 "letters" long

Received his 2nd Nobel in 1980

# The Beginning of the New "Chemistry"

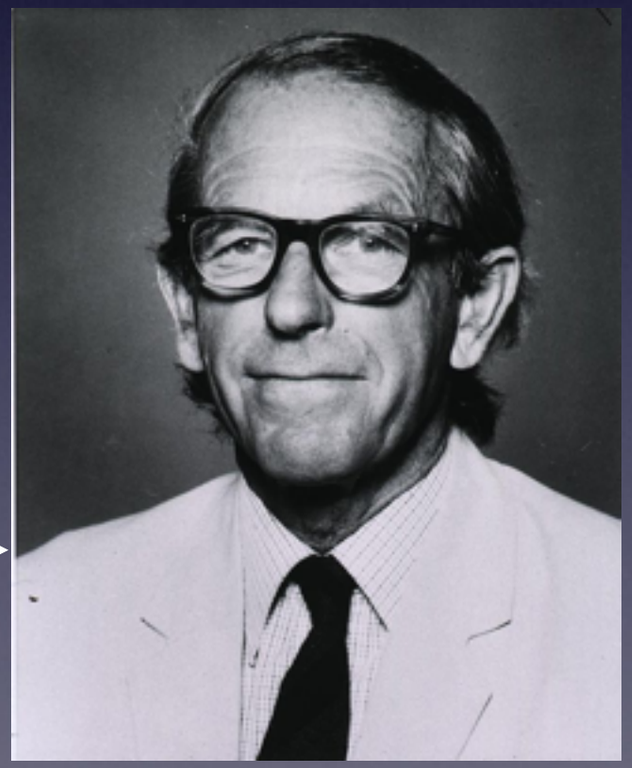
Lets look at the development DNA Sequencing

How to "read' these instructions?
1977 two new methods demonstrated and still widely used

Walter Gilbert

Published *PNAS*, Feb 1977

Published *PNAS*, Dec 1977



Frederick Sanger

They shared the 1980 Chemistry Nobel

# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing

How to "read' these instructions; the nitty gritty

The DNA Sequence: (Lady) Gaga gag a cat

Make four truncated "copy sets" of the DNA

| A Copy Set | T Copy Set | C Copy Set | G Copy Set |
|---|---|---|---|
| gA | GAGAGAGACAT | GAGAGAGAC | G |
| gagA | | | gaG |
| gagagA | | | gagaG |
| gagagagA | | | gagagaG |
| gagagagacA | | | |

# The Beginning of the New "Chemistry"

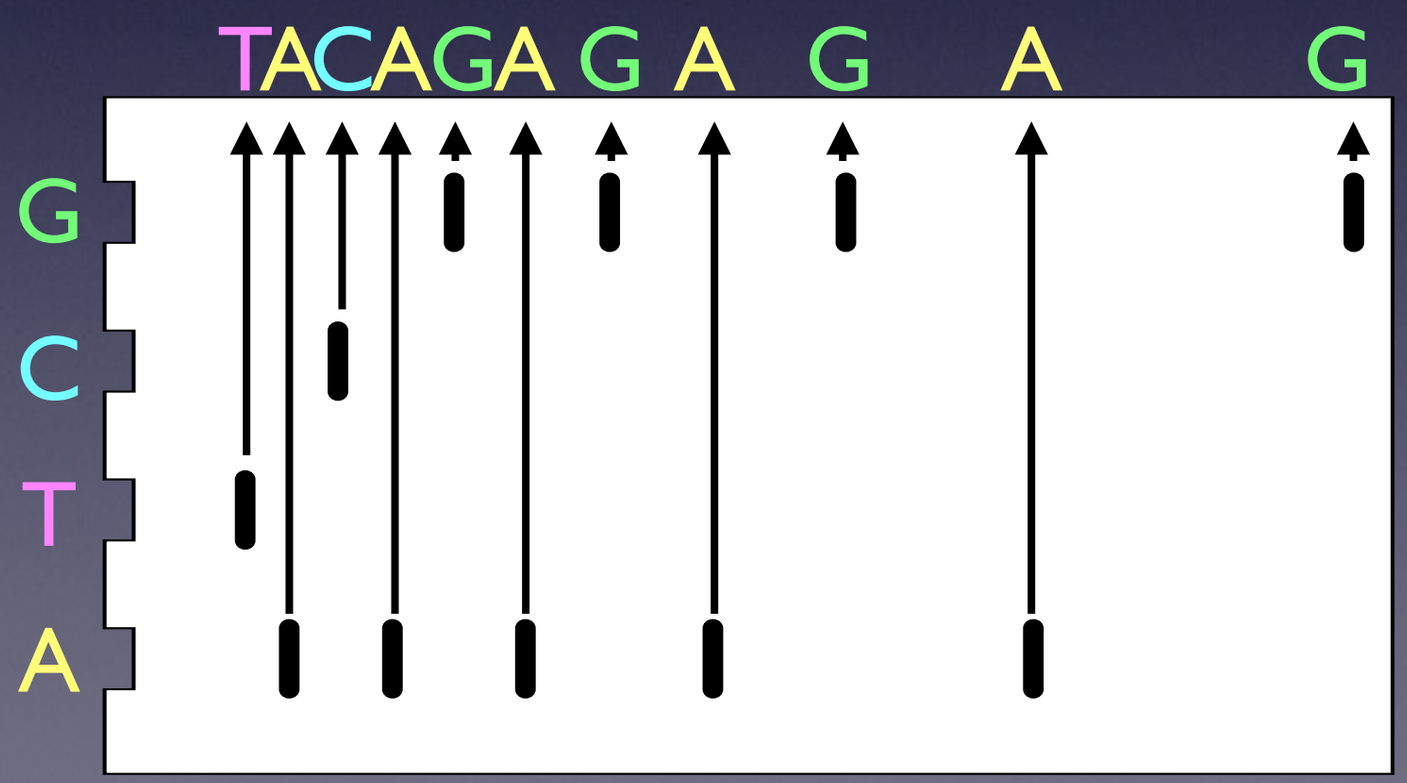
Lets look at the development DNA Sequencing

How to "read' these instructions; the nitty gritty

Now, measure the length of these DNA pieces with electrophoresis

LONG DNA moves slow

short DNA moves FAST



# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing

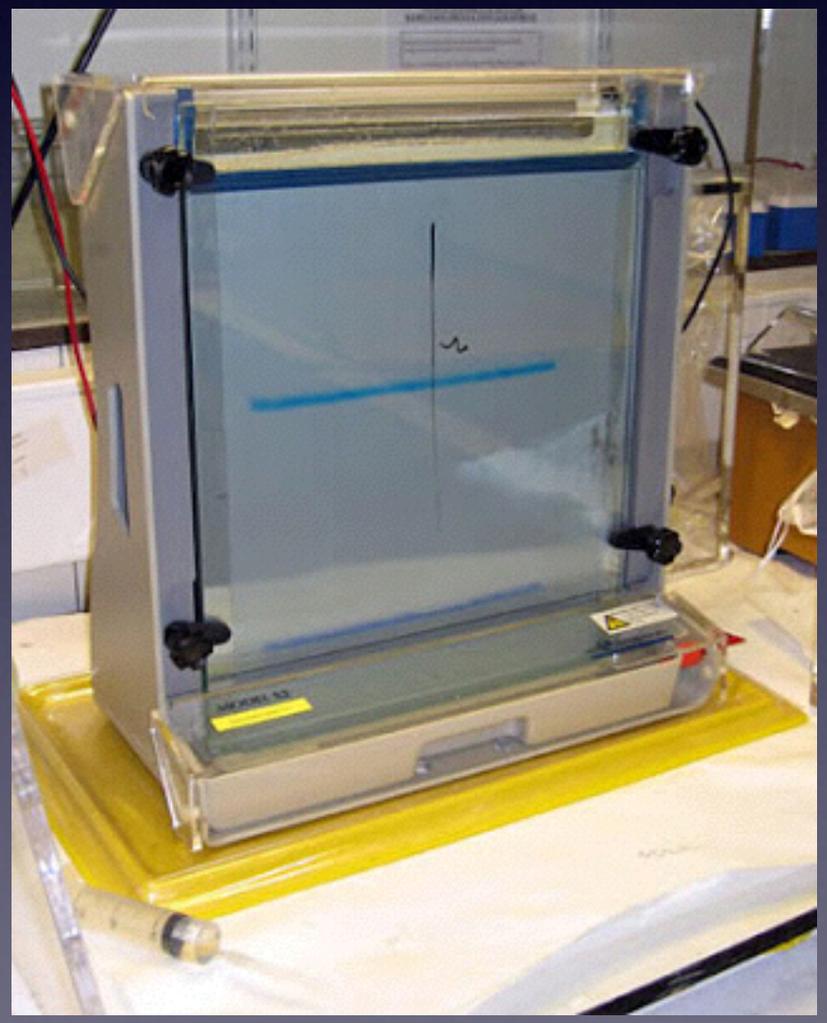
Until ~5 years ago, virtually all DNA sequencing was done with electrophoresis

# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing

Until the mid-early 1980's this was done in "Slab Gels"

with $^{32}P$ labels



Slow
Radioactive labels
Manual preparation
Manual data readout
Large chemical requirement

# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing

Starting in the mid 1980's radioactive labels were replaced with fluorescent labels and analysis was automated

VERY Slow

~~Radioactive labels~~

~~Manual preparation~~

~~Manual data readout~~

Large chemical requirement

# The Beginning of the New "Chemistry"

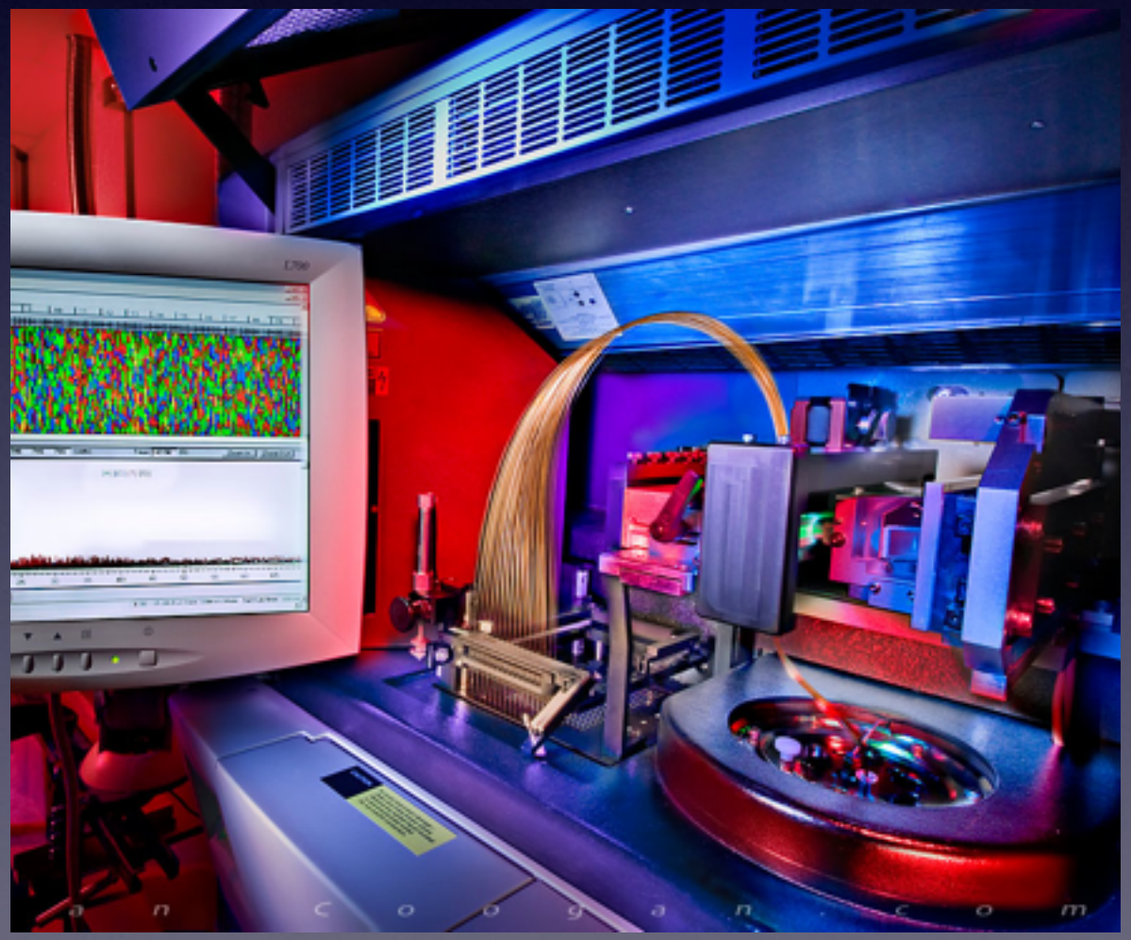
Lets look at the development DNA Sequencing

Starting in the mid 1990's this was done in capillaries

~~VERY~~ Slow
~~Radioactive labels~~
~~Manual preparation~~
~~Manual data readout~~
~~Large chemical requirement~~
Finicky, high failure rate
Limited sample capacity

# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing
Starting in the late 1990's this was done in 96 capillary arrays



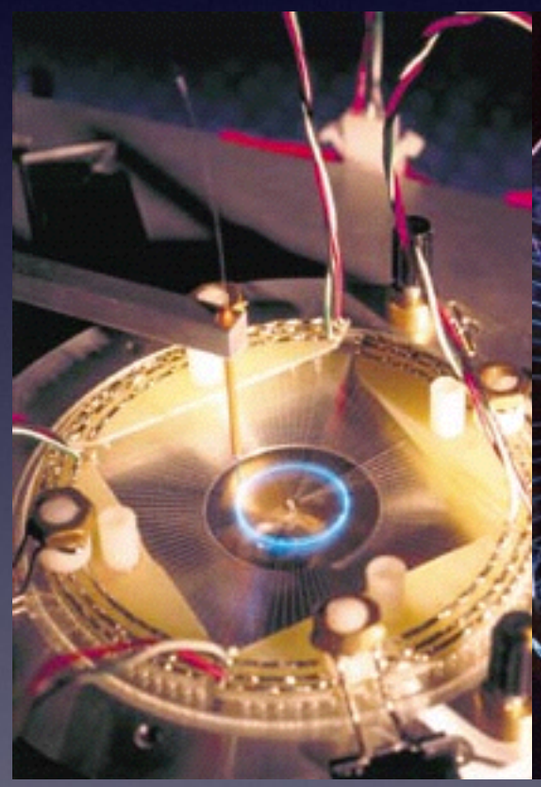
~~VERY~~ Slow
~~Radioactive labels~~
~~Manual preparation~~
~~Manual data readout~~
~~Large chemical requirement~~
Finicky, high failure rate
~~Limited sample capacity~~

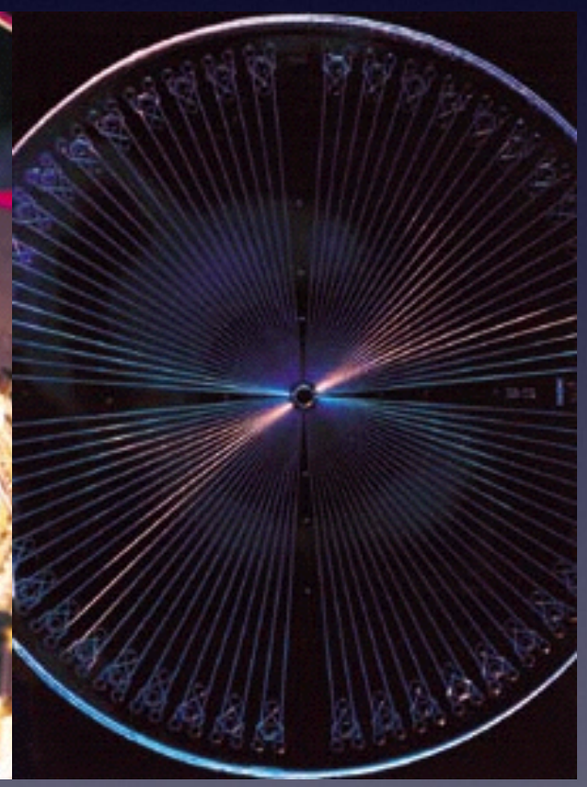
These instruments were the workhorse of the Human Genome Project

# The Beginning of the New "Chemistry"

Lets look at the development DNA Sequencing

In the early 2000's DNA moved into microfluidics

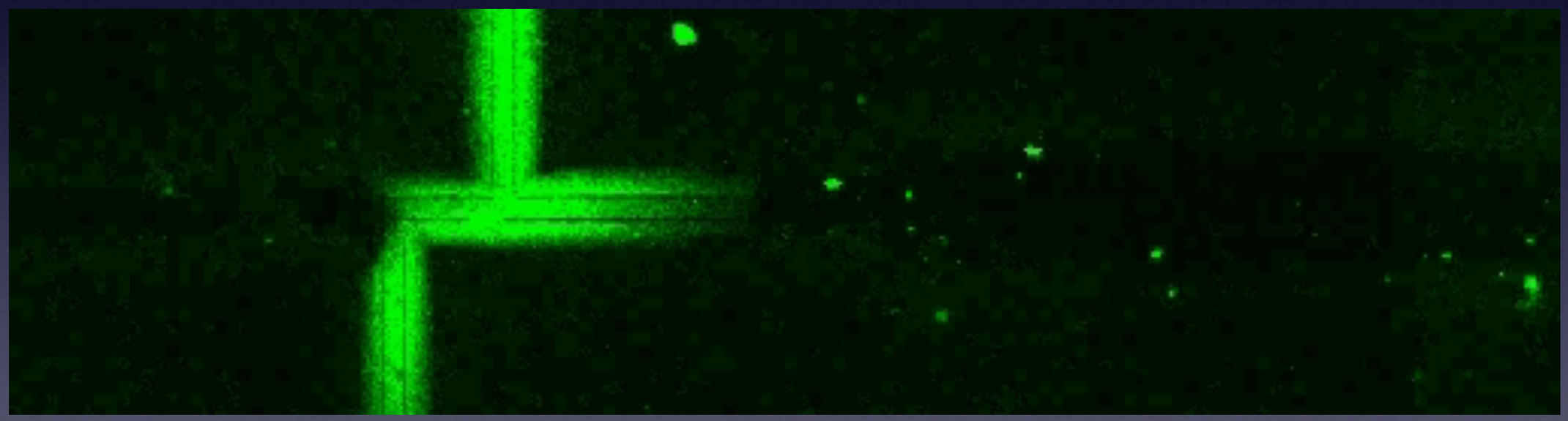




~~VERY Slow~~
~~Radioactive labels~~
~~Manual preparation~~
~~Manual data readout~~
~~Large chemical requirement~~
~~Finicky, high failure rate~~
~~Limited sample capacity~~
Really Expensive

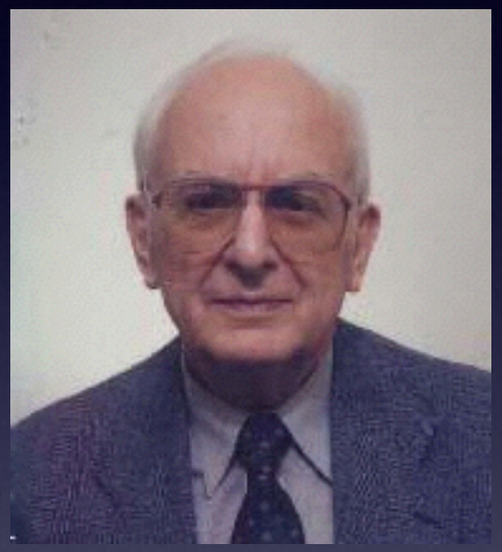
# The Beginning of the New "Chemistry"

A video of a DNA separation in a microfluidic device



# The Beginning of the New "Chemistry"

## An aside:
## There really is nothing new under the sun



Wolfgang Haller

After presenting some microfluidic research; an older NIST gentleman approached us:

(paraphrasing) "I am glad to see you guys are starting to work on these things again."

He then gave us a top-secret (in the 1950's) device

# The Beginning of the New "Chemistry"

## An aside:
## There really is nothing new under the sun

NIST (then NBS) housed the Diamond Ordnance Fuze Laboratory

- Designed devices to control bomb detonation
- Founded in 1940 at NBS
- Moved to Army in1952

This device is prototype analogue pneumatic computer to operate in a nuclear attack. (Electronics go crazy in an EMP)

# The Beginning of the New "Chemistry"

## The first thirty years of of DNA sequencing

In 1975 to sequence 5000 bases took:

- More than 1 year
- A world-class team
- Untold $ (well £)

In 2005 to sequence 1M bases took:

- One day
- One technician
- ~$ 1000

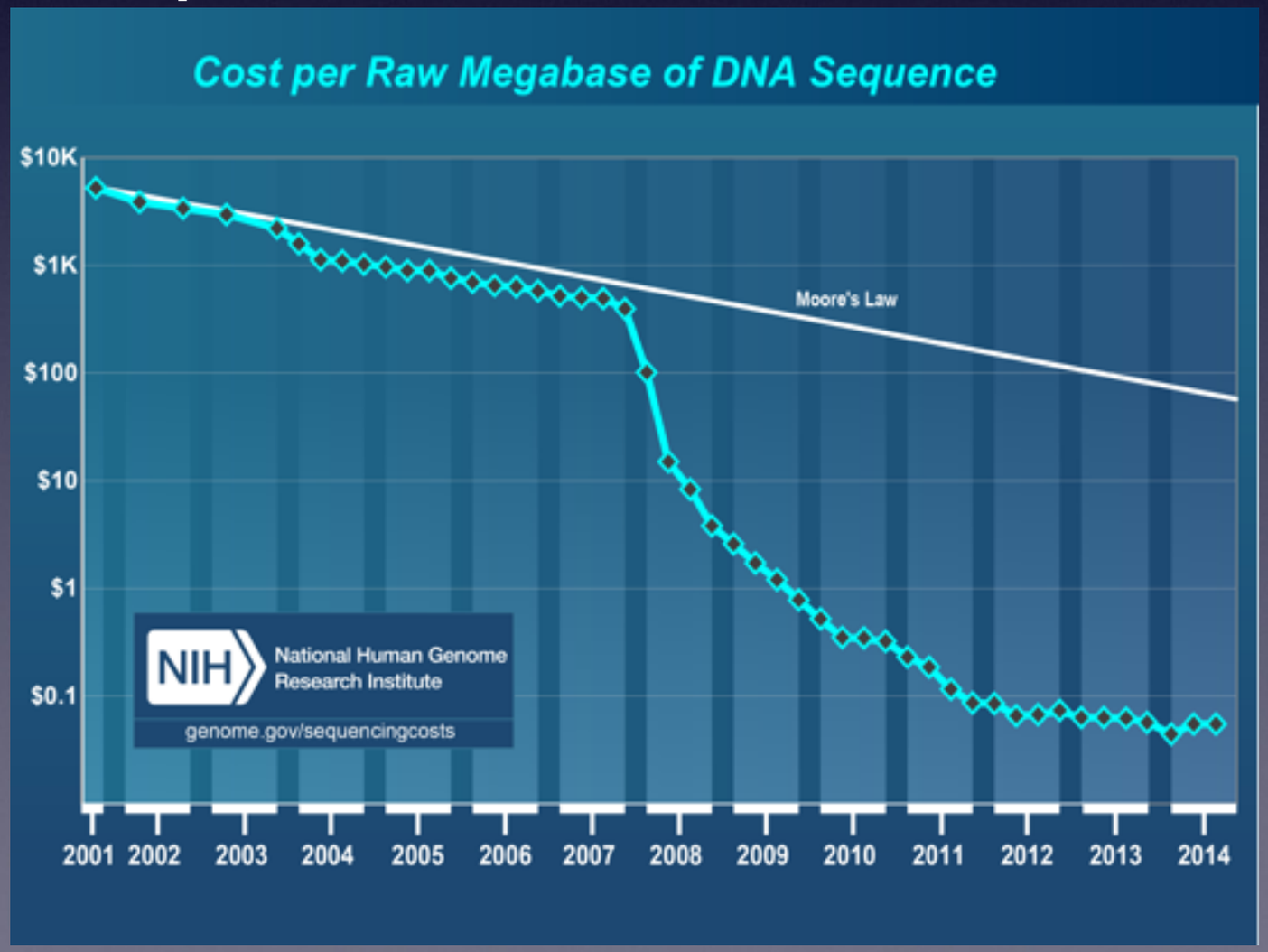
2 X

This is good progress, but we can do better
What is the *disruptive technology* happening *now*

# The Beginning of the New "Chemistry"

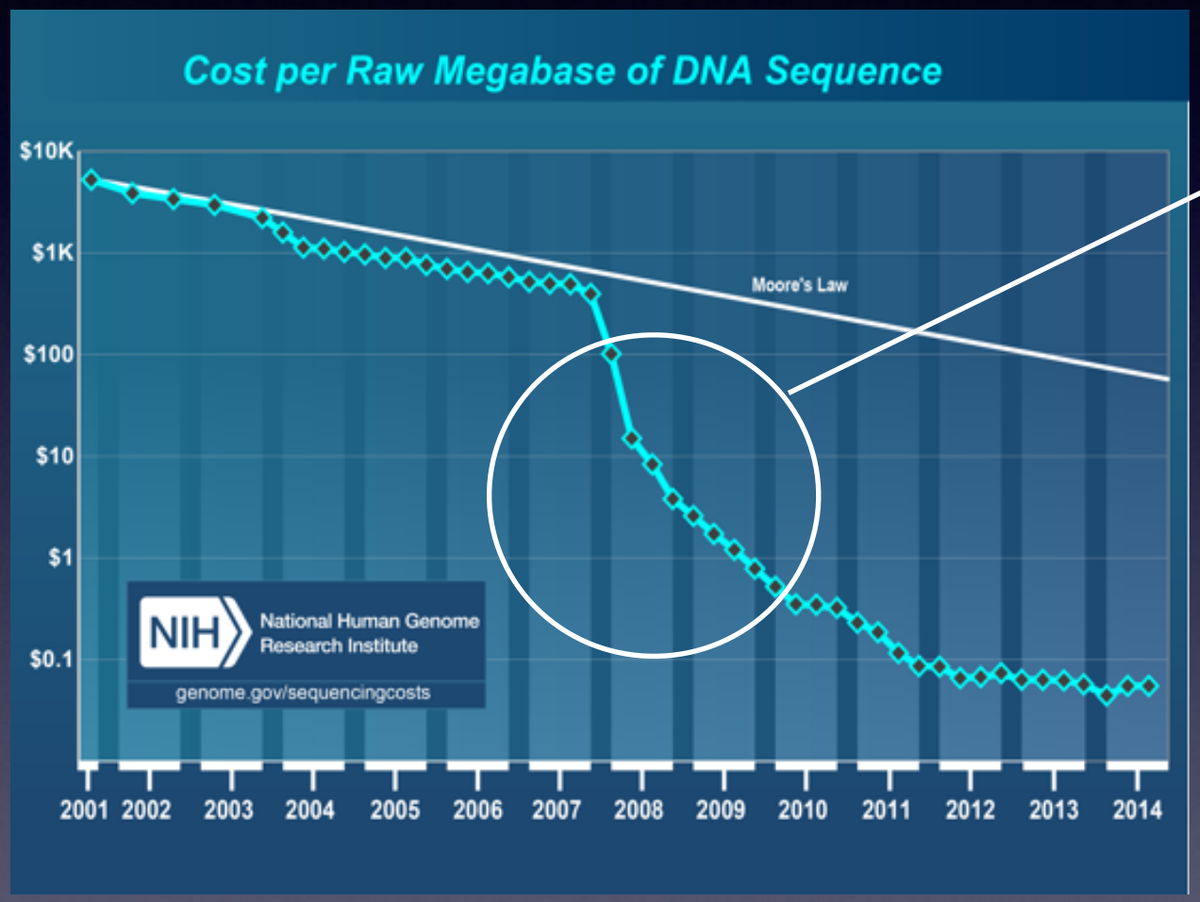
## The current state-of-the art

I would argue, DNA sequencing has just moved through an inflection point similar to that experienced in computer industry in 1972 with the introduction of the first Intel 8008 processor



# The Beginning of the New "Chemistry"

## The current state-of-the art




What happened here?

A new *disruptive technology*

The ability to interrogate individual, single molecules with great speed

This ability is facilitated by the *blurring the differences* between *biologists, chemists, physicists* and *material scientists*

# The Beginning of the New "Chemistry"

## The first forty years of of DNA sequencing

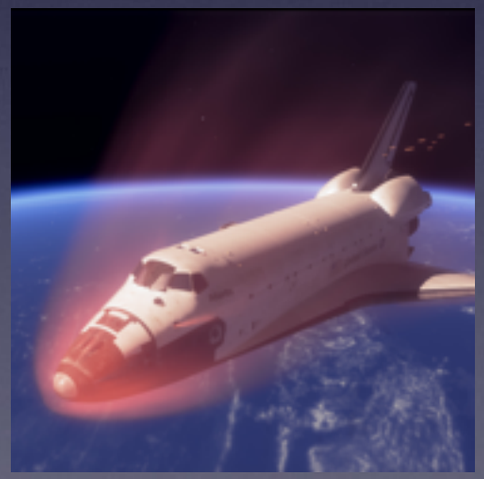
In 1975 to sequence 5000 bases took:

- More than 1 year
- A world-class team
- Untold $ (well £)

Now we can almost sequence 3Gbp in

- One day
- One technician
- ~$ 1000

4 X



# The Beginning of the New "Chemistry"

## The current state-of-the art

These technologies all have the same operational paradigm:

- Take a HUGE number of DNA molecules
- Interrogate each of those individual DNA strands simultaneously

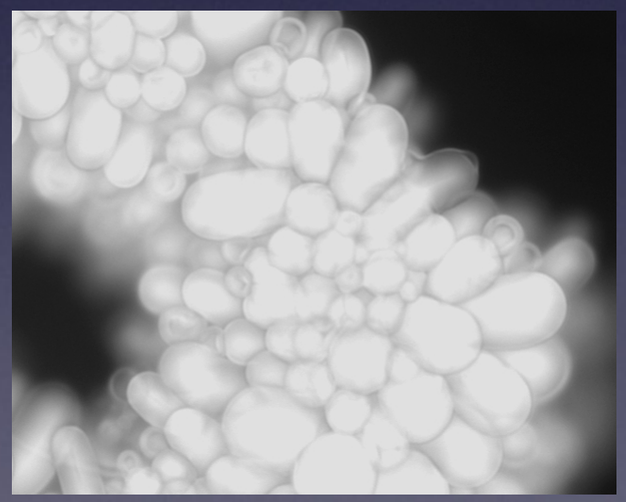
# The Beginning of the New "Chemistry"

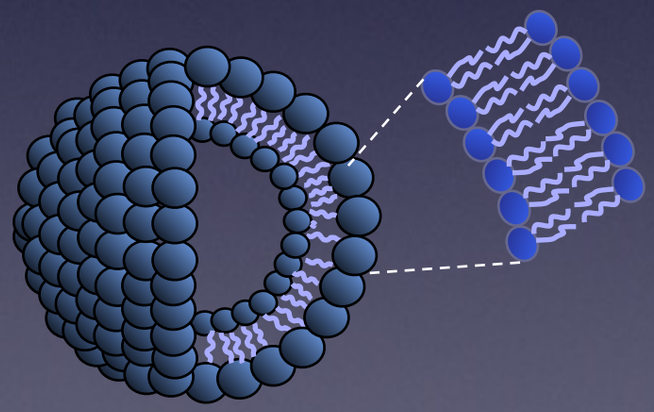
## NEW SUBJECT; NOT DNA

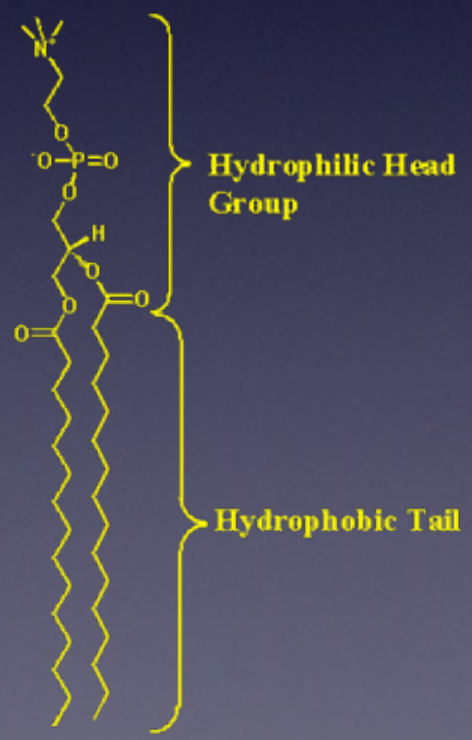
## Can we make new materials?

Consider nuclear medical imaging probes

These can be made of particles called "liposomes"







# The Beginning of the New "Chemistry"

## Can we make new materials?

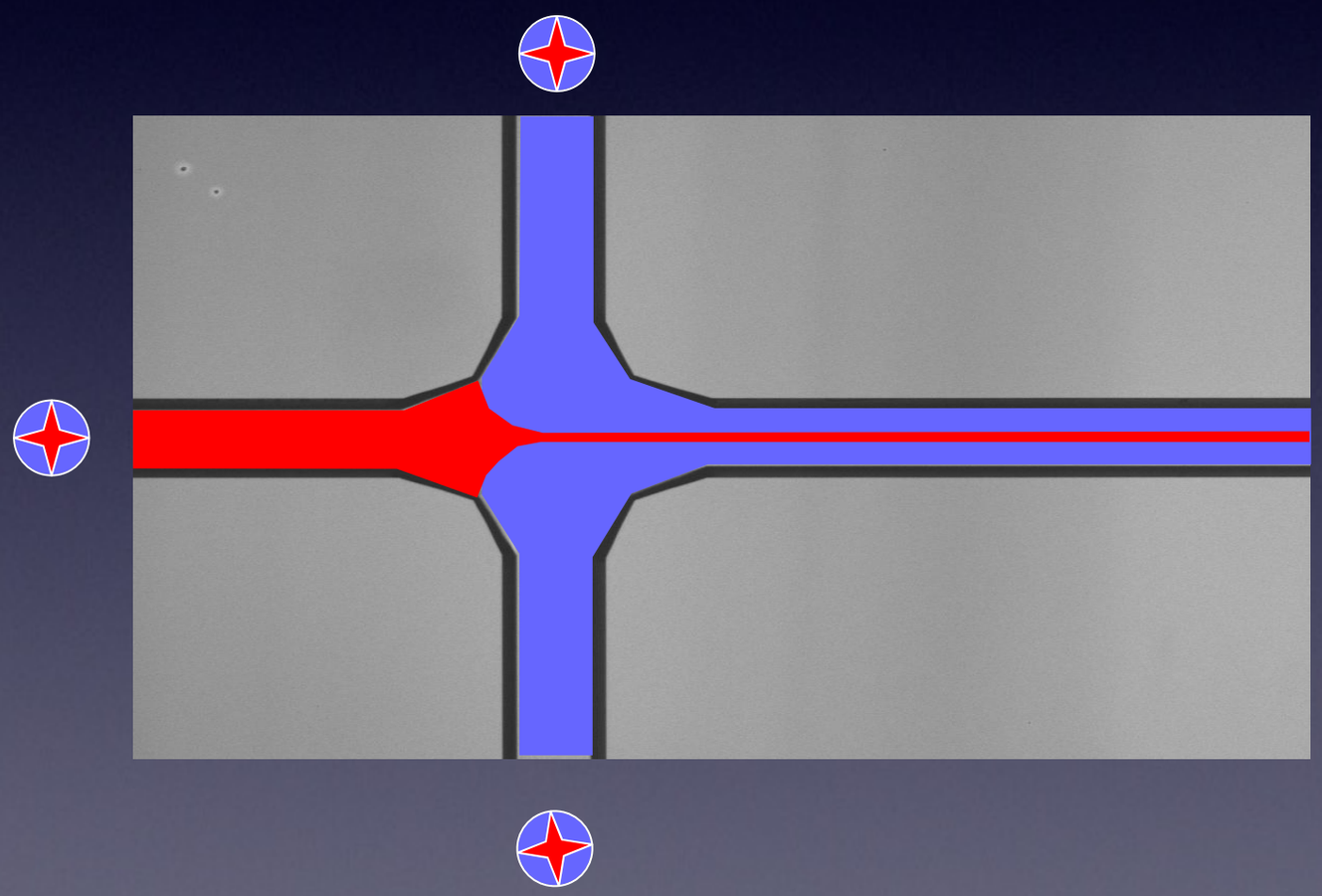
## The current industry state-of-the art

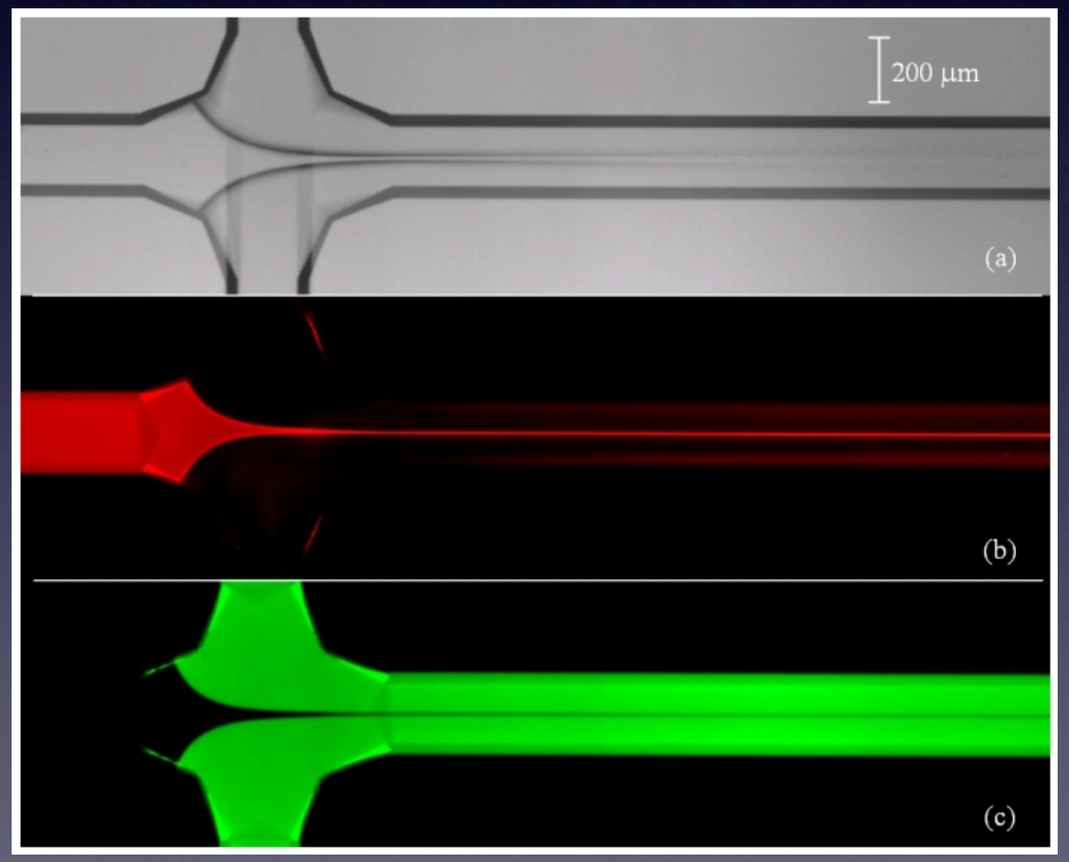
Weighs 50 kg
About 1 cubic meter
Expensive

# The Beginning of the New "Chemistry"

Can we make new materials?

What is the next *disruptive technology?*

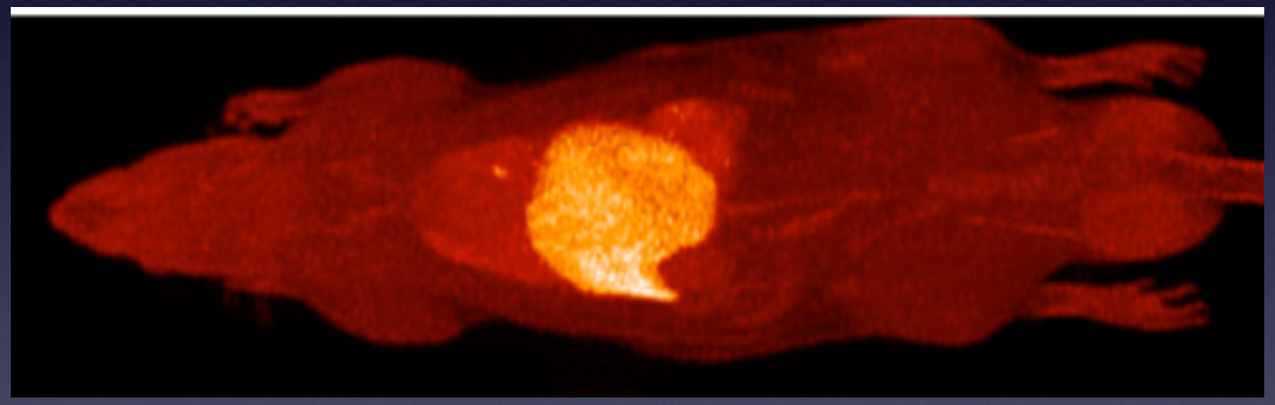




# The Beginning of the New "Chemistry"

## Can we make new materials?

If you make "bad" liposomes this is what you get….

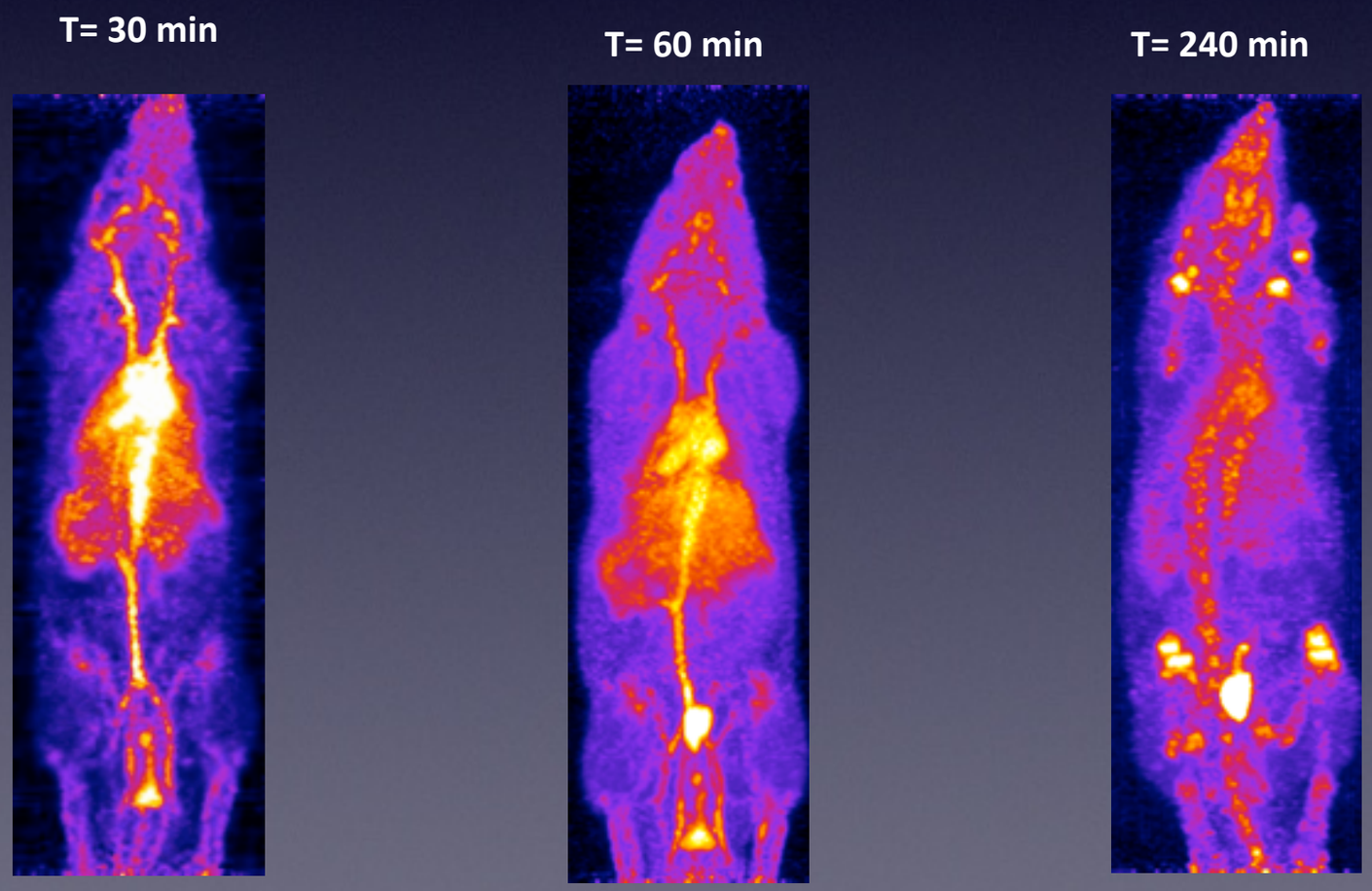


Ferrara, *et al,* Nuc Med Bio, 34 (2007) 165

# The Beginning of the New "Chemistry"

Can we make new materials?

But if you make "good" liposomes this what you get



# Thanks!!

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