Source BioScience
LifeSciences

DNA technology: a quick guide to its history and evolution

Tom Burr, Source BioScience

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What does DNA technology mean?

PCR?	Genetically Modified Organisms?	Data storage?
Molecular biology?	DNA/RNA analysis?	DNA computing?
Cloning?	Gene therapy?	Synthetic biology?

What DNA technology means to Source BioScience

PCR?	Genetically Modified Organisms?	Data storage?
Molecular biology?	DNA/RNA analysis	DNA computing?
Cloning?	Gene therapy?	Synthetic biology?

Who cares about DNA analysis?

Physiology or Medicine 1959: Severo Ochoa and Arthur Kornberg *(DNA polymerase)*

Physiology or Medicine 1962: Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins *(DNA structure)*

Physiology or Medicine 1968: Robert W. Holley, Har Gobind Khorana and Marshall W. Nirenberg *(Genetic code)*

Chemistry 1980: Walter Gilbert and Frederick Sanger *(DNA sequencing)*

Chemistry 1993: Kary B. Mullis *(PCR)*

Who uses DNA analysis?

- Forensics
- Paternity
- Diagnostics/screening
- Biomarkers
- Drug targets
- Authentication/typing
- Safety/testing
- Combinatorial biology & rational design
- Evolutionary biology
- .....

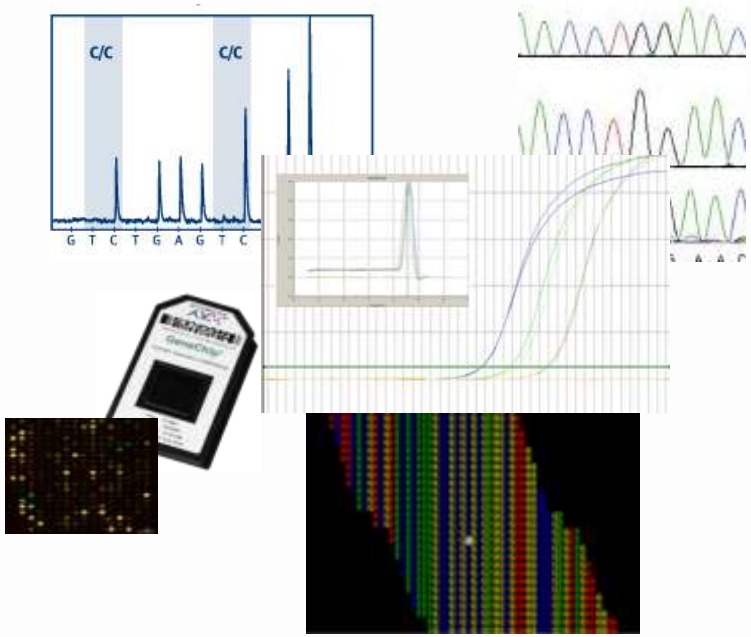
A variety of approaches

Capillary-/Pyro-sequencing

Real-time PCR

Microarrays

Next Generation Sequencing



From snapshot to bigger picture, from known to unknown.

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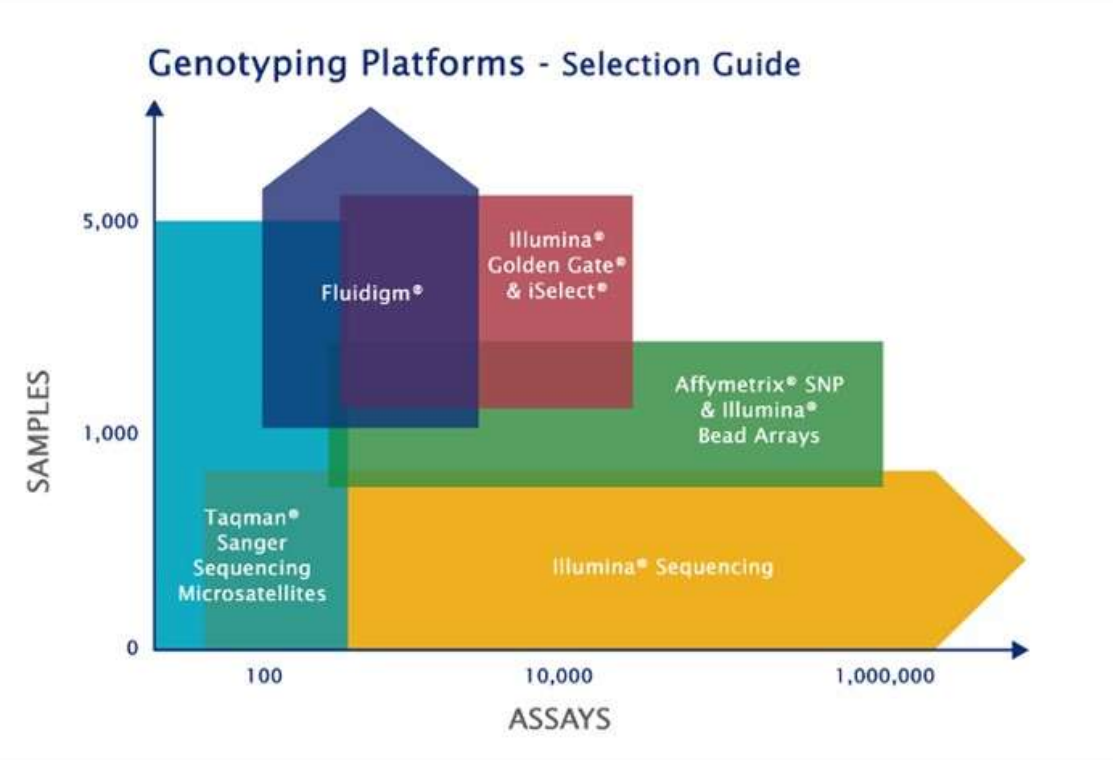
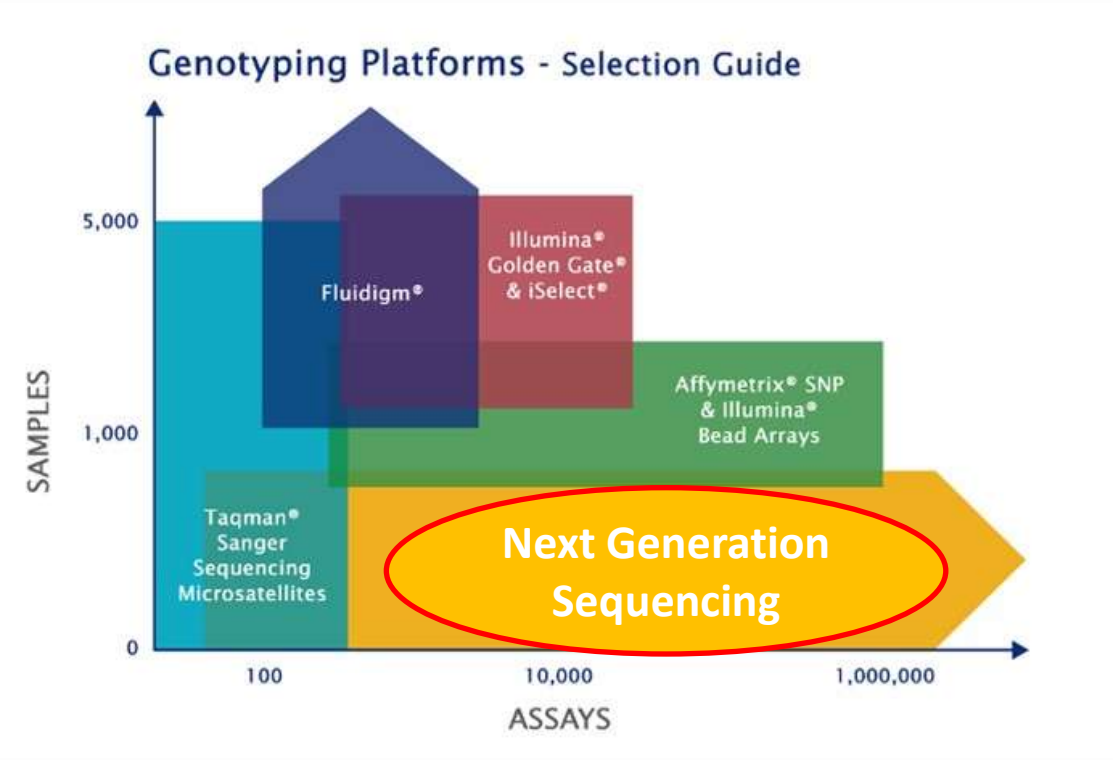
A *plethora* of platforms

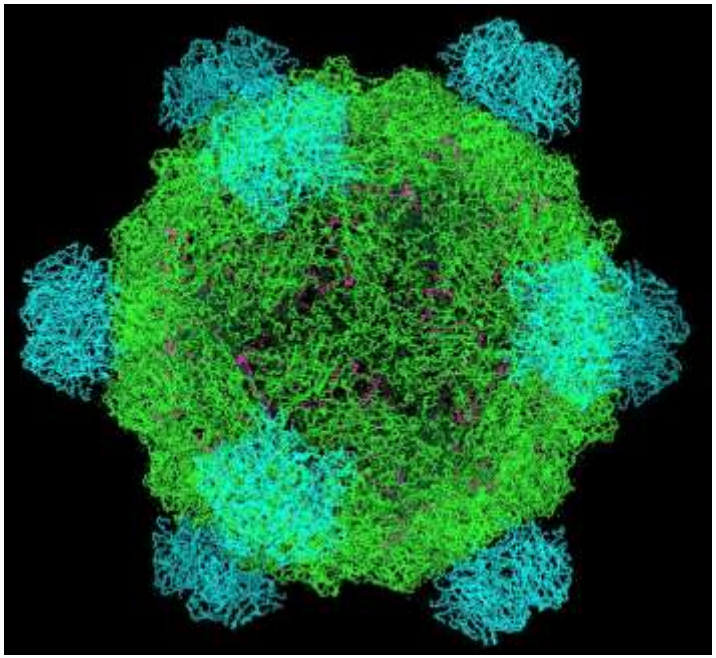


One size fits all?



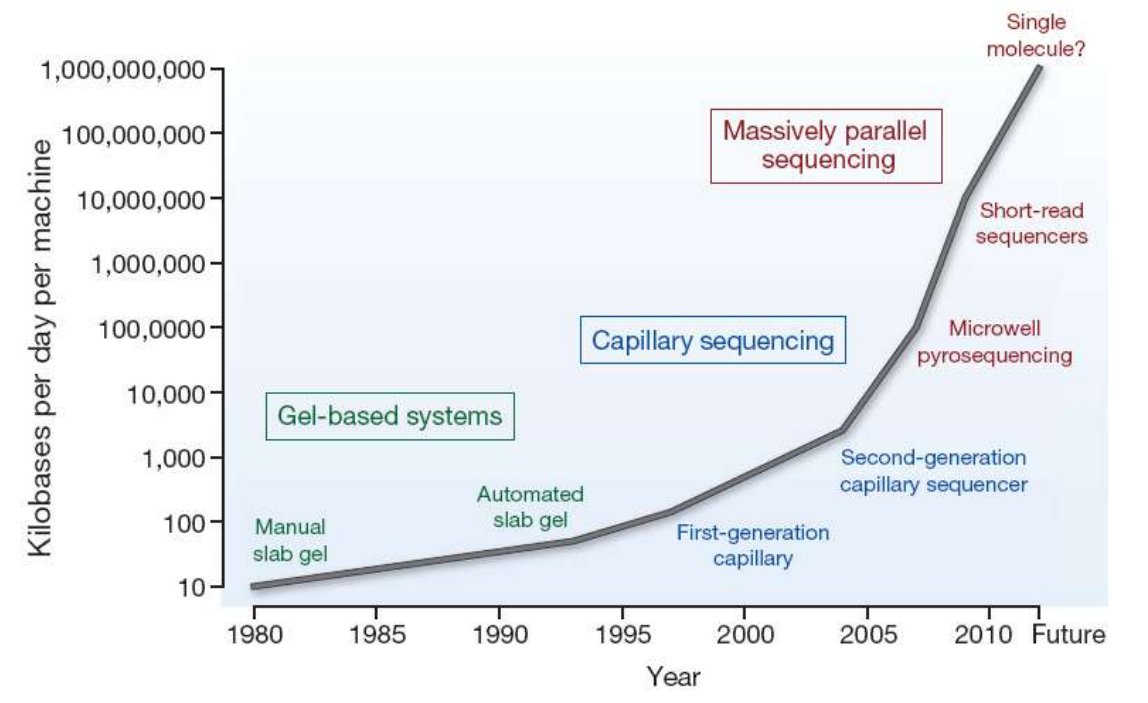
DNA sequencing – a historical perspective

First genome (1977), ϕ–X174: 5,386 bases.



Fdardel / CC-BY-SA-3.0

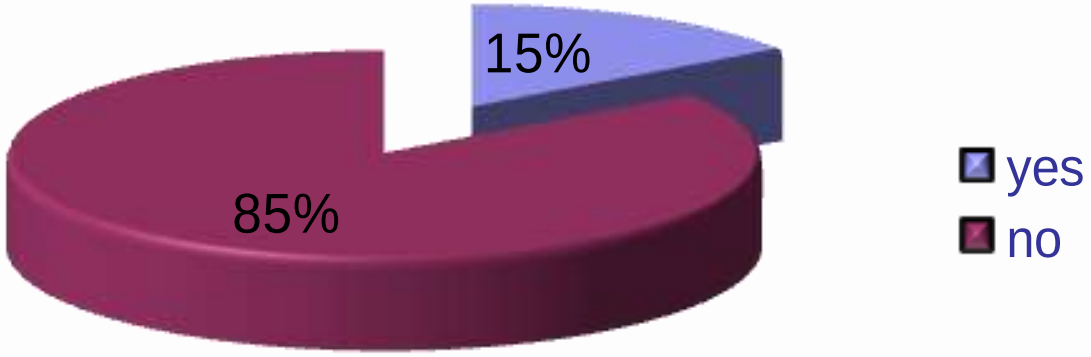
Progress in DNA sequencing



Stratton et al. Nature Vol 458 April 2009

The *'Next Generation'* in Sequencing

Q: *"Are you familiar with the new generation of emerging high throughput sequencing technologies eg, 454 Genome Sequencer 20, Agencourt SOLiD and Solexa 1G Genome Analyzer?"*



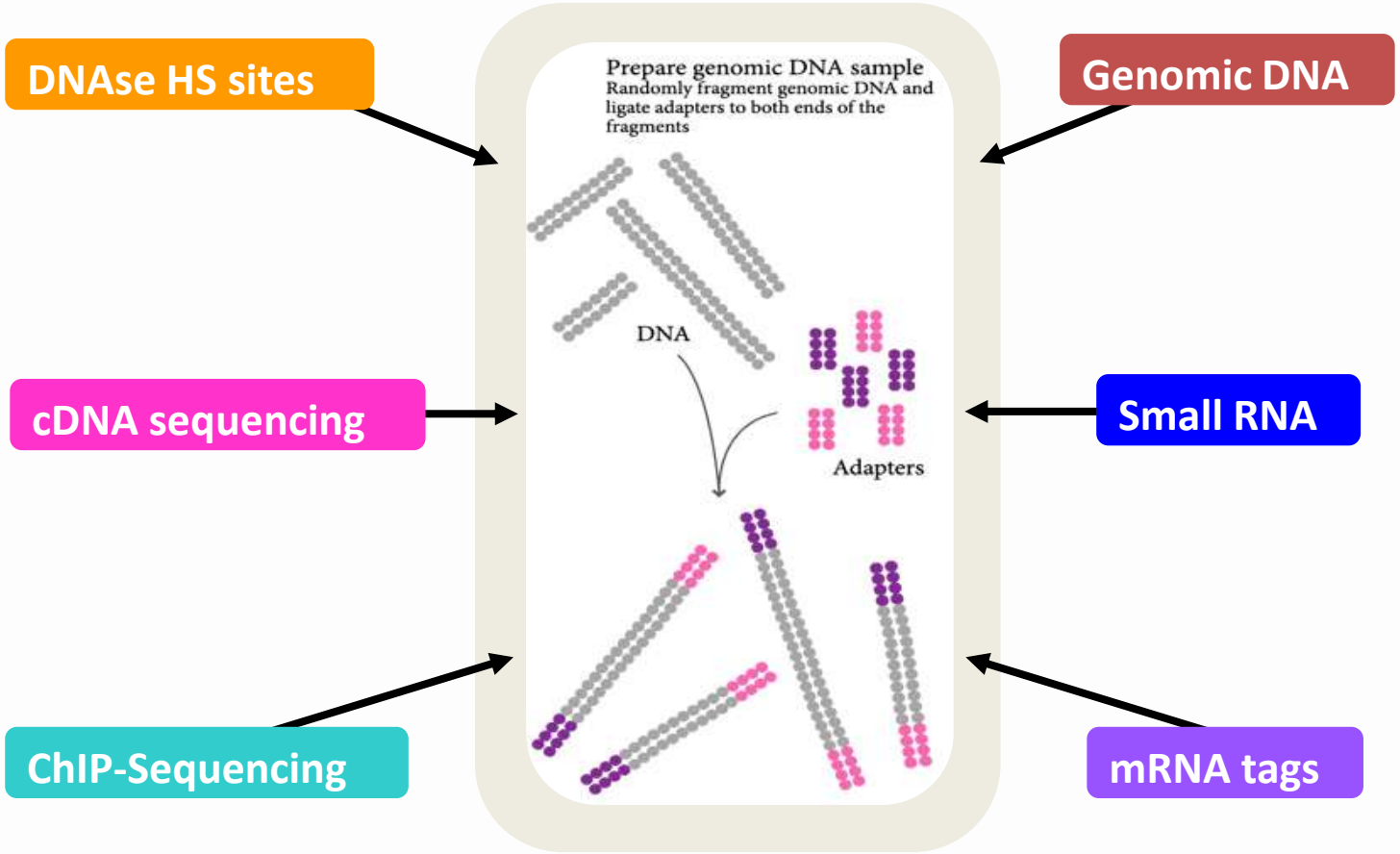
(April 2007)

Why sequence?

Sequencing of DNA, RNA and small RNA can reveal:

- SNPs
- somatic mutations
- copy number variations
- DNA methylation (methyl-seq/MeDIP-seq)
- genomic structural re-arrangements
- DNAse hypersensitivty
- Protein:DNA interactions (ChIP-seq)
- Protein:RNA interactions (RIP-seq)
- DNA:DNA interactions (3C-seq)
- mRNA structural variations (RNA-seq)
- mRNA expression levels
- small RNA (miRNA) discovery and expression levels
- RNA changes (RNA editing)

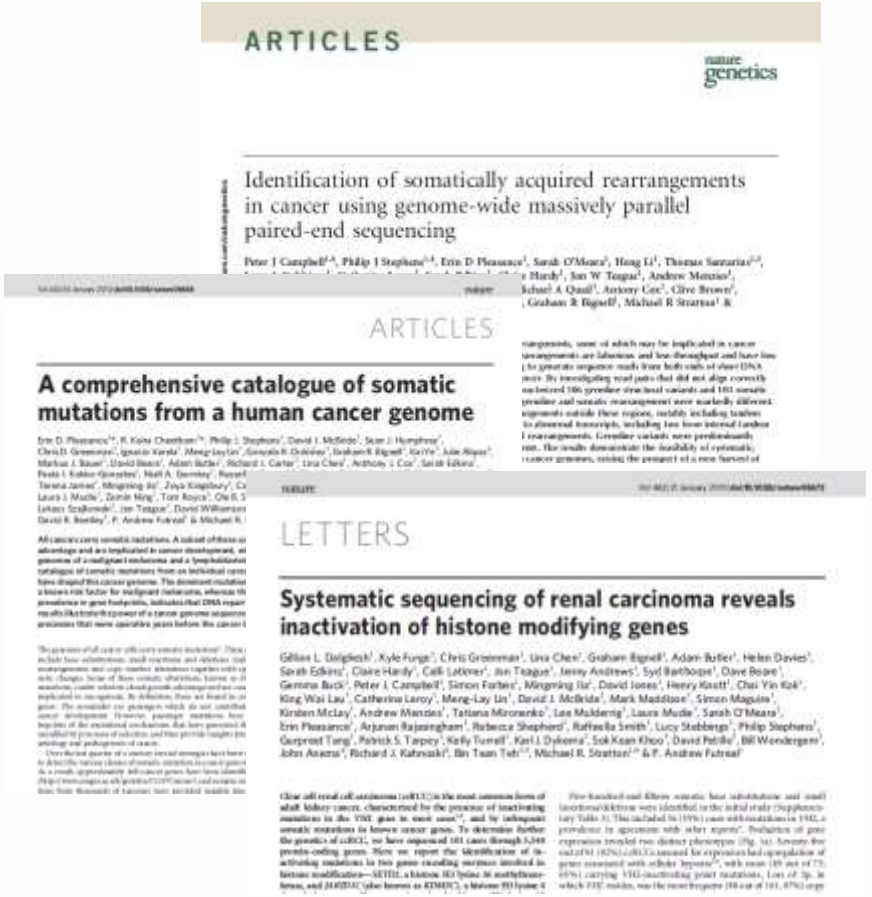
Sequencing applications



Whole genome sequencing

- Approaching point where whole genomes will be within reach.

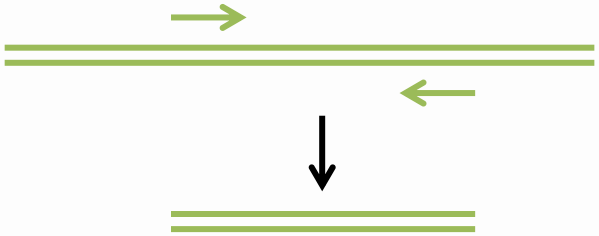
- Currently, sequencing costs still relatively high.



In the meantime: two principle methods for targeting regions of interest

1. Single-gene sequencing:

Gene-specific PCR (amplicon sequencing)



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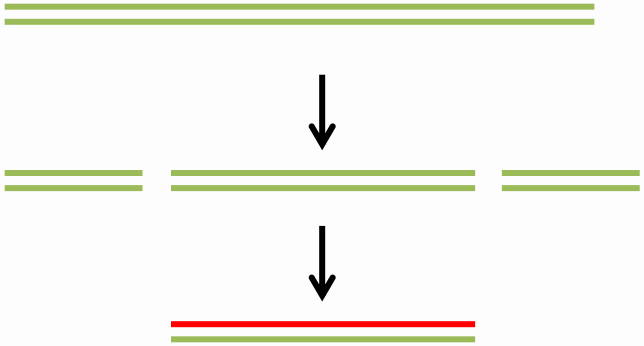
illumina ion torrent



2. 'Sequence capture' methods for larger regions:

NimbleGen illumina Agilent Technologies

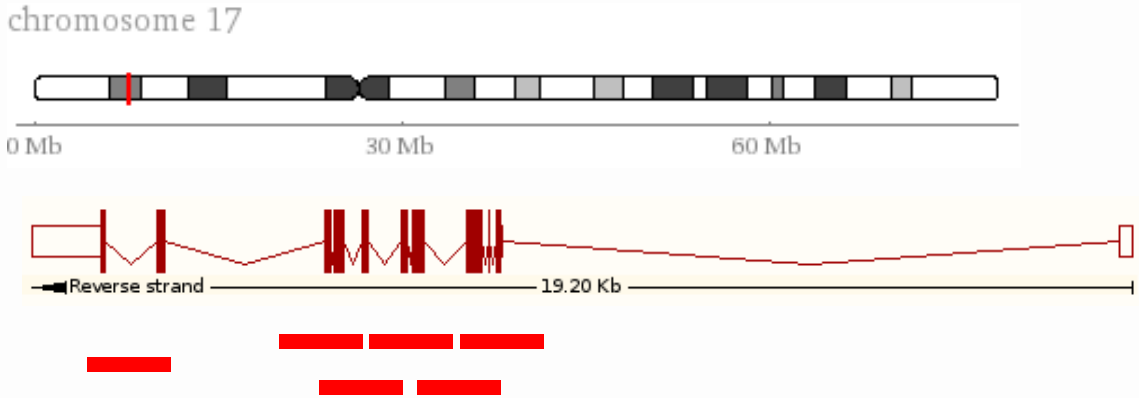
e.g. 'Exome' sequencing: ~50 x 10^6 bp including all known protein -coding regions.

Next Generation Sequencing @ SBS

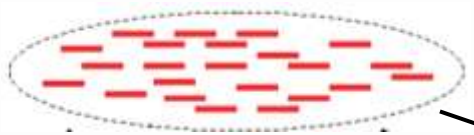
1. **Single-gene sequencing: ‘deep’ sequencing**

2. **‘Sequence capture’ methods for larger regions: *personalised medicine***

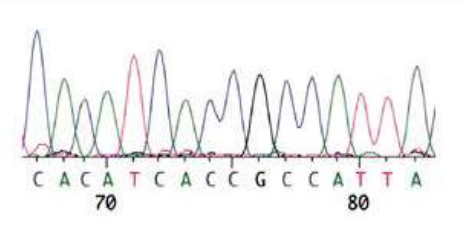
Deep sequencing



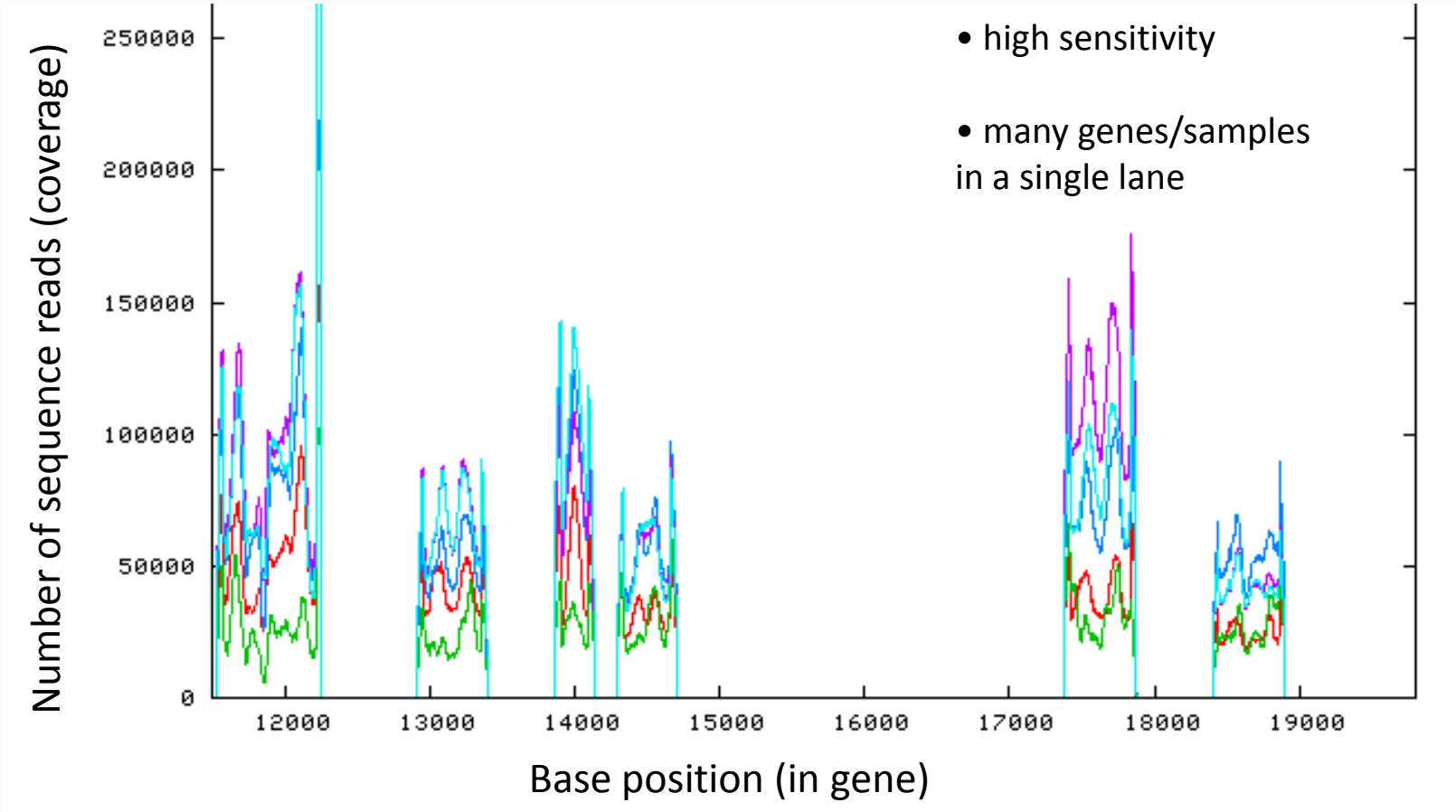
PCR amplicons



(from fresh, FFPE, CTCs)



Deep sequencing



The future of personalised medicine?

Personalised Medicine: “A medical model using molecular profiling technologies for tailoring the right therapeutic strategy for the right person at the right time.”

CRUK Stratified Medicines Programme

Aimed at demonstrating utiliity of molecular diagnostics in healthcare

- **Phase I:** (two year pilot programme)
  - 9000 samples, multiple cancers (breast, bowel, lung, protstate, ovary, melanoma), multiple tests
- **Phase II:**
  - to extend into general practice, ***to integrate innovative testing platfoms***

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The future of personalised medicine?

Technology Strategy Board
Driving Innovation

Stratified medicines programme: Tumour profiling and data capture to improve cancer care

COMPETITION FOR COLLABORATIVE R&D FUNDING
JANUARY 2011

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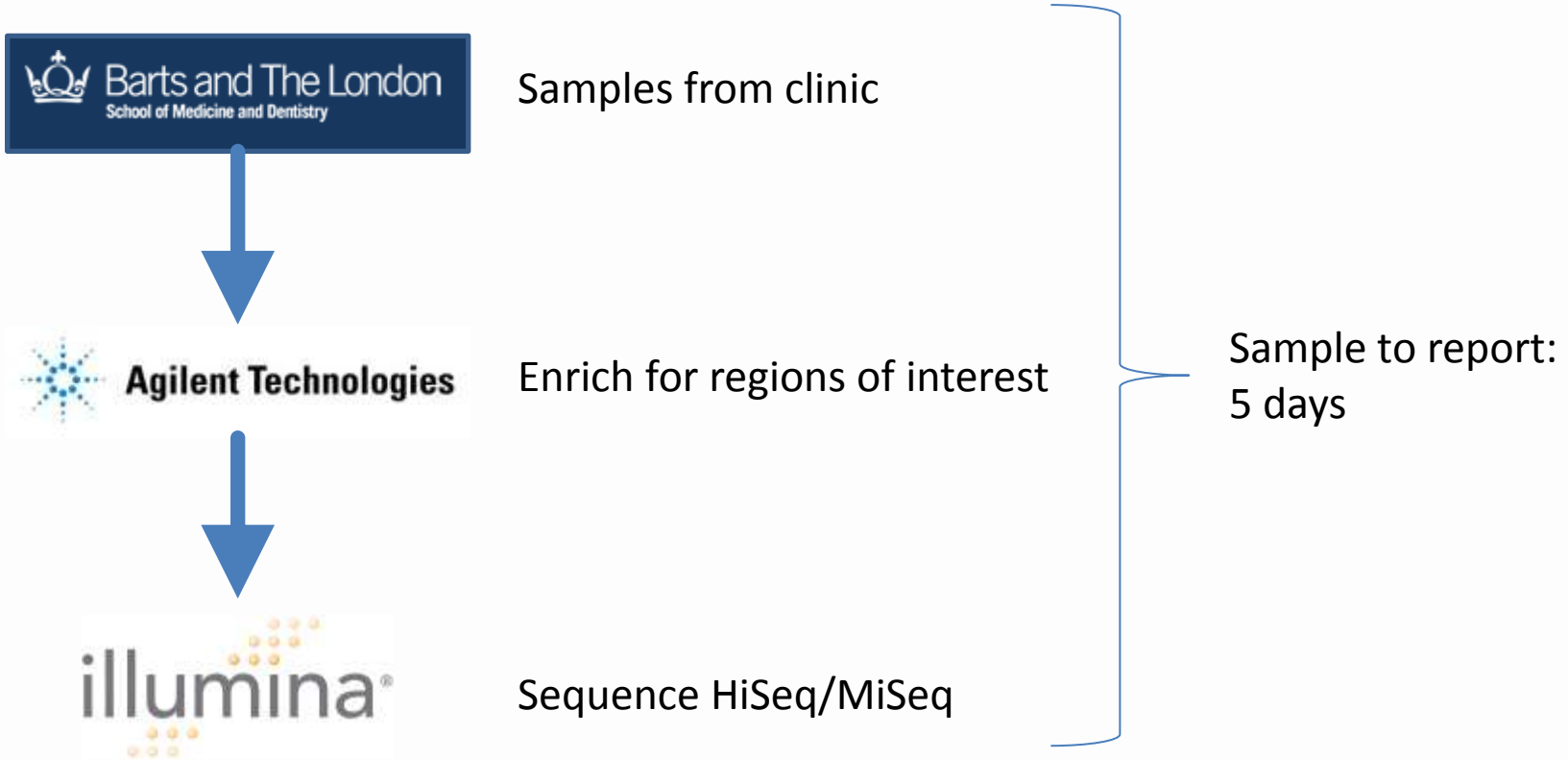
Barts and The London
School of Medicine and Dentistry

Agilent Technologies

illumina®

The future of personalised medicine?



The sequencing race … no sign of slowing down

medco 100 OVER 100
ARCHON GENOMICS X PRIZE

Complete genomics
HALCYON MOLECULAR
PACIFIC BIOSCIENCES
picoseq
Helicos BioSciences Corporation
ion torrent by life technologies
LIGHTSPEED GENOMICS
VISIGEN BIOTECHNOLOGIES, INC
Oxford NANOPORE Technologies
IBM
Intelligent Bio Systems

$10 million
100 ‘medical-grade’ genomes