UCDAVIS Bioinformatics Core

Bioinformatics: A perspective

Dr. Matthew L. Settles

Genome Center
University of California, Davis
settles@ucdavis.edu

UCDAVIS Bioinformatics Core

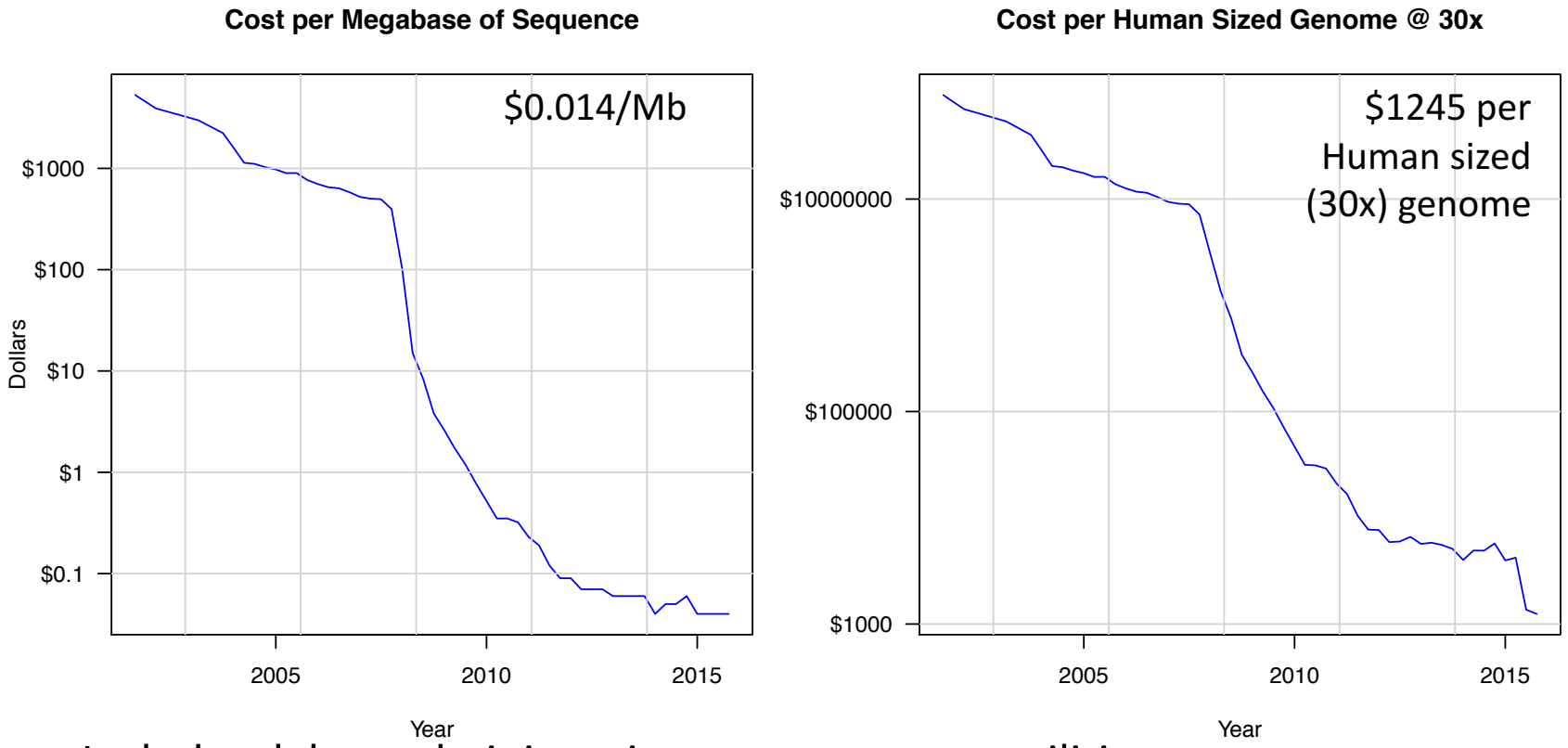
Outline

- The World we are presented with
- Advances in DNA Sequencing
- Bioinformatics as Data Science
- Viewport into bioinformatics
- Training
- The Bottom Line

UCDAVIS Bioinformatics Core

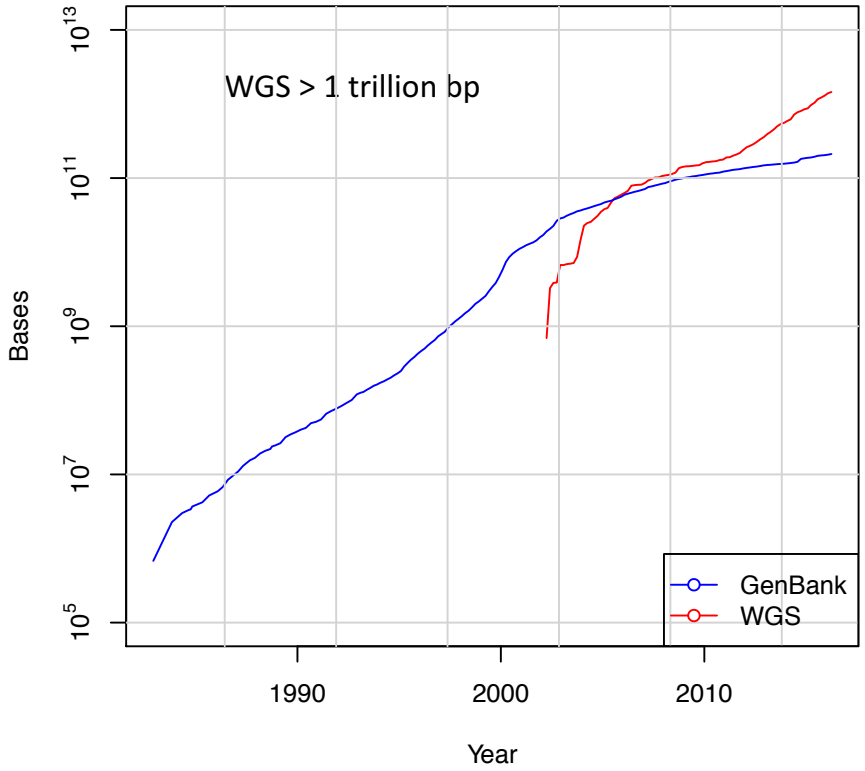
Sequencing Costs

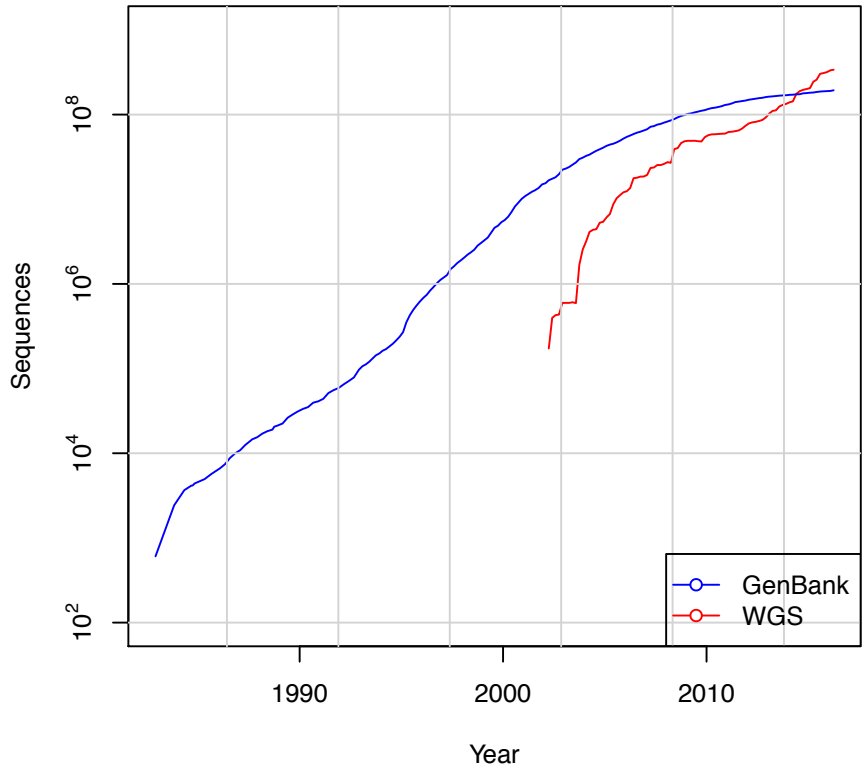
October 2016



- Includes: labor, administration, management, utilities, reagents, consumables, instruments (amortized over 3 years), informatics related to sequence productions, submission, indirect costs.
- http://www.genome.gov/sequencingcosts/

Growth in Public Sequence Database

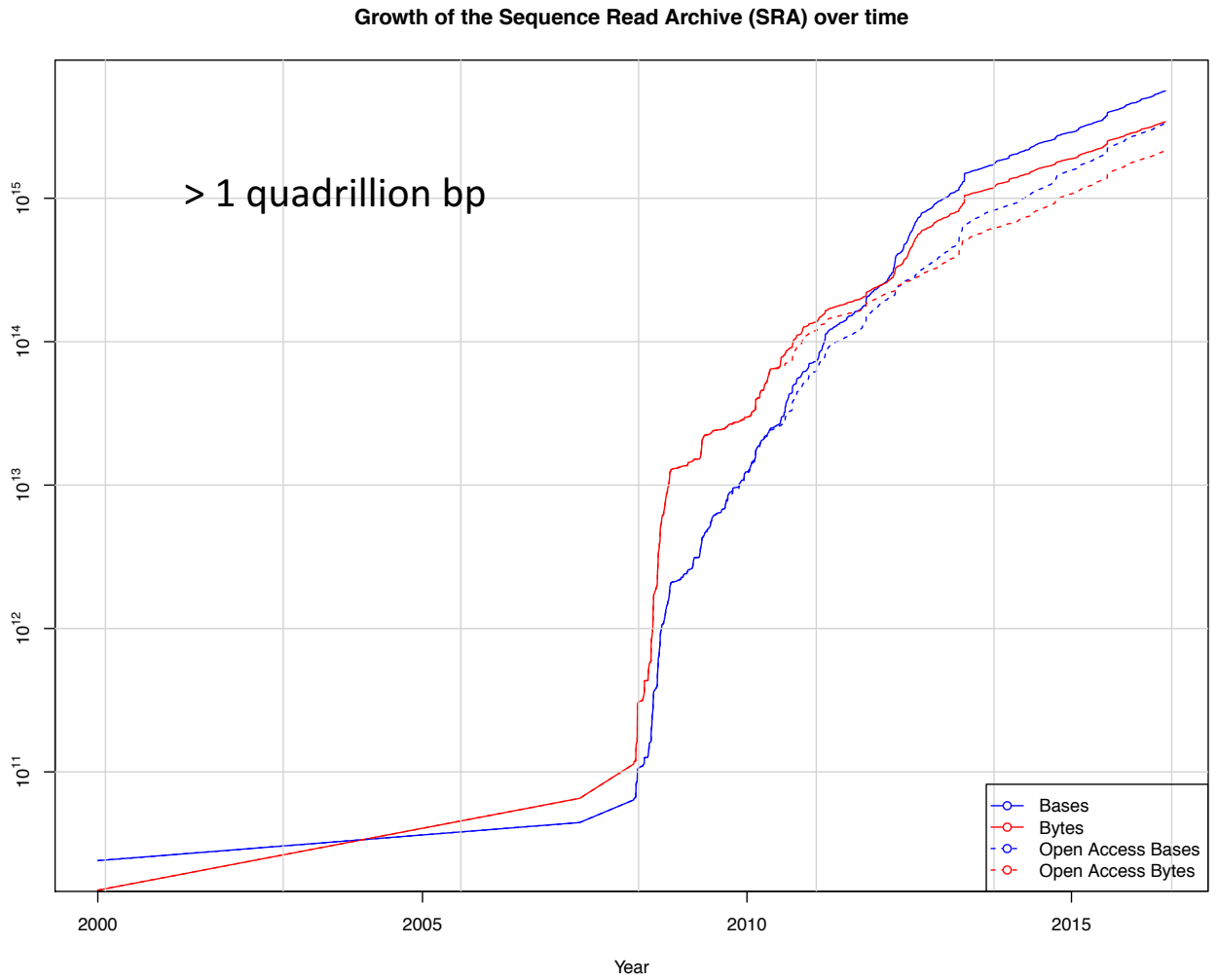




- http://www.ncbi.nlm.nih.gov/genbank/statistics

UCDAVIS Bioinformatics Core

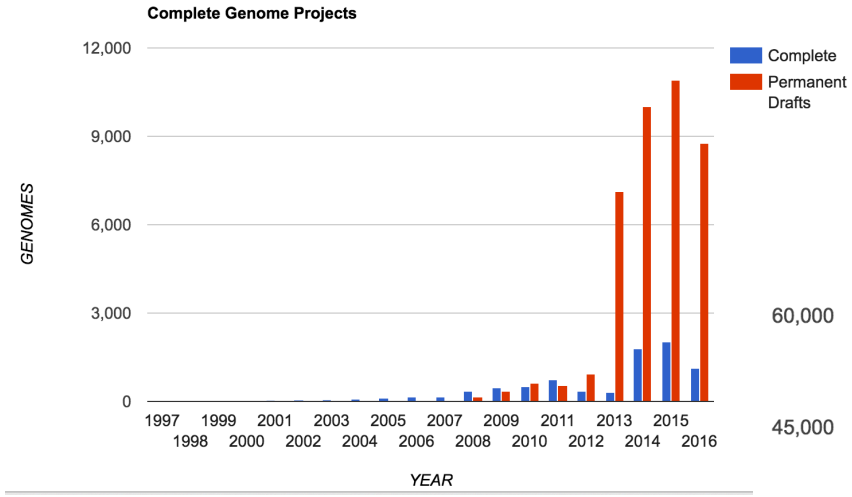
Short Read Archive (SRA)



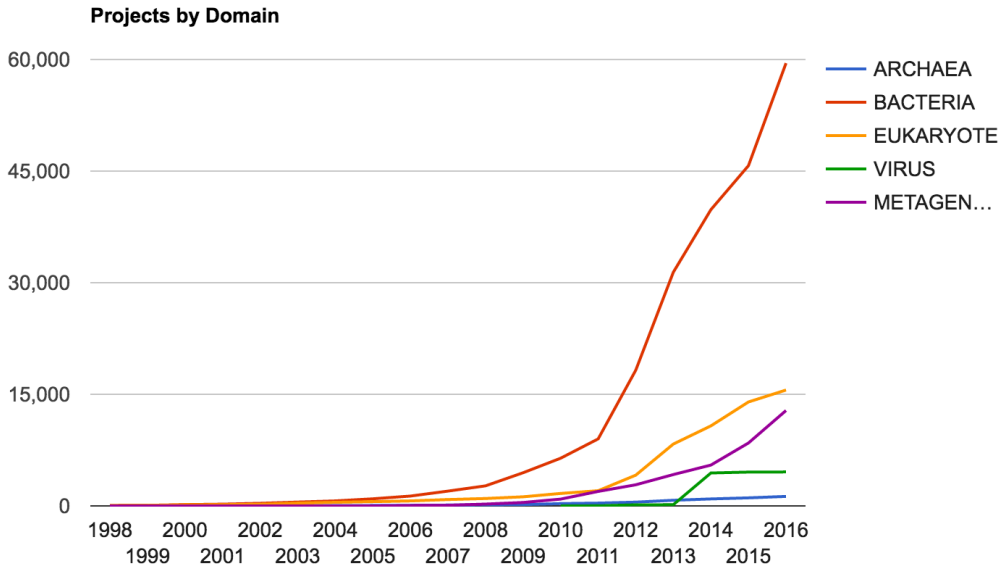
http://www.ncbi.nlm.nih.gov/Traces/sra/

UCDAVIS Bioinformatics Core

Increase in Genome Sequencing Projects



Lists > 3700 unique genus



- JGI – Genomes Online Database (GOLD)
- 67,822 genome sequencing projects

UCDAVIS Bioinformatics Core

Brief History

Sequencing Platforms

- 1986 - Dye terminator Sanger sequencing, technology dominated until 2005 until “next generation sequencers”, peaking at about 900kb/day

‘Next’ Generation

- 2005 – ‘Next Generation Sequencing’ as Massively parallel sequencing, both throughput and speed advances. The first was the Genome Sequencer (GS) instrument developed by 454 life Sciences (later acquired by Roche), Pyrosequencing 1.5Gb/day

Discontinued

Illumina

- 2006 – The second ‘Next Generation Sequencing’ platform was Solexa (later acquired by Illumina). Now the dominant platform with 75% market share of sequencer and and estimated >90% of all bases sequenced are from an Illumina machine, Sequencing by Synthesis > 200Gb/day.

New
NovaSeq

Complete Genomics

- 2006 – Using DNA nanoball sequencing, has been a leader in Human genome resequencing, having sequenced over 20,000 genomes to date. In 2013 purchased by BGI and is now set to release their first commercial sequencer, the Revolocity. Throughput on par with HiSeq

NOW DEFUNCT

Human genome/exomes only.

10,000 Human Genomes per year

Bench top Sequencers

- Roche 454 Junior

- Life Technologies
- Ion Torrent
- Ion Proton

- Illumina MiSeq

The 'Next, Next' Generation Sequencers (3rd Generation)

- 2009 – Single Molecule Read Time sequencing by Pacific Biosystems, most successful third generation sequencing platforms, RSII ~2Gb/day, newer Pac Bio Sequel ~14Gb/day, near 100Kb reads.

SMRT Sequencing

Iso-seq on Pac Bio possible, transcriptome without 'assembly'

UCDAVIS Bioinformatics Core

Oxford Nanopore

- 2015 – Another 3rd generation sequencer, founded in 2005 and currently in beta testing. The sequencer uses nanopore technology developed in the 90's to sequence single molecules. Throughput is about 500Mb per flowcell, capable ofnear 200kb reads.

Fun to play with but results are highly variable

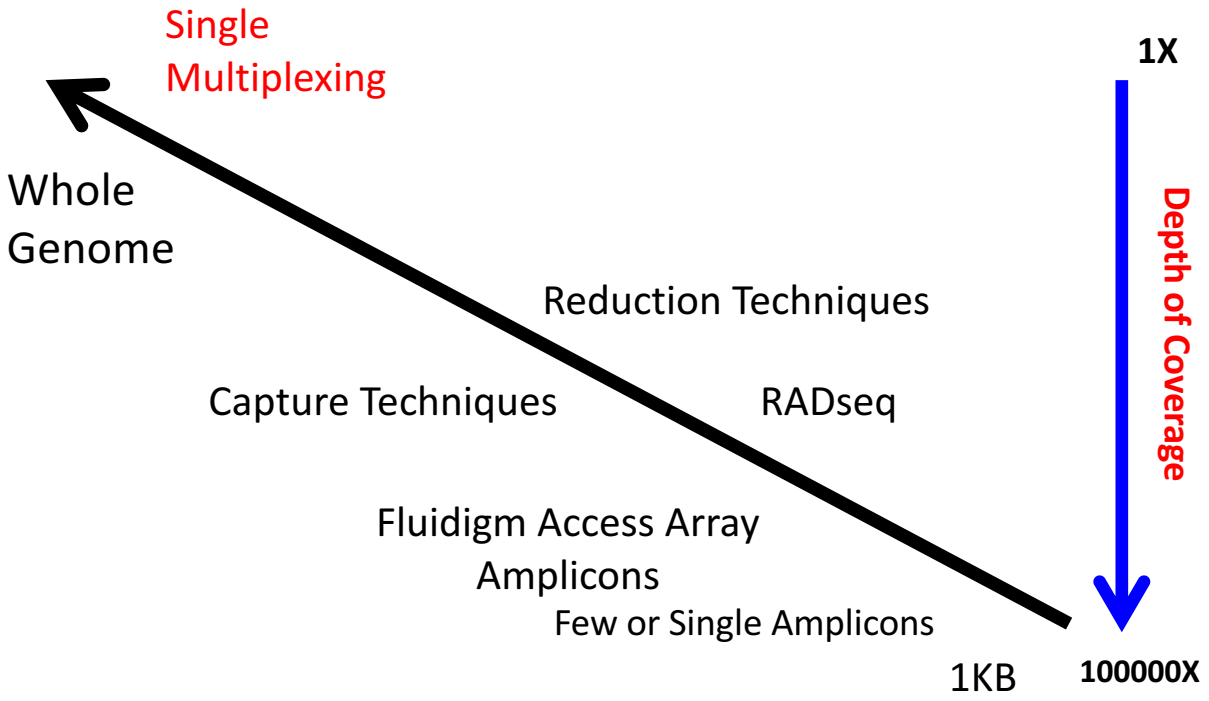
Nanopore Sequencing

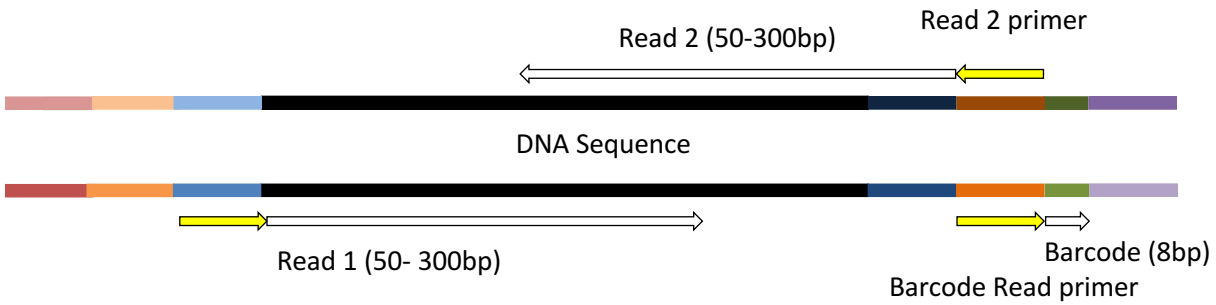
FYI: 4th generation sequencing is being described as In-situ sequencing

Flexibility

Genomic reduction allows for greater coverage and multiplexing of samples.

You can fine tune your depth of coverage needs and sample size with the reduction technique





Sequencing Libraries

- DNA-seq
- RNA-seq
- Amplicons
- CHiP-seq
- MeDiP-seq
- RAD-seq
- ddRAD-seq
- Pool-seq
- EnD-seq

DNase-seq

ATAC-seq

MNase-seq

FAIRE-seq

Ribose-seq

smRNA-seq

mRNA-seq

Tn-seq

QTL-seq

tagRNA-seq

PAT-seq

Structure-seq

MPE-seq

STARR-seq

Mod-seq

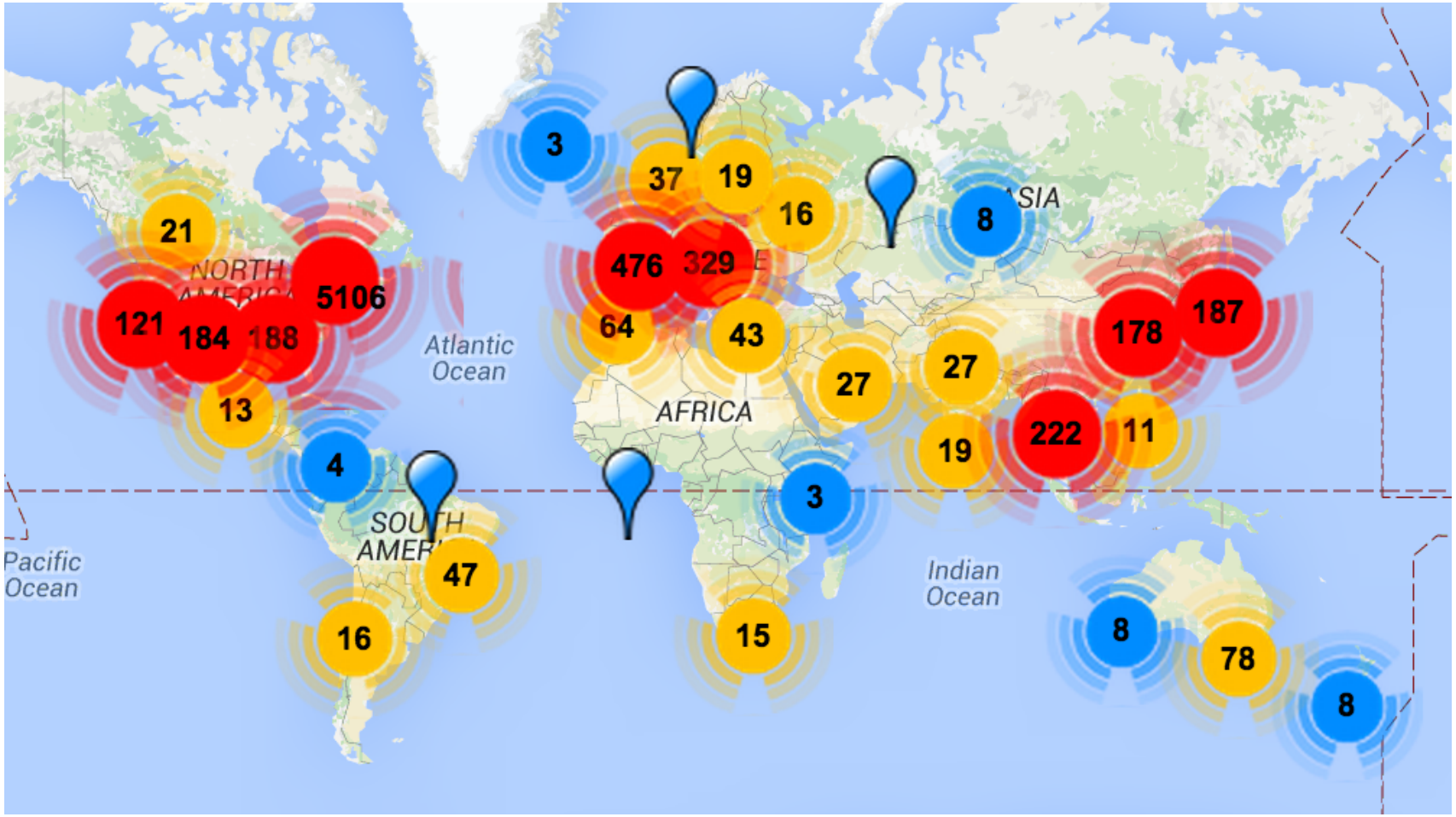
BrAD-seq

SLAF-seq

G&T-seq

UCDAVIS Bioinformatics Core

omicsmaps.com



The data deluge

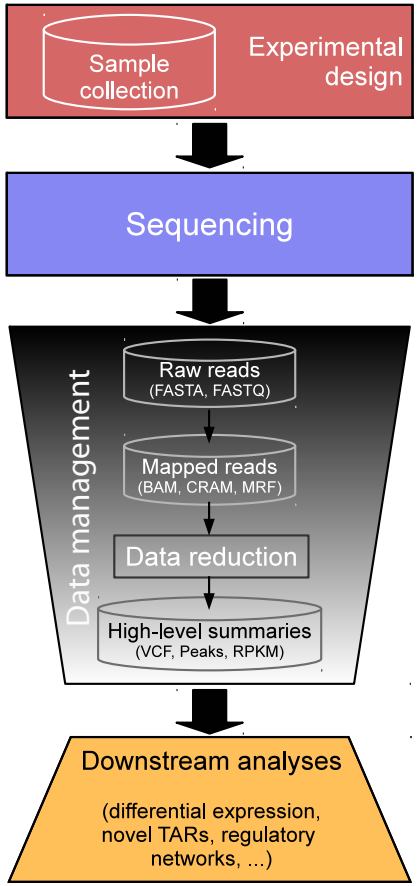
- Plucking the biology from the Noise

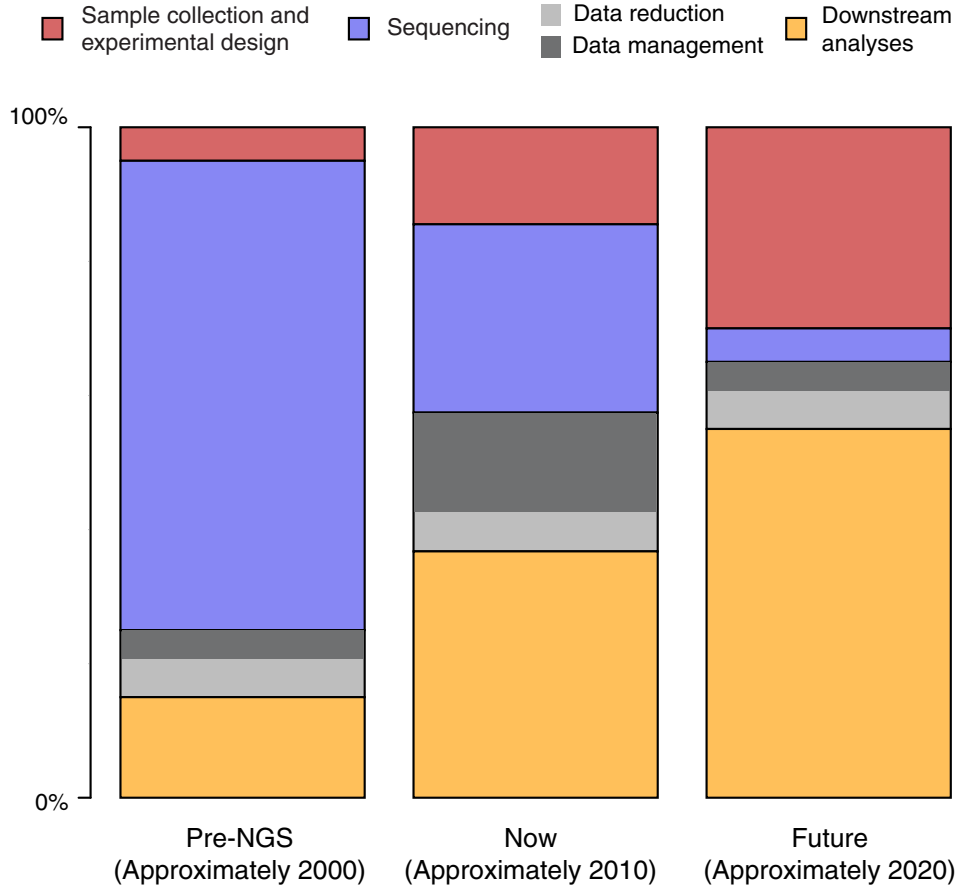
Reality

- Its much more difficult than we may first think

UCDAVIS Bioinformatics Core

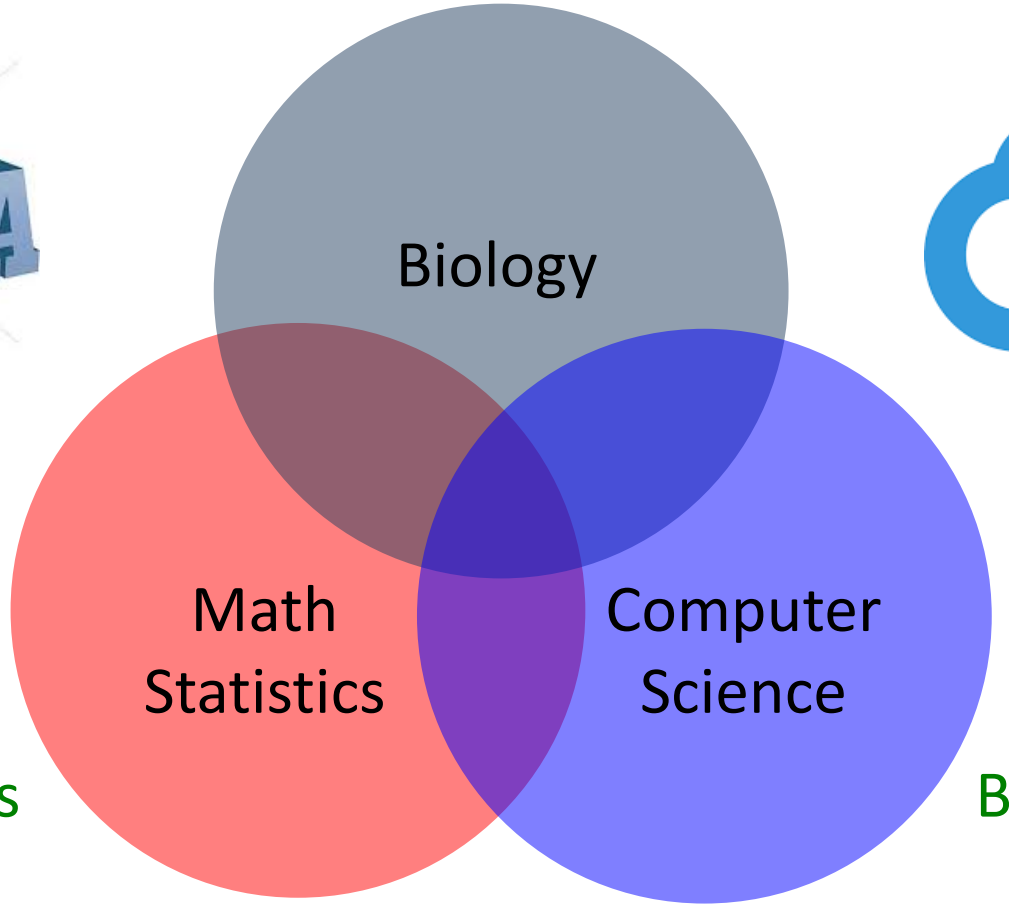
The real cost of sequencing





Sboner et al. Genome Biology 2011 12:125 doi:10.1186/gb-2011-12-8-125

Bioinformatics is Data Science



'The data scientist role has been described as "part analyst, part artist."'
Anjul Bhambhri, vice president of big data products at IBM

Data Science

Data science is the process of formulating a quantitative question that can be answered with data, collecting and cleaning the data, analyzing the data, and communicating the answer to the question to a relevant audience.

Five Fundamental Concepts of Data Science
statisticsviews.com November 11, 2013 by Kirk Borne

7 Stages to Data Science

1. Define the question of interest

2. Get the data
3. Clean the data
4. Explore the data

5. Fit statistical models

6. Communicate the results
7. Make your analysis reproducible

1. Define the question of interest

Begin with the end in mind!

what is the question
how are we to know we are successful
what are our expectations

dictates

the data that should be collected
the features being analyzed
which algorithms should be use

2. Get the data
3. Clean the data
4. Explore the data

Know your data!

know what the source was
technical processing in producing data (bias, artifacts, etc.)
“Data Profiling”

Data are never perfect but love your data anyway!

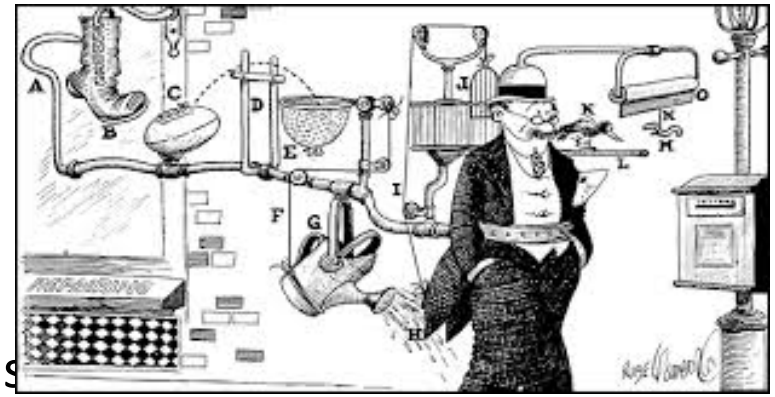
the collection of massive data sets often leads to unusual , surprising, unexpected and even outrageous.

5. Fit statistical models

Over fitting is a sin against data science!

Model's should not be over-complicated

- If the data scientist has done their job correctly the statistical models don't need to be incredibly complicated to identify important relationships
- In fact, if a complicated statistical model seems necessary, it often means that you don't have the right data to answer the question you really want to answer.



6. Communicate the results
7. Make your analysis reproducible

Remember that this is 'science'!

We are experimenting with data selections, processing, algorithms, ensembles of algorithms, measurements, models. At some point these ***must all be tested for validity and applicability*** to the problem you are trying to solve.

Data science done well looks easy – and that's a big problem for data scientists

simplystatistics.org
March 3, 2015 by Jeff Leek

Training: Data Science Bias

Data Science (data analysis, bioinformatics) is most often taught through an apprentice model

Different disciplines/regions develop their own subcultures, and decisions are based on cultural conventions rather than empirical evidence.

- Programming languages
- Statistical models (Bayes vs. Frequentist)
- Multiple testing correction
- Application choice, etc.

These (and others) decisions matter **a lot** in data analysis
"I saw it in a widely-cited paper in journal XX from my field"

The Data Science in Bioinformatics

Bioinformatics is not something you are taught, ***it's a way of life***

*"The best bioinformaticians I know are **problem solvers** – they start the day not knowing something, and they enjoy finding out (themselves) how to do it. It's a great skill to have, but for most, it's not even a skill – it's a passion, it's a way of life, it's a thrill. It's what these people would do at the weekend (if their families let them)."*

Mick Watson – Rosland Institute

UCDAVIS Bioinformatics Core

Training - Models

- Workshops
  - Often enrolled too late
- Collaborations
  - More experience persons
- Apprenticeships
  - Previous lab personnel to young personnel
- Formal Education
  - Most programs are graduate level
  - Few Undergraduate

Bioinformatics

- Know and Understand the experiment
  - "The Question of Interest"
- Build a set of assumptions/expectations
  - Mix of technical and biological
  - Spend your time testing your assumptions/expectations
  - Don't spend your time finding the "best" software
- Don't under-estimate the time Bioinformatics may take
- Be prepared to accept 'failed' experiments

Bottom Line

The Bottom Line:
Spend the time (and money) planning and producing **good quality, accurate and sufficient data** for your experiment.

Get to know to your data, develop and test expectations

Result, you'll **spend much less time** (and less money) extracting biological significance and results during analysis.

Substrate

Cloud Computing

Cluster Computing

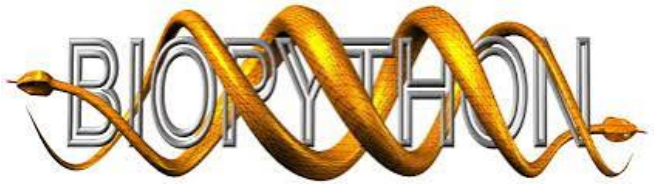
LINUX

BAS™

Laptop & Desktop

Environment

“Command Line” and “Programming Languages”



VS

Bioinformatics Software Suite

Prerequisites

- Access to a multi-core (24 cpu or greater), ‘high’ memory 64Gb or greater Linux server.
- Familiarity with the ’command line’ and at least one programming language.
- Basic knowledge of how to install software
- Basic knowledge of R (or equivalent) and statistical programming
- Basic knowledge of Statistics and model building