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Bioinformatics: A perspective

Dr. Matthew L. Settles

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

Outline

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

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 > 1600Gb/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

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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'

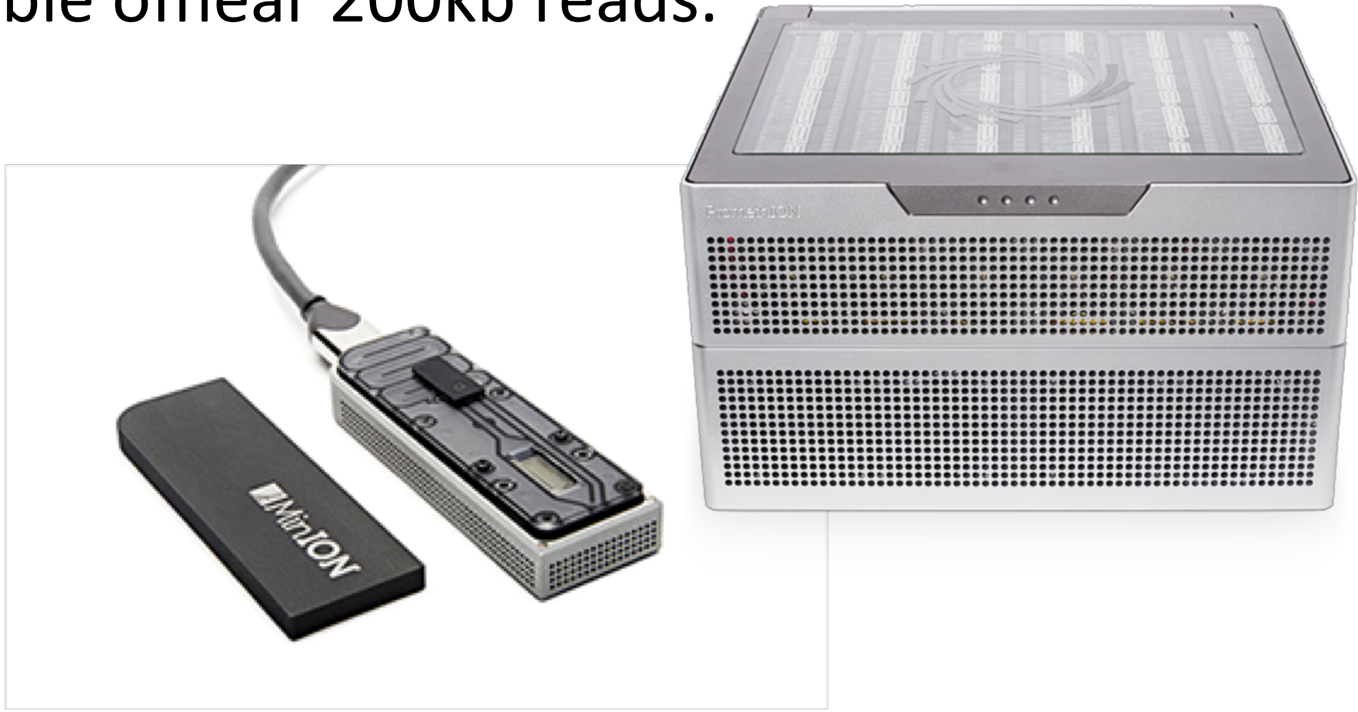
SmidgION: nanopore sensing for use with mobile devices

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]

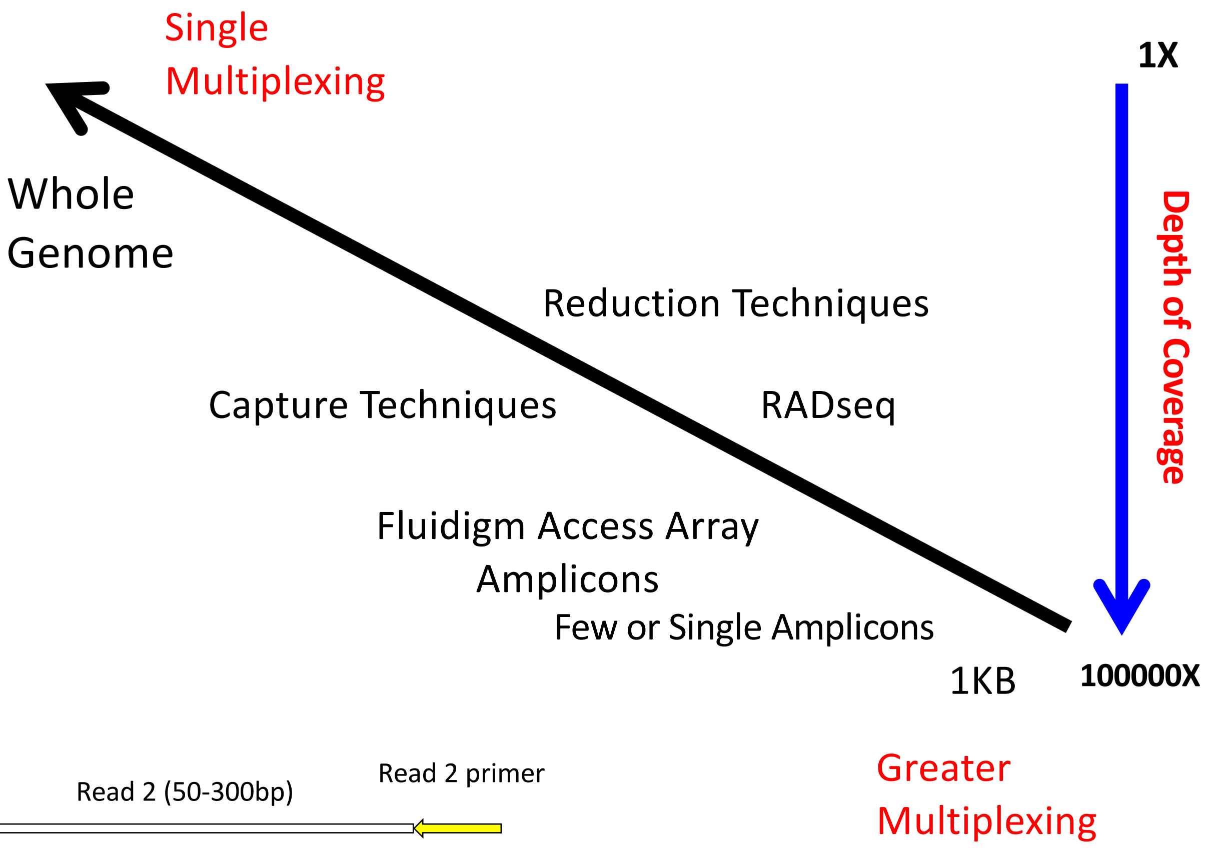


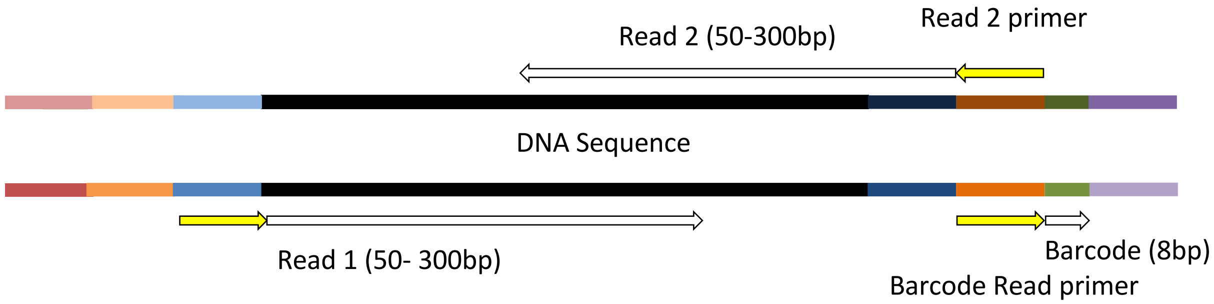
FYI: 4th generation sequencing is being described as In-situ sequencing

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 : MLA-seq

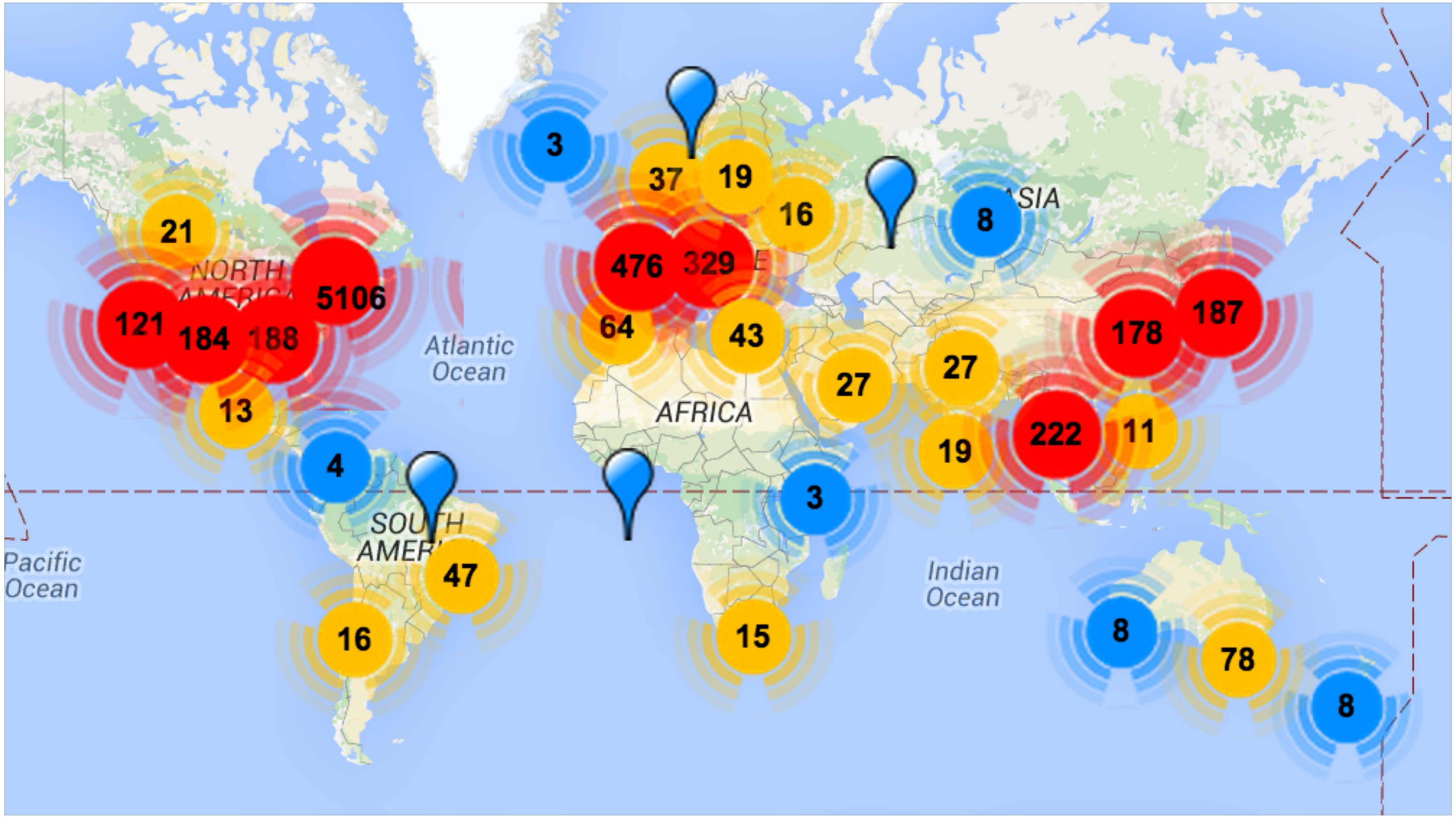
DNA-seq	DNase-seq	tagRNA-seq	EnD-seq
RNA-seq	ATAC-seq	PAT-seq	Pool-seq
Amplicons	MNase-seq	Structure-seq	G&T-seq
CHiP-seq	FAIRE-seq	MPE-seq	Tn-Seq
MeDiP-seq	Ribose-seq	STARR-seq	BrAD-seq
RAD-seq	smRNA-seq	Mod-seq	SLAF-seq
ddRAD-seq			

Methods. 2018 Jun 11. pii: S1046-2023(18)30064-1. doi: 10.1016/j.ymeth.2018.06.004. [Epub ahead of print]

fCLIP-seq for transcriptomic footprinting of dsRNA-binding proteins: lessons from DROSHA.

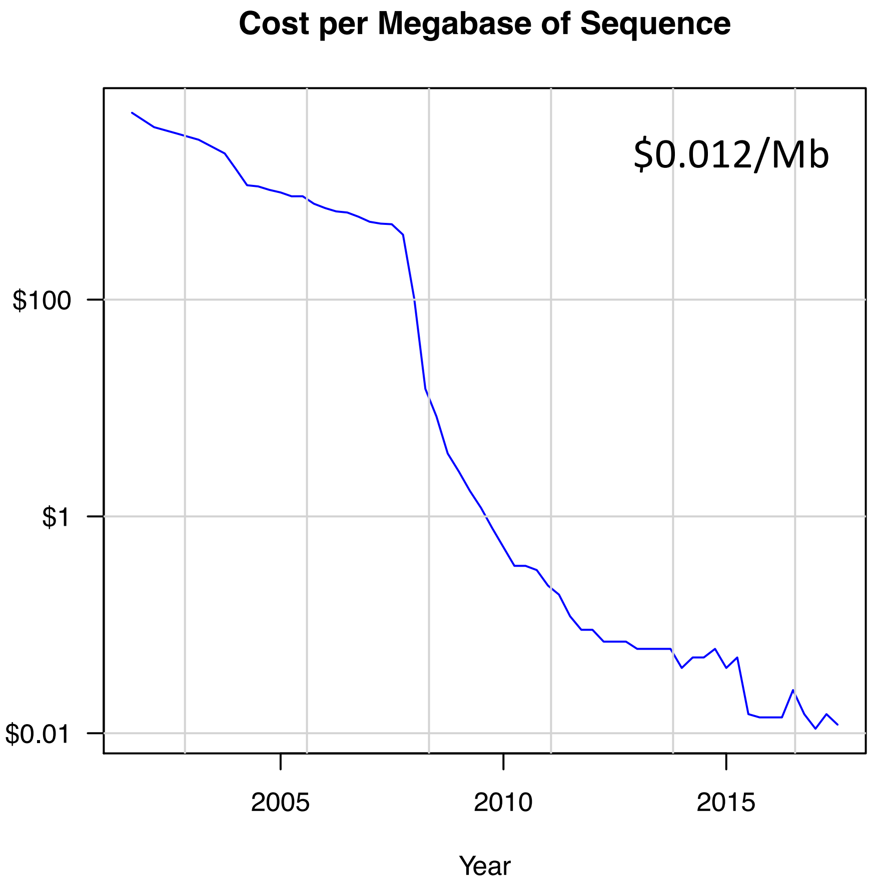
Kim B[1], Kim VN[2].

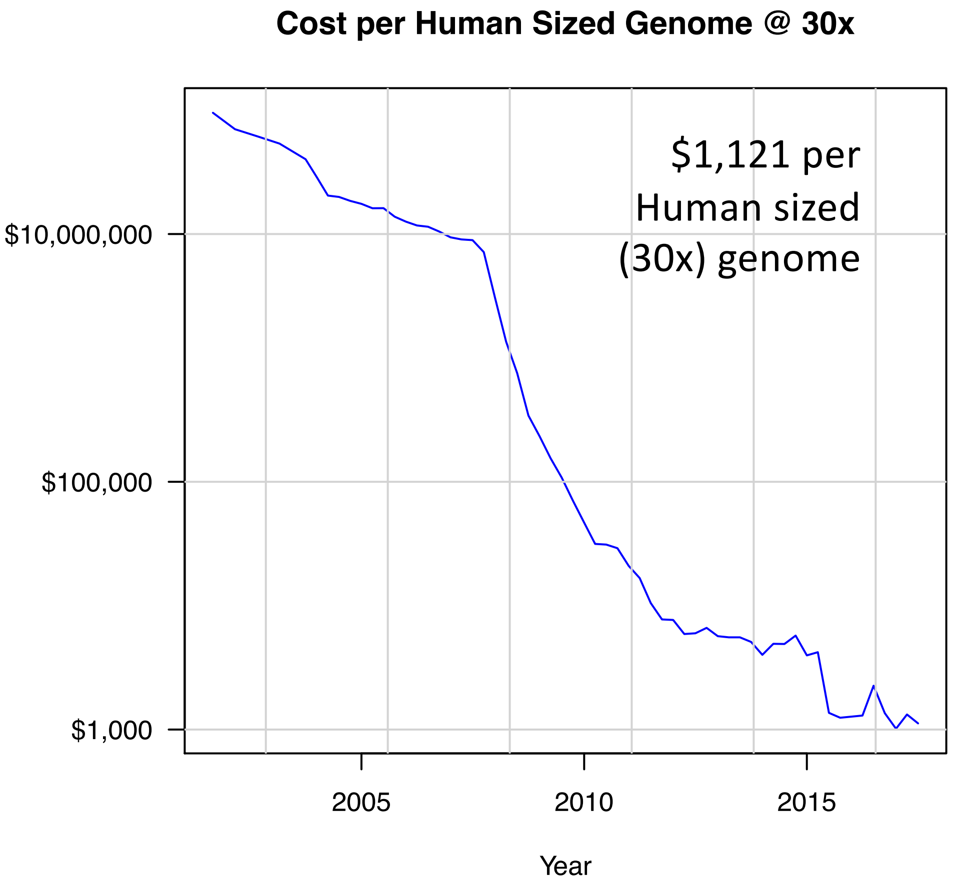
omicsmaps.com



Sequencing Costs

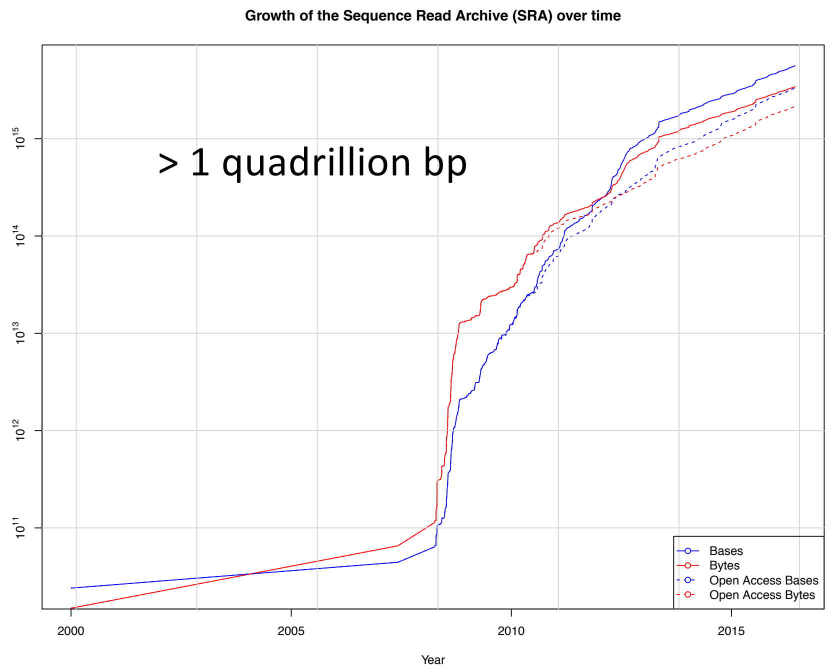
July 2017



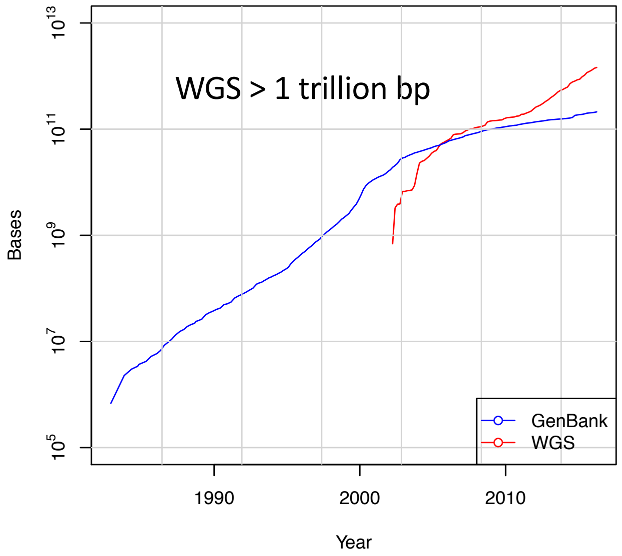


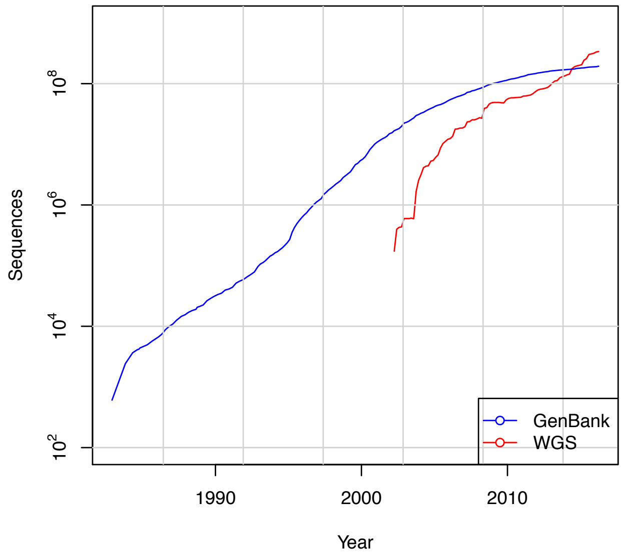
- Includes: labor, administration, management, utilities, reagents, consumables, instruments (amortized over 3 years), informatics related to sequence productions, submission, indirect costs.
- http://www.genome.gov/sequencingcosts/

Growth in Public Sequence Database



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





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

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The data deluge

- Plucking the biology from the Noise

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Reality

- Its much more difficult than we may first think

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!

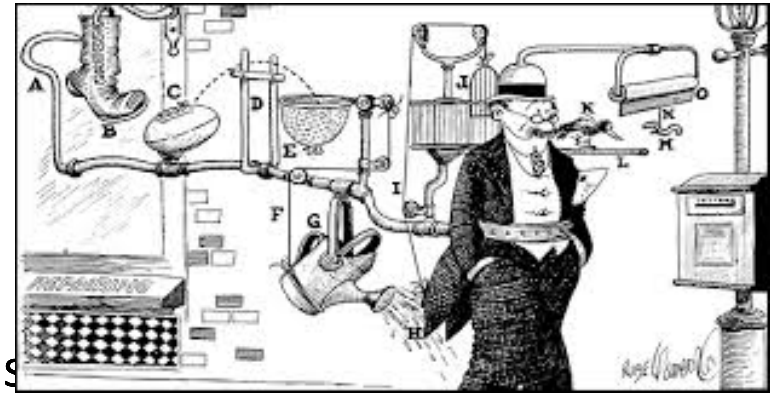
the collection of massive data sets often leads to unusual , surprising, unexpected and even outrageous.

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

Bad data science (bioinformatics) also looks easy

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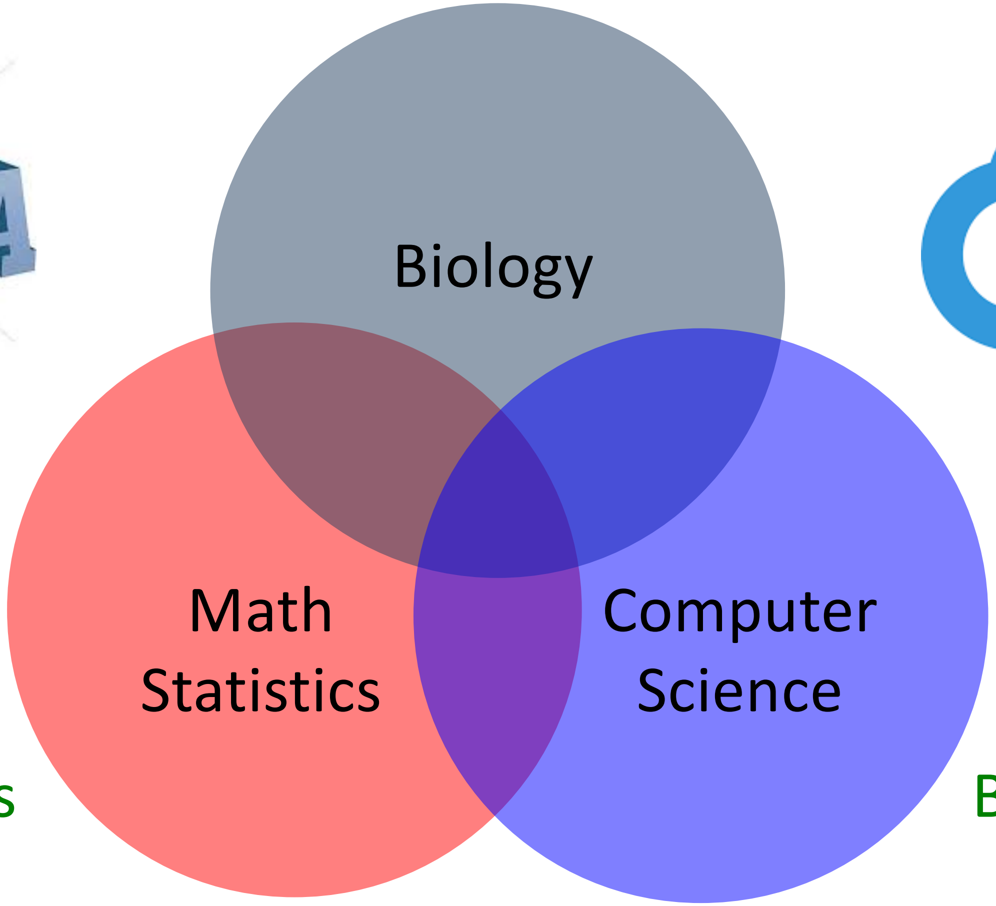
Bioinformatics is Data Science

Computational Biology



Biostatistics

Bioinformatics

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

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

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

DATA CARPENTRY

MAKING DATA SCIENCE MORE EFFICIENT

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"

Substrate

Cloud Computing

Cluster Computing

LINUX

BAS™

Laptop & Desktop

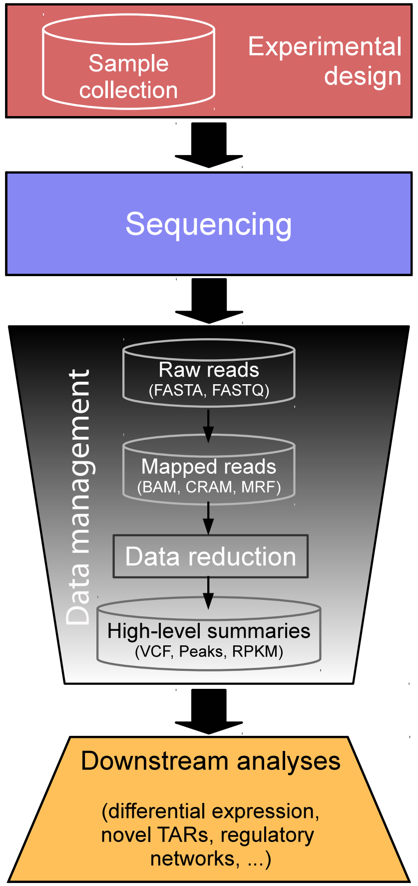
Environment

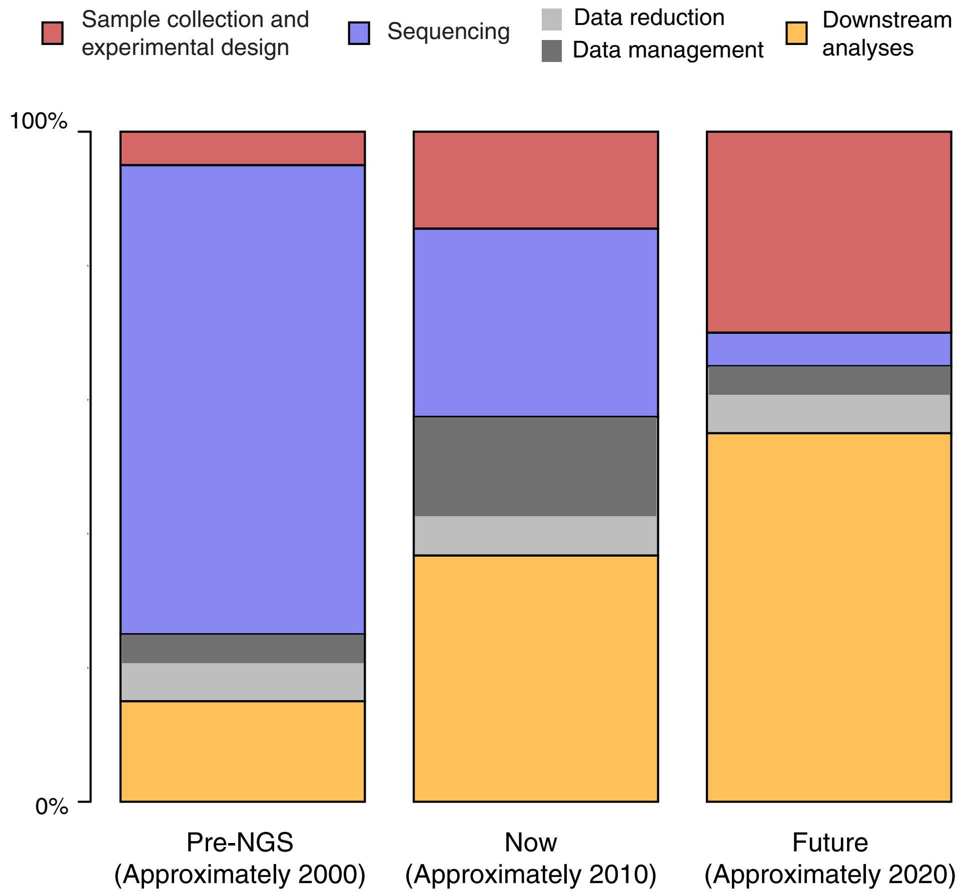
“Command Line” and “Programming Languages”

VS

Bioinformatics Software Suite

The real cost of sequencing





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

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

In 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.

The last mile

http://www.bikeblanket.com/blog/suisse