Biol 365 – Computer applications in biology

Class intro

Computers have become extremely powerful

- The computer used to operate the Apollo 11 moon landing (1969)
  - Used about 5,000 circuits (number of calculations per cycle possible)
  - Had a clock speed of 1.024 MHz (number of times the 5,000 operations can be done per second = 1,024,000)
- It had 4 kb of RAM (working memory)
- How does this compare to our modern machines?

Onboard computer from a Ford Ranger

- Runs at 40 MHz
- But, many more transistors on the CPU chip (can do many more calculations per cycle)
- Several MB memory
- Way more powerful than the Apollo moon landing computers

General-purpose, desktop computing has also advanced

- Desktop computing was just for hobbyists initially
- Hardware was not up to tasks like graphics, audio
- Not multi-tasking – could only run one program at a time
- Coincidentally, my own computer history parallels the development of desktop computers pretty well

My computing history

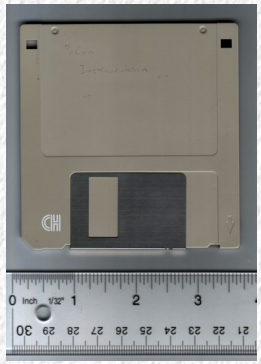
- First (family) computer – Apple IIe, late 1970's
- No hard drive, monochrome (green) display
- Two floppy drives recommended – one for programs, one for data
- Floppies held 512 KB
- No graphical interface
- 1.023 MHz clock speed
- 64 KB RAM
- Usable – word processing

College days – terminals, not home PC's

- PC's were very expensive, few students had their own in the mid/late 80's
- When we used computers, we used terminals like this one
- Monochrome display (green or amber)
- Printed to a central print facility – send it a print job, pick it up later
- Used for “real” work – PC's were still considered too limited for serious scientific computing

Mac SE

- Acquired in 1989 – senior in college
- CPU ran at 7.8 MHz
- 40 MB hard drive (!)
- 1.2 MB floppy drive
- 1 MB RAM
- Monochrome display (black, white, and shades of gray)
- Graphical, mouse-driven interface
- Multi-tasking – could have more than one program running at a time
- Access campus network (no Internet yet) through an external modem over phone lines (remember those?)



The mighty Gateway 486DX

- Upper-end PC in 1990
- 33 MHz CPU
- 250 MB hard drive
- 4-64 MB RAM
- MS-DOS or Windows 3.1
- 16 or 256 colors on display
- No network connection (not considered necessary)
- Not my own – used to do Geographic Information Systems analysis for my MS thesis

Mac IIci

- Acquired in early 1990's
- 25 MHz
- Separate FPU for doing math with decimal numbers quickly
- 1-68 MB RAM
- 40 MB hard drive
- True color (like today, millions of colors but less screen resolution)
- Dial-up modem built in

Power Mac G3

- Acquired in mid-late 1990's
- 300 MHz
- 256 MB – 1 GB RAM
- Hard drives up to 27 GB
- Graphics card with 16 MB RAM
- Ethernet built in, but most people still used modems from home
- Started my PhD dissertation on this computer

Compaq Presario

- Acquired in 2001
- 1.33 GHz
- 256 MB RAM
- 64 MB video card
- 80 GB hard drive
- Ethernet built in, broadband internet was becoming common, but no WiFi yet
- Finished my PhD dissertation on this one

Dell Inspiron 531

- Acquired in 2006
- 2 GHz dual-core processor
- 1-8 GB RAM
- 160 GB hard drive

My current computer – Dell Optiplex 9010

- Standard faculty computer
- Octo core processor, 3.4 GHz
- 16 GB RAM
- 500 GB solid state drive

- GIS analysis that took 4+ hours on the Gateway in 1991 would take less than 30 sec on this machine

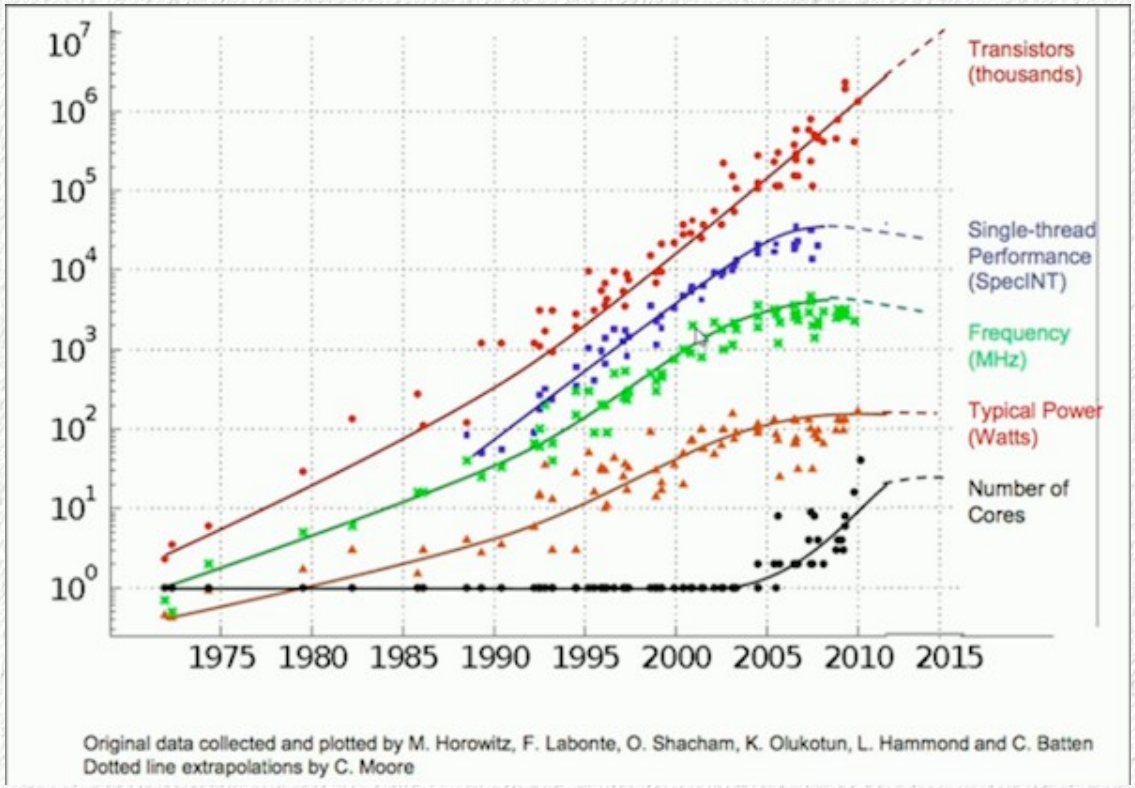
My smart phone

- 2.2 GHz quad-core CPU
- Millions of transistors
- 32 GB internal storage
- 2 GB RAM

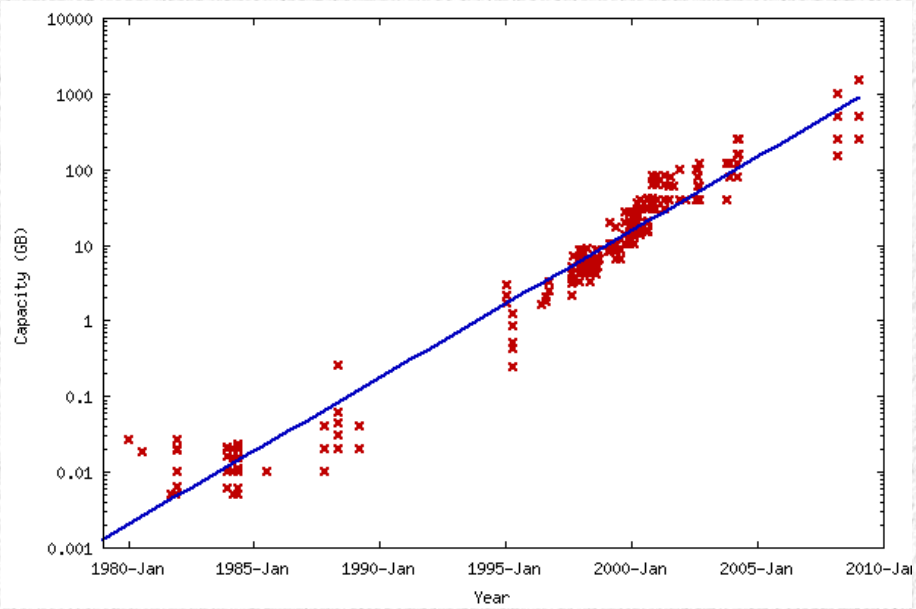
- Nowhere near the best available today, but still more than enough to go to the moon!

Increase in computing power over time

CPU



Hard drive capacity



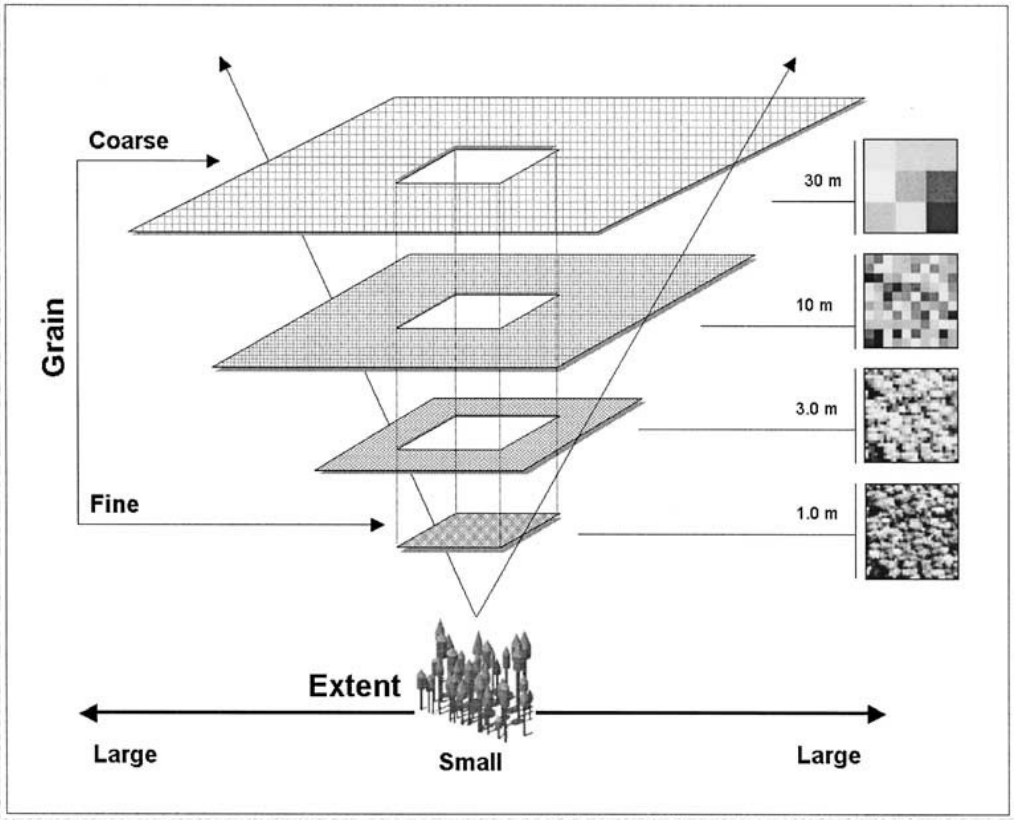
At the same time, cost has declined (both in absolute $ and adjusted for inflation)

Quantitative increases in computing power qualitatively changed Biology

- The increase in computing power has allowed us to use computers very differently
  - Not just for math, data management, statistical analysis
  - Used now for sound, images, video – big files, very processor intensive
- We are now able to address questions that couldn't be addressed before...
  - Genome-level analysis
  - Change detection at global scales
- ...using methods that weren't practical before
  - Numerical methods of analysis
  - Stochastic simulation modeling

Sizes of data sets can be bigger

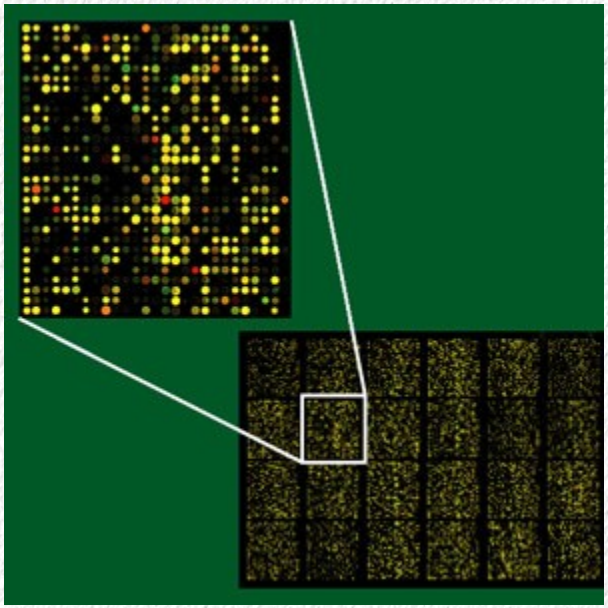
- Example: GIS – computer mapping
- For a given level of computing power, trade-off grain and extent
- As computers get more powerful, it's possible to record finer grain detail over larger extents



- Result is better cover type mapping, change detection

Example: genomic analysis

- We can look at expression at huge numbers of genes (10,000 +) simultaneously
- Conducting the experiments, and then collecting, managing, and analyzing these data would not be possible without computers



Example: statistical analysis

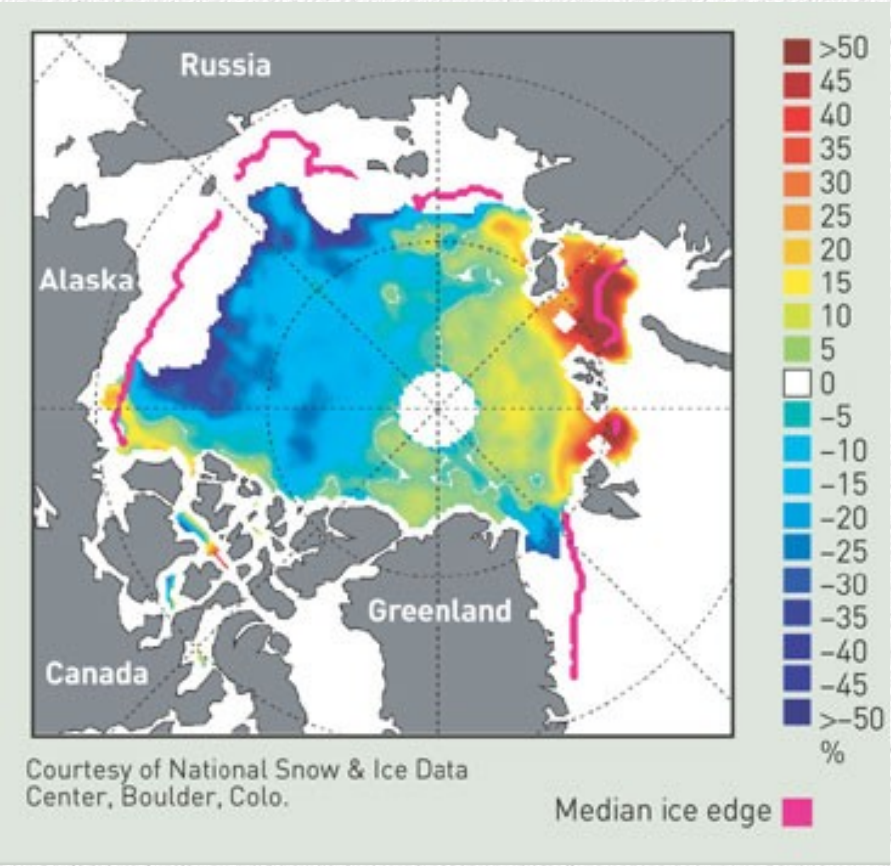
- Complex data sets – we have known how to analyze them for a long time, but couldn't
  - Multivariate data – calculations done by hand would take years to complete, less than a second today
- Computer-intensive methods:
  - Randomization tests
  - Neural networks
  - Tree-based methods
  - Maximum likelihood

Computers allow automation of data collection

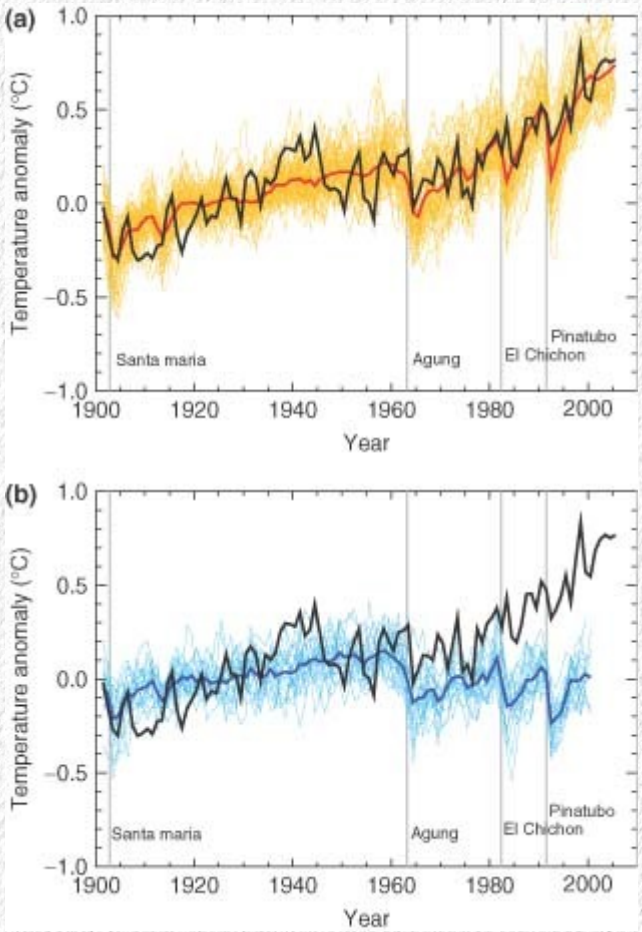
- Digital sensors of various kinds have been developed that can collect vast amounts of data
- Examples:
  - Imagery – microarrays, LandSat, x-rays
  - Position – GPS collars
  - Physiological state – continuous monitoring of heart rate, environmental conditions

Example: change detection

- Improvements in technology (remote sensing) along with computing power allows us to detect changes over large areas over time
- Changes in arctic ice shown here



Example: simulation modeling



- When you can't do experiments, next best thing is to simulate the system in a computer
- Global climate models can be built that:
  - Include all potentially important variables
  - Use high enough spatial resolution to account for geographic variation
- Here we're seeing that we can't reproduce historic temperatures unless we include anthropogenic CO_2 emissions

Numerical methods become practical

- Statistical methods
  - Maximum likelihood
  - Randomization methods (bootstrap, Monte Carlo)
- Numerical optimization
- Sequence alignments

Identifying function of unknown genes

- You sequence a gene, but don't know what it does
- How do you find out?
- Need to check if the function of the gene is already known in your own organism, or another
- Even if it's only known from another species, good chance that it has a similar function in your organism

BLAST searches

- Aligning DNA sequences – need two components
  - A database (or “library”) of sequences and their known functions
  - A routine (or “algorithm”) for aligning an unknown sequence with a known sequence
- BLAST is a common alignment method
  - Basic Local Alignment Search Tool
  - Aligns the unknown sequence to those in the database
  - Gives a measure of sequence similarity
  - Genes that are similar above a user-defined threshold are likely to have similar function
- Any database can be used, but large databases built from contributed sequences from all over the world are the most useful

The BLAST approach

- Matching one sequence of nucleotides to another
- Assign a score
  - Matching bases get a +1
  - Mismatching bases get a penalty, $-\mu$
  - Inserting or deleting a base gets a penalty, $-\sigma$
  - Score = # matches – μ(# mismatches) – σ(# indels)
- Score the sequences, unmodified
- At the first mismatch, try an insertion or deletion, see how the score changes – if it improves, keep it and try an indel at the next mismatch
- Keep going until the score is as high as you can get it

Example

```
Seq. 1: AGCTTATAAGCCAA
Seq. 2: AGTTATAAGACCAA
```

Matches: 8
Mismatches: 6

```
Seq. 1: AGCTTATAAGCCAA
Seq. 2: AG-TTATAAGACCAA
```

Matches: 11
Mismatches: 2
Indels: 1

```
Seq. 1: AGCTTATAAG-CCAA
Seq. 2: AG-TTATAAGACCAA
```

Matches: 13
Mismatches: 0
Indels: 2

Repeat for all the genes in the database

- The sequence may have thousands of bases
  - Alignment against one sequence in the database takes time
- May be thousands of sequences in the database
  - Multiply time per sequence x thousands
- Pick the gene with the highest score as the match

- Huge amount of computation – could be done by hand, but would take inordinate amounts of time
- Thanks to computers, this is now a routine part of molecular genetics work

Computers are ubiquitous

- As of 2013, 78.5% of US households have desktop or laptop computers in them (up to 83.8% if you include tablets)
  - 92% or more for younger households (less than 44 years old)
  - Over 95.5% of households of college graduates
- Powerful computers are now in everyday items (smart phones)
- It's increasingly difficult to avoid computer use entirely, even for people who do not personally own one
- Kids are growing up using them → no fear!

What's missing

- Students today are more comfortable with using computers, but are not expected to learn as much about them
- Computer programming classes are not required for Bio majors
- Computer literacy courses no longer required at CSUSM
  - Did not cover MS Excel, MS Access for data management and analysis even when it was required

In this class:

- We will learn how computers are used in Biology
  - Not in bioinformatics/biotech – there's another class for that
- We will use a spreadsheet as the primary computational tool
  - The “swiss army knife” of scientific computing – general purpose, can do most things
  - Will mention more specialized tools for particular purposes, but won't use them in class