High Performance Computing Facility

Center for Health Informatics and Bioinformatics

Accelerating Scientific Discovery and Innovation in Biomedical Research at NYULMC through Advanced Computing

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Technical Director

NYU Langone Medical Center

Center for Health Informatics and Bioinformatics

NYU Langone MEDICAL CENTER

NYU Langone Medical Center

- One of nation's premier centers for excellence in clinical care, biomedical research and medical education.
- The Medical Center's tri-fold mission is to serve, discover and educate.
- NYULMC Consists of:
  - NYU School of Medicine (a division of New York University)
  - NYU Hospitals Center
- The NYU Hospitals Center is composed of 4 hospitals:
  - Tisch Hospital
  - Rusk Institute of Rehabilitation Medicine
  - NYU Hospital of Joined Diseases
  - Clinical Cancer Center
- Located in the center of Manhattan, NYC
- 17,000 employees
- www.nyulmc.org

NYU Langone
MEDICAL CENTER

Center for Health Informatics and Bioinformatics

Mission: To catalyze transformative changes in biomedicine through breakthrough computational methodological research, best practices services, state of the art infrastructure and cutting edge education.

- Informatics Research and Education
  - Computational Causal Discovery methods in biomedicine
  - Next Generation Sequencing informatics
  - Information Retrieval
  - Computational Proteomics
  - Microbiomics
  - Graduate Training Program in Biomedical Informatics
  - …..
- Service and Infrastructure
  - HPC: data storage and computing
  - Research Enterprise Data Warehouse
  - ….
- Operational and applied Collaborative Projects

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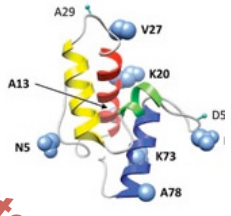
MiSeq

HiSeq 2000

GA IIx

Roche/454 FLX

RNAi



Proteomics

Leica SCN400F

Histopathology

Genome Technology Center

Data Storage

Microscopy

External Data Sources

S.O.L.V.E.

THE CANCER GENOME ATLAS

HMP

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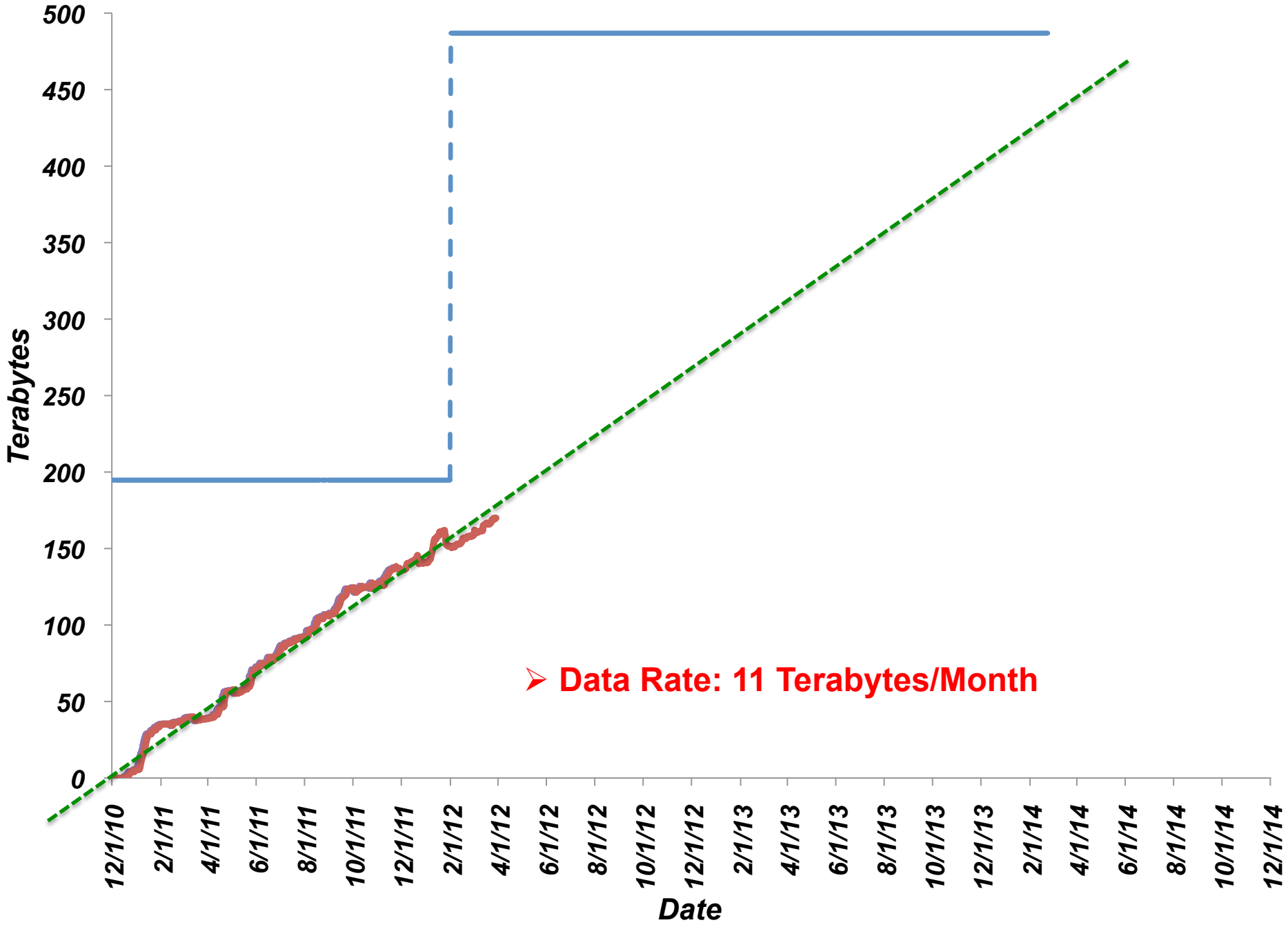
Simulation & Analysis

Asclepius HPC Linux Cluster


500
450
400
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200
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Terabytes
12/1/10
2/1/11
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4/1/14
6/1/14
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10/1/14
12/1/14
Date
➢ Data Rate: 11 Terabytes/Month

HPC Challenges in Next Generation Sequencing (NGS)

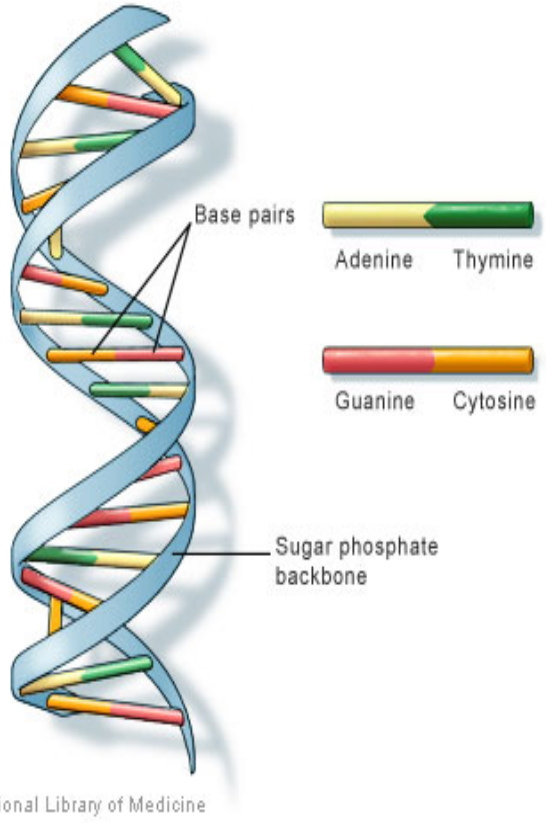
DNA Sequencing: The process of determining the exact order of the 3 billion nucleotides or bases, **A** (Adenine), **G** (Guanine), **C** (Cytosine), and **T** (Thymine) that make up a DNA molecule.

Next Generation Sequencing

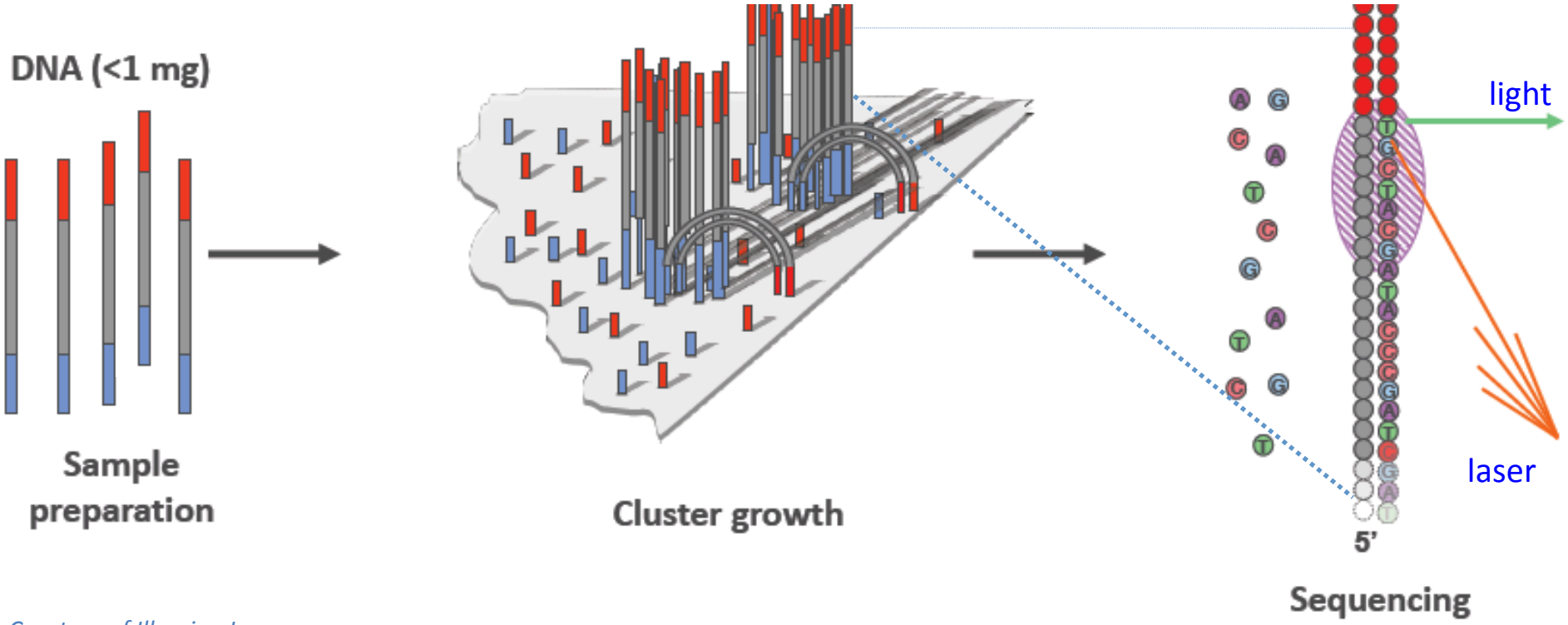
Massively Parallel
High Throughput
Low cost per base

February 2001:
Ten-year international effort produced 22.5 x 10^9 bases of DNA sequence, costing $3B

February 2011:
One NGS instrument produces 60 x 10^9 bases per day, costing several thousand dollars



Sequencing By Synthesis



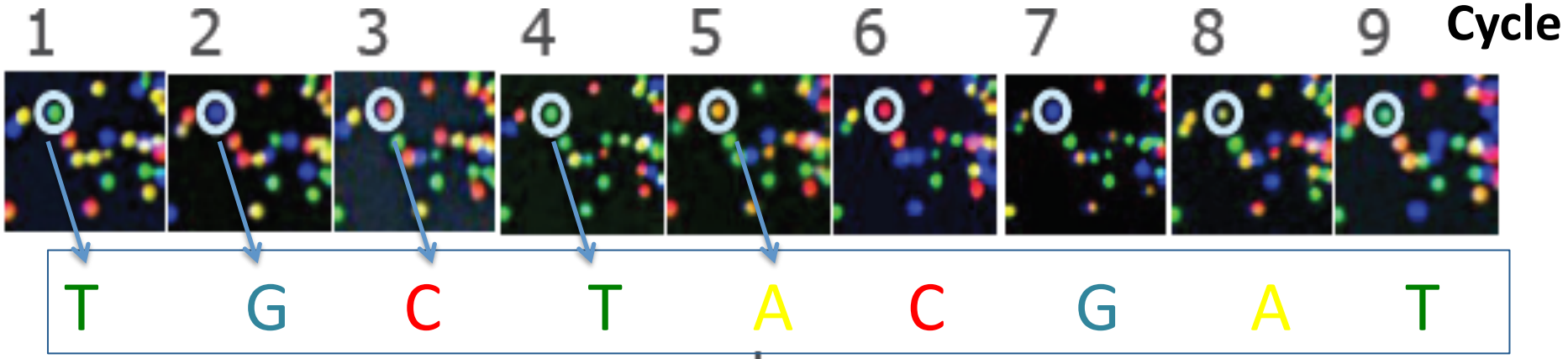
Courtesy of Illumina Inc.

High Throughput Sequencing ➔ High Data Throughput ➔ Dramatic increase in data storage and computing requirements

Dramatic Increase in Data Storage and Computing Requirements

Image Acquisition

Very Precise, High Resolution imaging: millions of images (.tiff) ➔ Terabytes of data



Courtesy of Illumina Inc.

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AGCAATGCCAATA
+SRR014849.1 EIXKN4201CFU84 length=93
3+&$#""""""""""""7F@71,'";C?,B;?6B;:EA1EA
1EA5'9B:?:#9EAOD@2EA5':>5?:%A;A8A;?9B;D@
/=<?7=9<2A8==
```

Gigabytes of Text Output

Millions of DNA reads (Billions of Nucleotides and associated quality scores)

NGS Data Output

Whole Human Genome Sequencing requires a ~30x coverage

- **Uneven Coverage** - Poisson distribution of small DNA reads
- **Sequencing Errors** - machine/chemistry (~ 1% => 30Mbp)
- **Systematic Biases** - some regions are harder to sequence
- **Alignment Problems** - gaps, repeats, etc.
- **Quality Factor** - additional data/metadata

Making Sense of the Data

Raw Data ➔ Genetic Variation ➔ Biological Function

- Where in the Genome did each of the reads originate from?
- Identify Genetic Variations: How is the individual different from the "idealized" individual represented by the reference or other genomes?

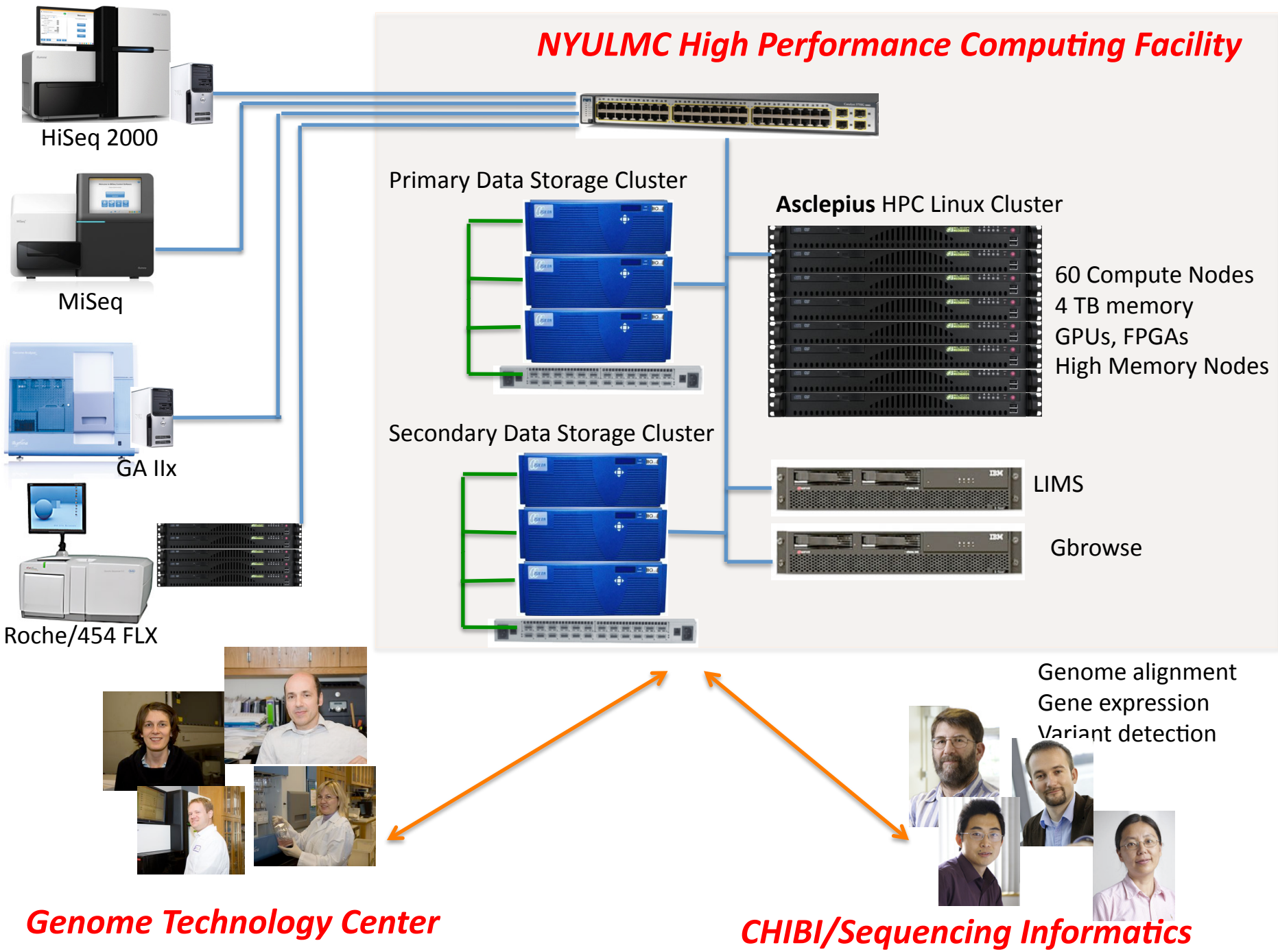
Sequence Alignment: Computationally and Data Intensive task

- A *Moving Target*:
  - Changes in sequencing technology
  - Shifting of biologists' interests.

- *Large volumes of sequencing data*:
  - Fast, Sophisticated algorithms (often trading accuracy for speed)
  - Scalable tools (multi-threaded/multi-process)
  - Efficient memory use (GPUs seem to be a good fit!)

- Plethora of unsupported, serial tools, developed from "scratch" by researchers.

- No commercial commitment


NYULMC High Performance Computing Facility
HiSeq 2000
MiSeq
GA IIx
Roche/454 FLX
Primary Data Storage Cluster
Secondary Data Storage Cluster
Asclepius HPC Linux Cluster
60 Compute Nodes
4 TB memory
GPUs, FPGAs
High Memory Nodes
LIMS
Gbrowse
Genome alignment
Gene expression
Variant detection
Genome Technology Center
CHIBI/Sequencing Informatics

Cloud Computing in Next-Gen Sequencing

(1) Infrastructure as a Service (IaaS) and Data Sharing

- Self-Service, easy to deploy, ability to scale, availability of resources (reference genomes, public databases, etc.)

(2) Cloud-enabled services made available over the internet

- Ready to use services deployed on the cloud with predefined (and configurable) pipelines, no need for local installation.
- Examples: Galaxy, UCSC Genome Browser, etc.

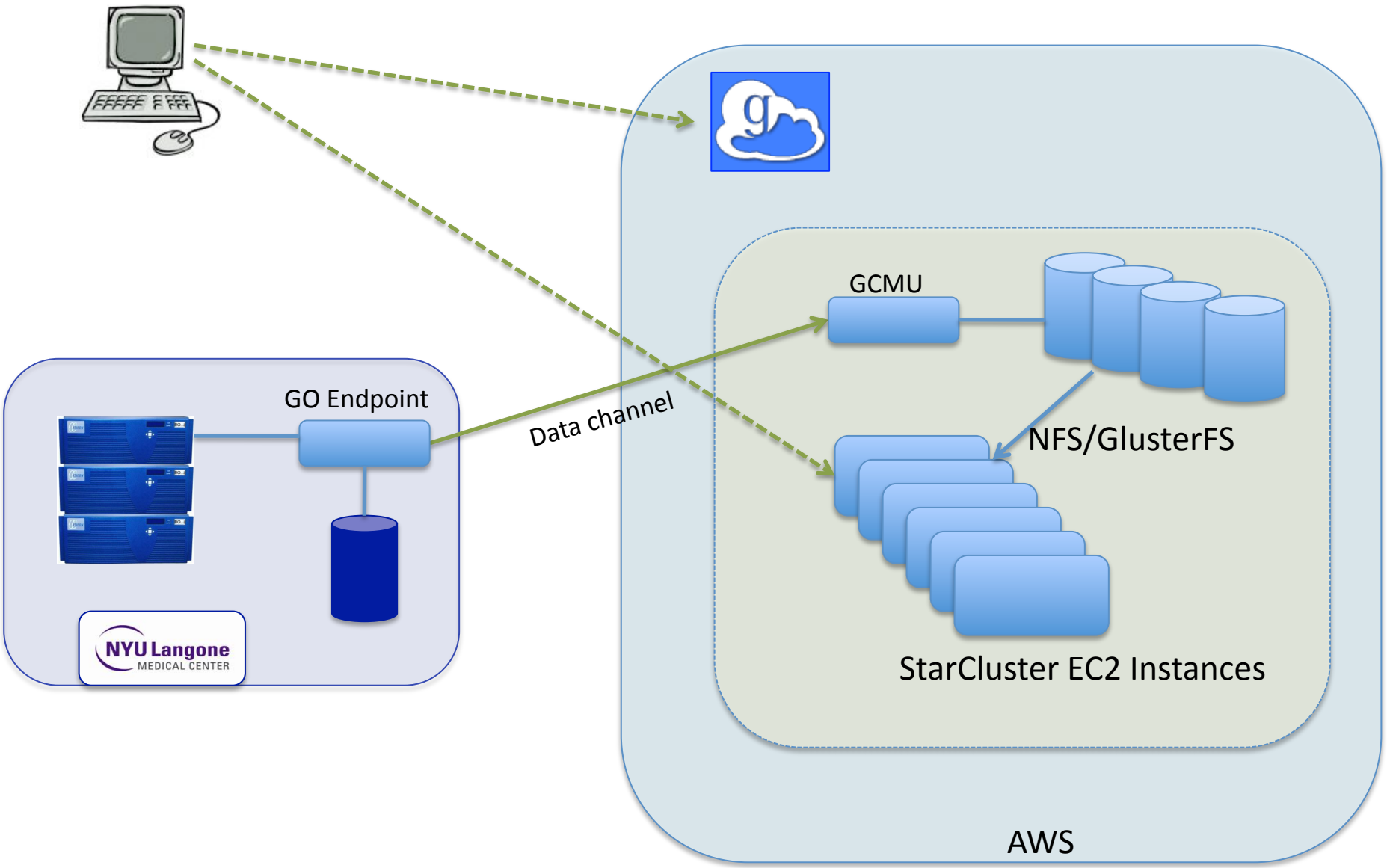
(3) NGS as a Service: Commercial pipelines use cloud resources to analyze customer NGS data. Examples: DNAnexus, Genome Quest, etc.

(4) Ready-to-use, scalable pipelines.

- Pre-configured pipelines that use virtualization and Map Reduce to expedite NGS data analysis
- Examples: CloudBurst, CloudBLAST, cloVR, crossbow, etc.

- Biggest Challenge:
  - Uploading large data sets to the cloud, in an efficient, cost-effective, fault-tolerant, easy to use way.
- Typical data set: A few hundred GigaBytes of FASTQ or BAM files. It should take ~ 1 hr over Gbps

- scp, sftp, http: known limitations in WAN
- Shipping disks: huge latencies, low automation potential, error prone
- GridFTP: Challenging GSI infrastructure


GCMU
GO Endpoint
Data channel
NFS/GlusterFS
StarCluster EC2 Instances
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AWS

- GO enabled data intensive analysis on the cloud.
  - Performance (a factor of 10 improvement over scp/sftp)
  - Minimum Firewall Requirements
  - Eliminates unnecessary duplication of large data sets
  - No need to VPN/on-site login to initiate transfers
  - Cost-effective

- Increasing Need for Data Sharing solutions:
  - New York Genome Center
  - NYC Workshop on HPC for Biomedical Research coming up in May