Technical developments within NGS

05/02/2026

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Brussels University Alliance

VUB VRIJE UNIVERSITEIT BRUSSEL

UCL

ULB UNIVERSITÉ LIBRE DE BRUXELLES

Universitair Ziekenhuis Brussel

Cliniques universitaires SAINT-LUC UCL BRUXELLES

ULB CANCER RESEARCH CENTER

Hôpital Erasme | ULB

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What we offer

- Whole Genome sequencing
- Viral/bacterial whole genome sequencing
- Gene panel and exome sequencing
- SNP array (Illumina, Agilent, Affymetrix)
- Methylation sequencing
- RNA sequencing
- Spatial transcriptomics
- ATAC-sequencing
- ChIP-sequencing
- Single-cell RNA sequencing
- Long-read sequencing
- Optical genome mapping

35.000 analyses / year

Equipment

Illumina
NovaSeq 6000

Illumina
MiSeq

NanoPore
GridION x5

NanoPore
PromethION P2i

Bio-Rad
QX600 + AutoDG

Bionano
Stratys

MGI Tech
DNBSEQ-T7

2017 2018 2019 2020 2021 2022 2023 2024 2025

Revvity
Victor Nivo 3F

Formulatrix
Mantis

10x Genomics
Chromium controller

Diagenode
Bioruptor

10x Genomics
Chromium X

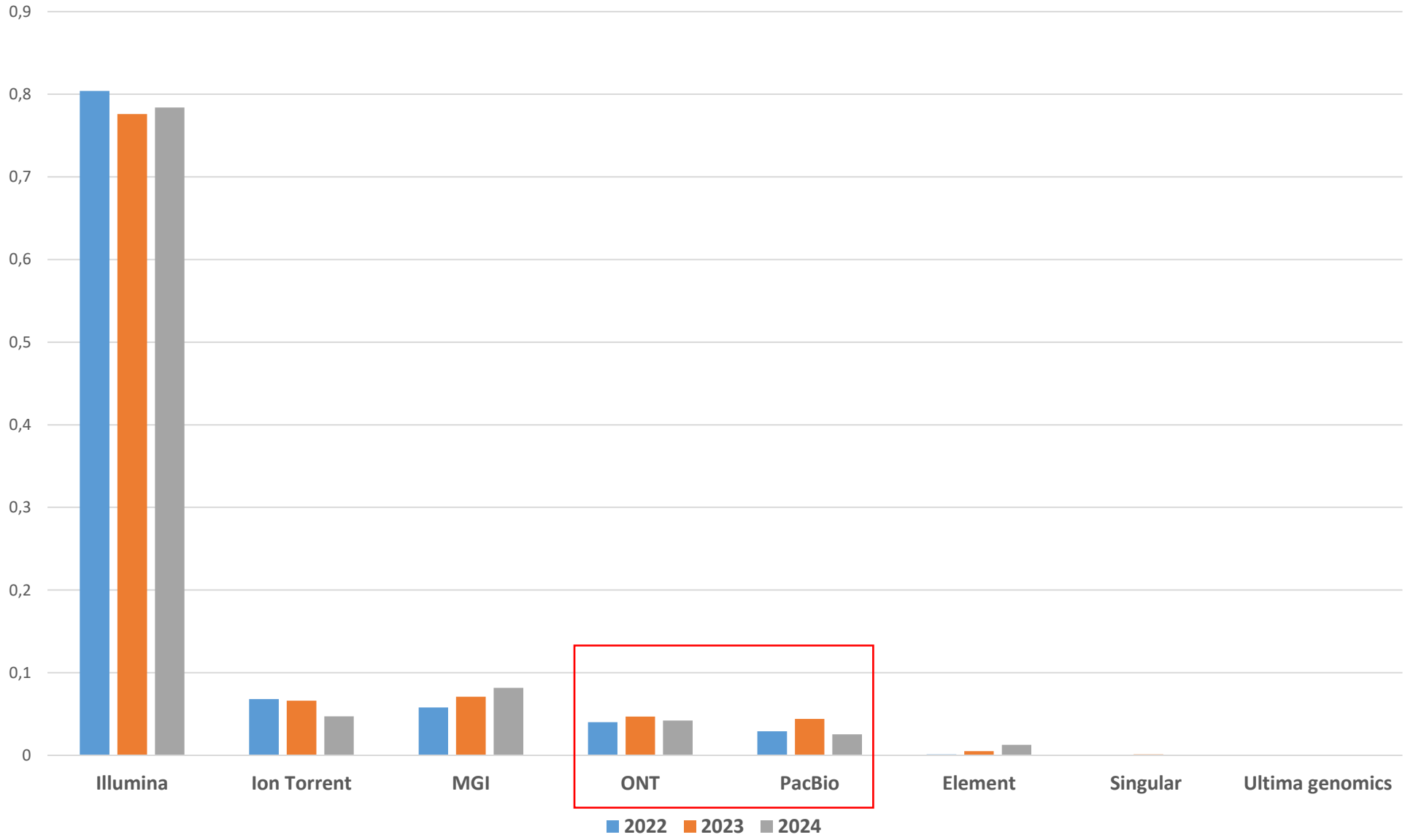
Hamilton
NGS STAR V

MGI Tech
DNBelab C – TaiM 4

Next Generation Sequencing

Current state

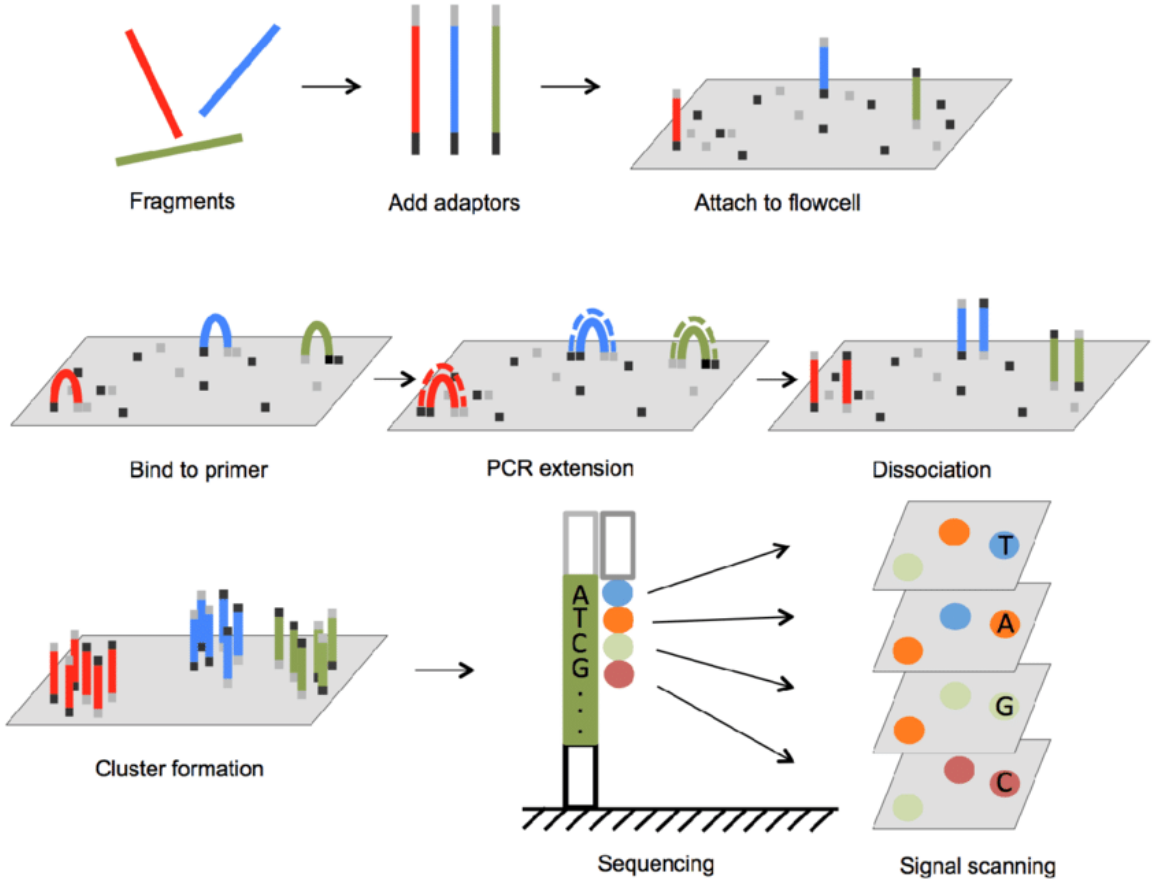
Evolution market share next generation sequencing



Illumina SBS sequencing

- Known technology

illumina®



Next Generation Sequencing

Short read sequencing improvement 1

QUALITY

MGI Tech

T20x2

Ultra-High Throughput Sequencers

T10x4RS

Large-Scale Population Genomics

T7+

Unmatched Power and Speed

T7

Turbocharged Sequencing

T1+

Built for Productivity

G400

Experience Seamless Sequencing

G99

Lightning-Fast, High-Precision

E25

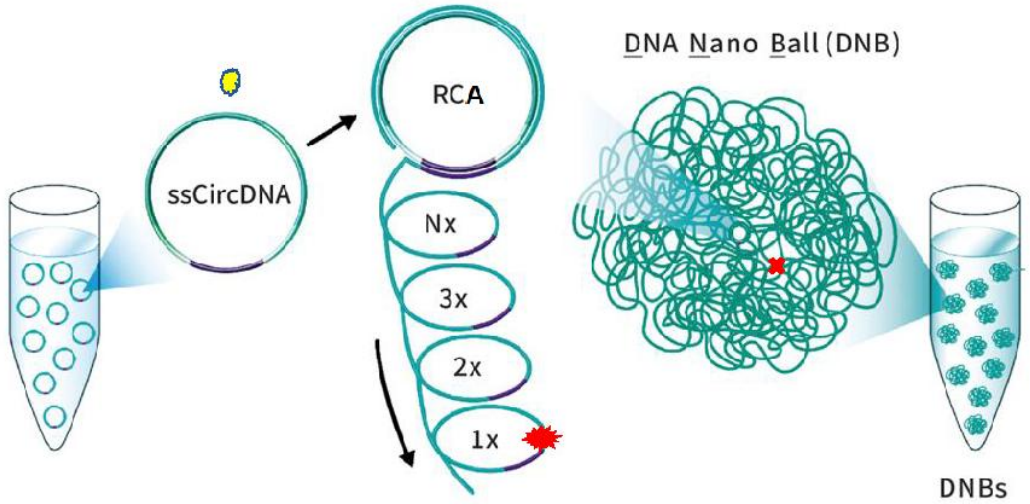
Sequencing on the Go

G50

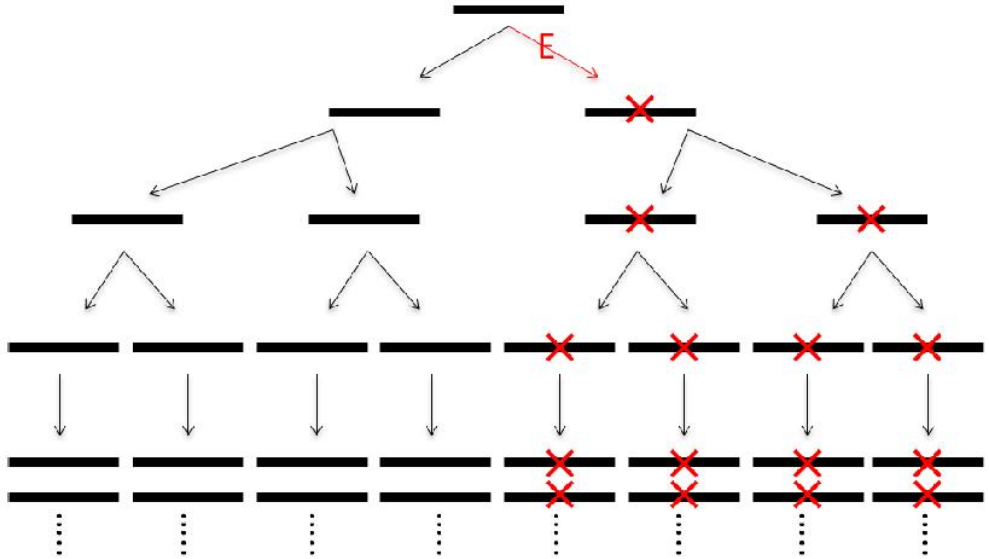
Small yet Mighty

MGI sequencing – error accumulation

RCA (Rolling Circle Amplification)

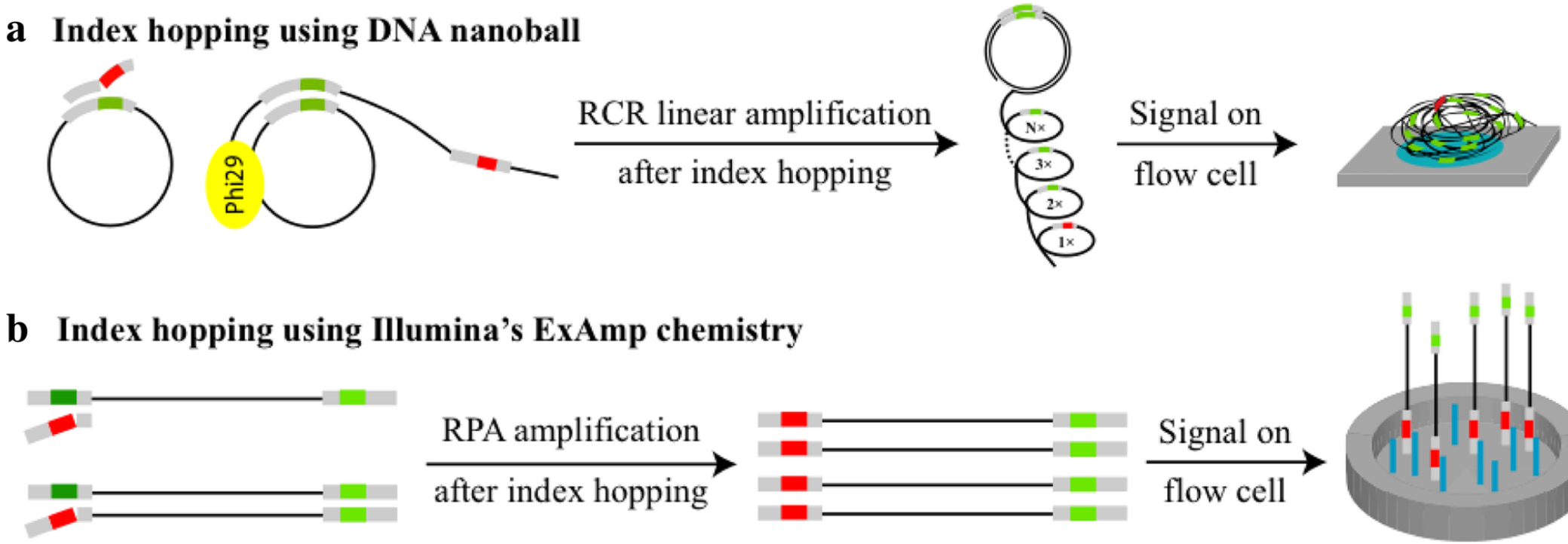


PCR (Polymerase Chain Reaction)



- No error accumulation & amplification
- Low amplification bias
- Phi29 enzyme: highest fidelity of any known enzyme (1 error in 10^6 – 10^7 bases) & processivity
- Controlled RCA, 100% of DNA are direct copies of the original ssCirDNA

MGI sequencing – index hopping

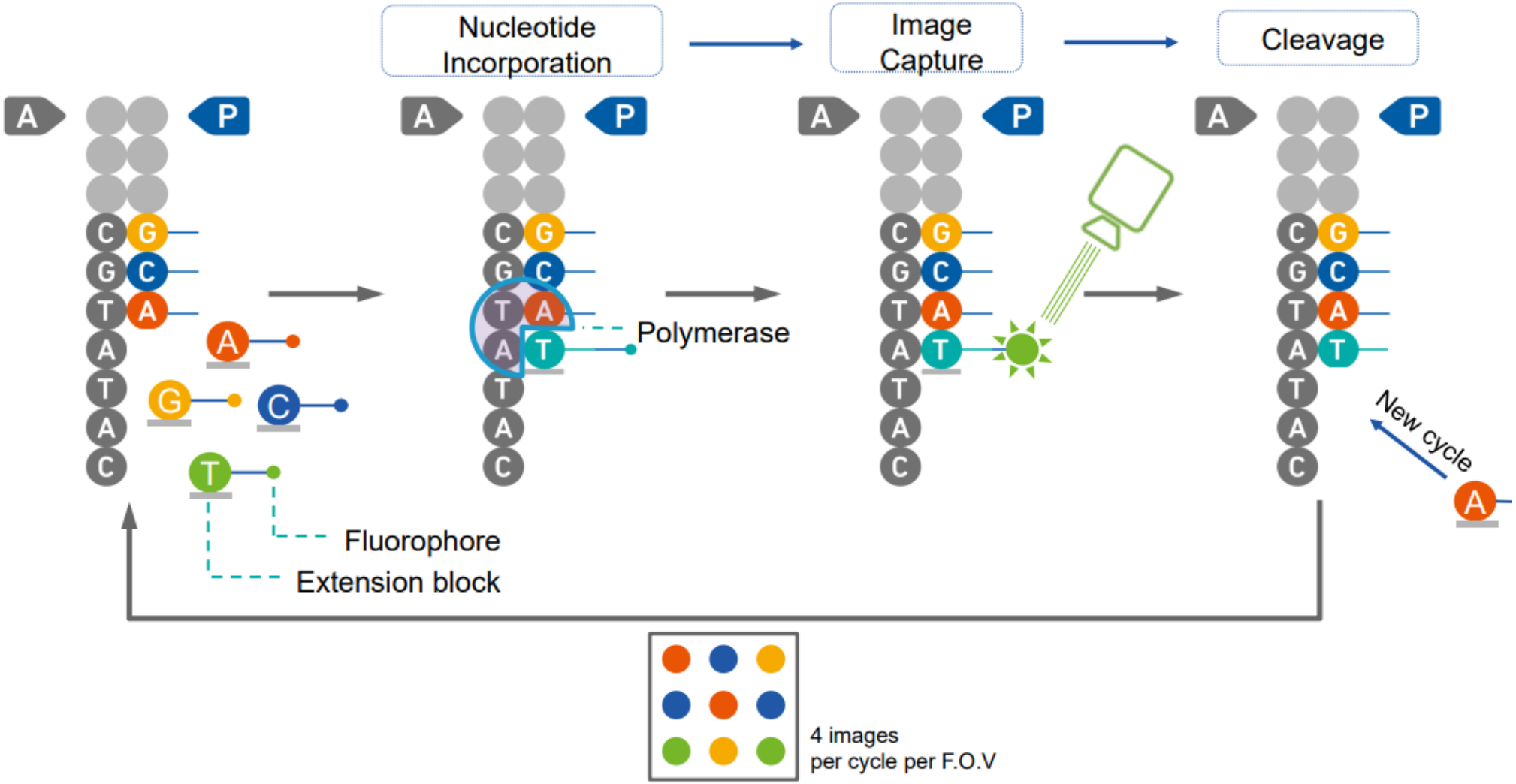


INCREASED ACCURACY
SNP Prec & Sensi>99%
Indel Prec & Sensi > 98%

DECREASED DUPLICATES
<3%

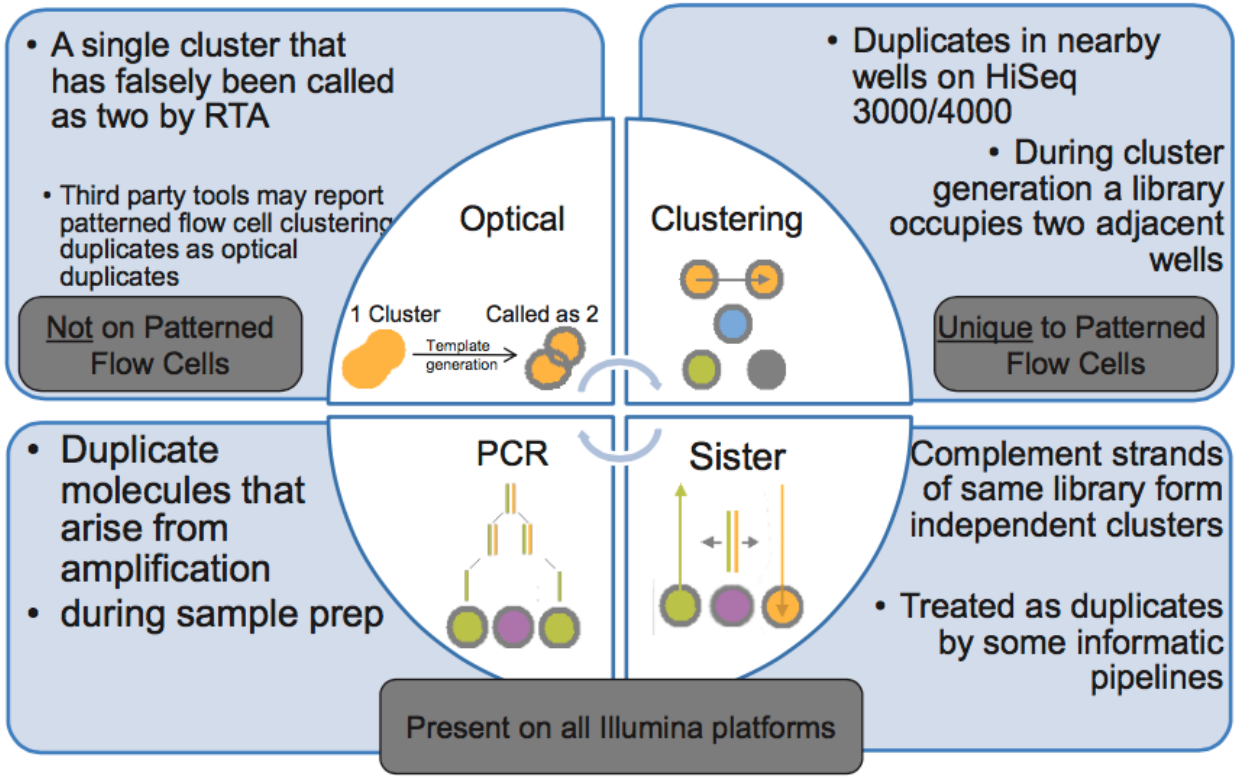
REDUCED INDEX HOPPING
0.0001%~0.0004%

MGI – cPAS sequencing

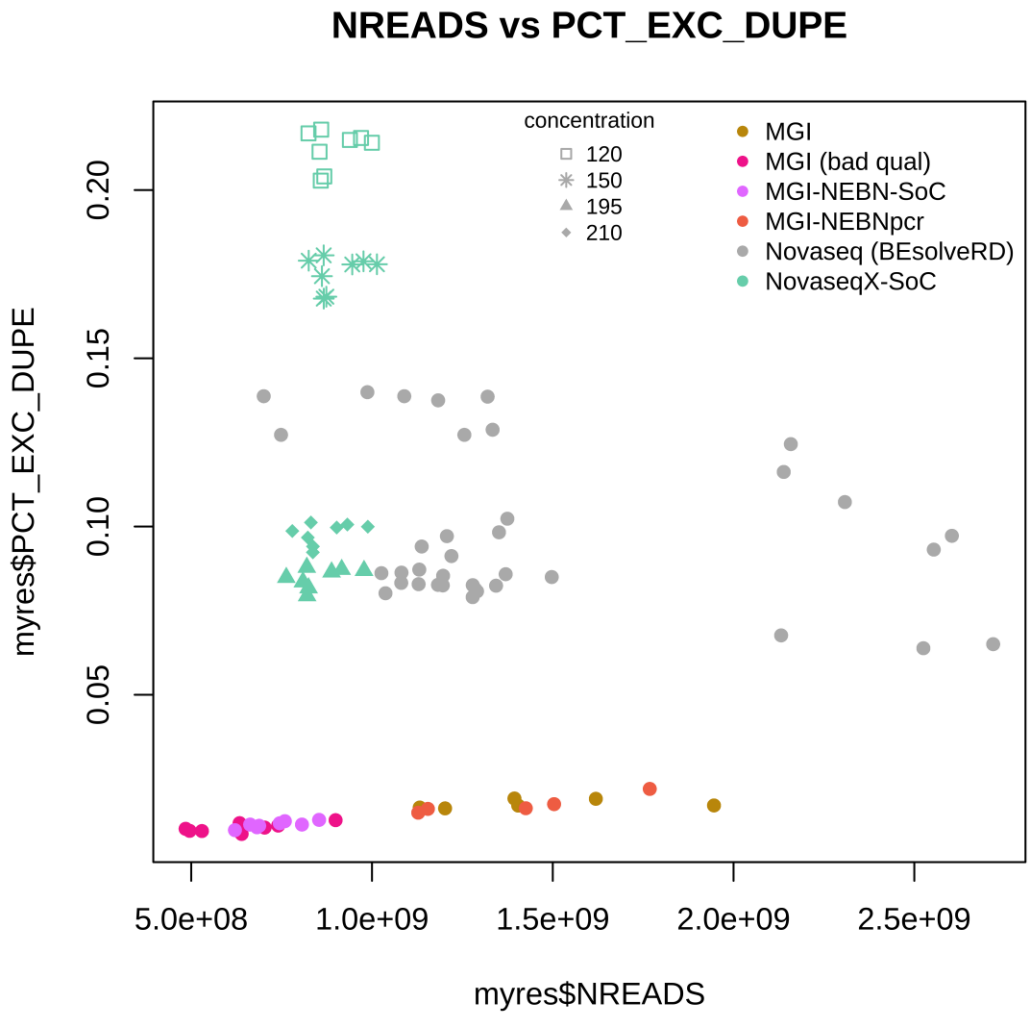


MGI sequencing - duplicates

- No cluster generation on flowcell
- Cluster generation on MGIDL-T7 loader (manual step)
- Significantly less duplicates



Alignment stats
Duplicates



Novaseq X:

- Duplication rate depends on the input concentration **-> lowest at 195**
- Titration of libraries is key but hard to quantify libraries with this accuracy
- “The NovaSeq X further increases cluster density compared to the NovaSeq 6000”

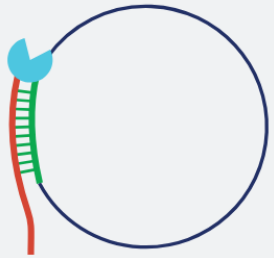
Element Biosciences

Element Biosciences - Cloudbreak

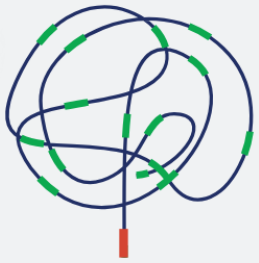
Error accumulation

Index hopping

< Optical duplicates



Hybridize DNA
Circular DNA template attaches to **surface primers** coating the flow cell via an **adapter**.



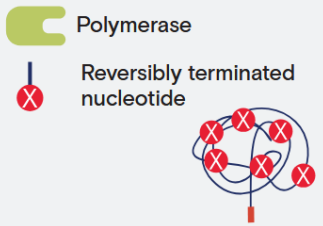
Generate Polonies
RCA copies the template DNA and rolls each strand into a tightly bound polony—no PCR, no copies of copies.

SBS combines base detection and strand extension, consuming micromolar reagent concentrations to complete the reaction while signal persists. In contrast, ABC separates the steps and leverages multivalent binding stability to require only nanomolar avidite concentrations. Multiple binding events for each avidite ensure persistent signal for base detection.

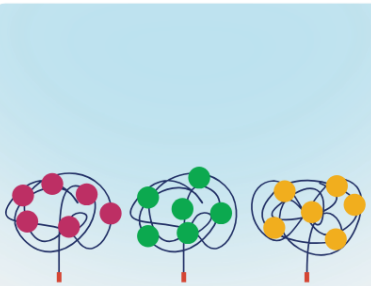
An **avidite** is a dye-labeled polymer with multiple nucleotide arms carrying the same nucleotide base.

Bind Polonies and Avidites
An engineered polymerase binds a primer-hybridized polony and an avidite nucleotide arm without incorporation or extension. Many arms bind to primer-hybridized regions in a polony, creating an ultrastable multivalent complex. Polymerase base-pair discrimination binds the correct avidite to each polony.

Remove Blocks
Removing and converting blocking groups to terminal 3' hydroxyl groups allows the next cycle to begin on the primer strands, through ~600 cycles.

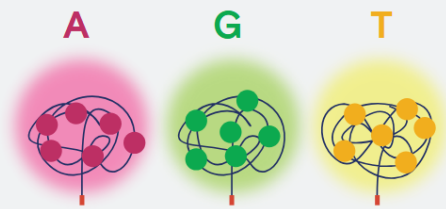


Step and Block
An engineered polymerase incorporates an unlabeled, blocked nucleotide to extend hybridized primers by a base.



Wash Avidites
A wash removes unbound avidites to leave only avidites bound to polonies. Ultratight binding enables a 100x reagent dilution, fundamentally decreasing cost.

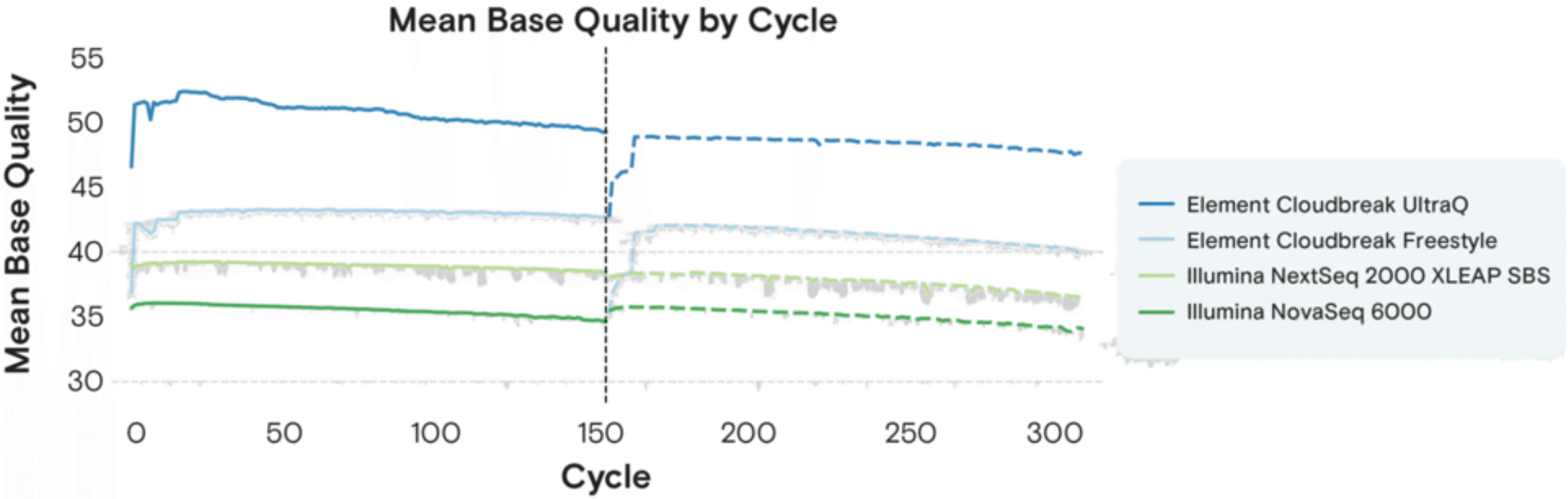
Remove Avidites
Buffers remove avidites from the polonies.



Detect Bases
Florescent signals in four channels correlate with A, T, G, or C avidites. Low-binding surface chemistry makes the signals more prominent for highly accurate detection.

Element Bioscience – Q50+

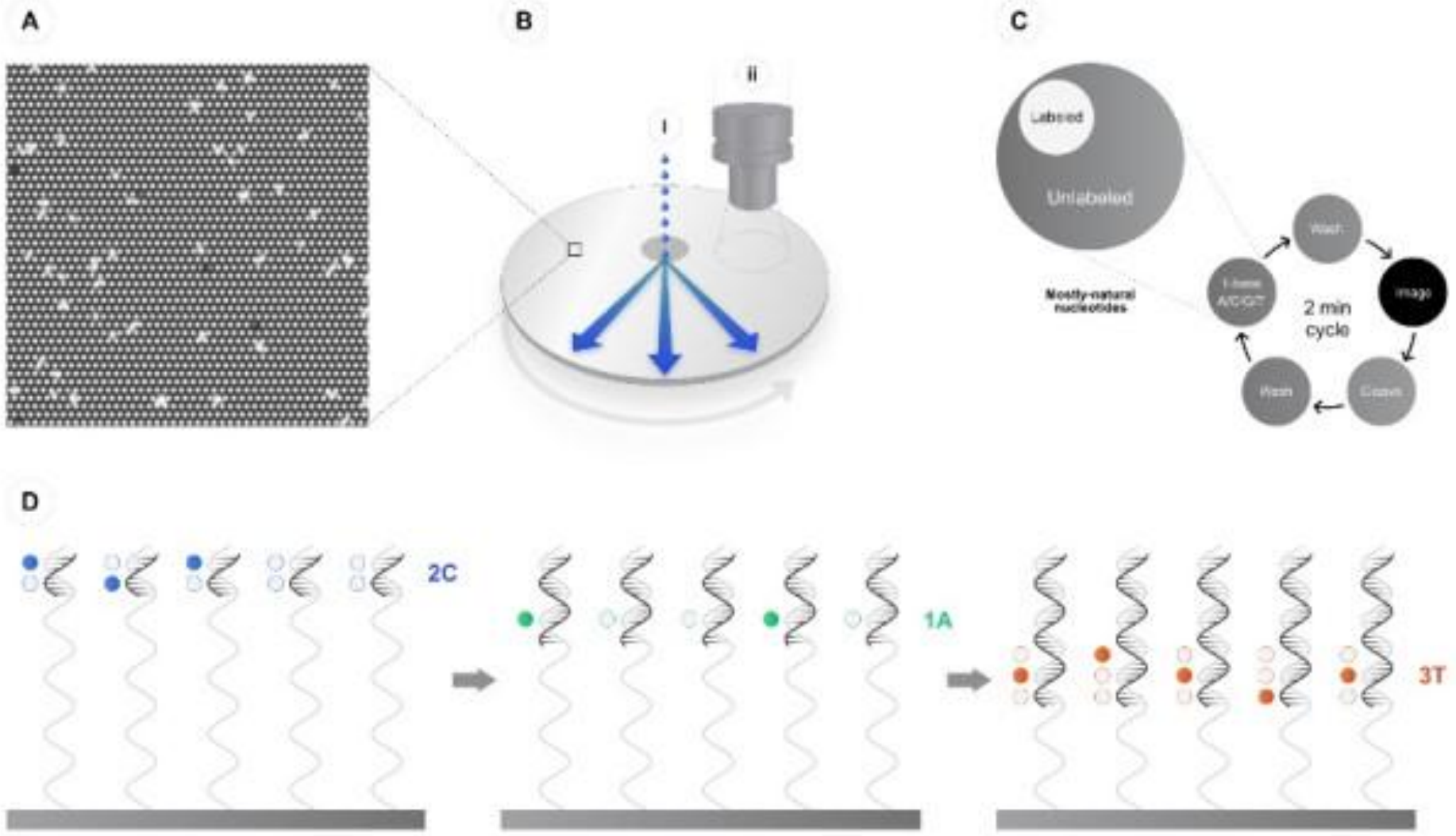
- Cloudbreak UltraQ :
  - Sequencing chem. : New enzymes, avidite modifications (core/dye/linker), recipe changes
  - Library prep changes
  - Data analysis



Ultima Genomics

Reduce molecular scarring

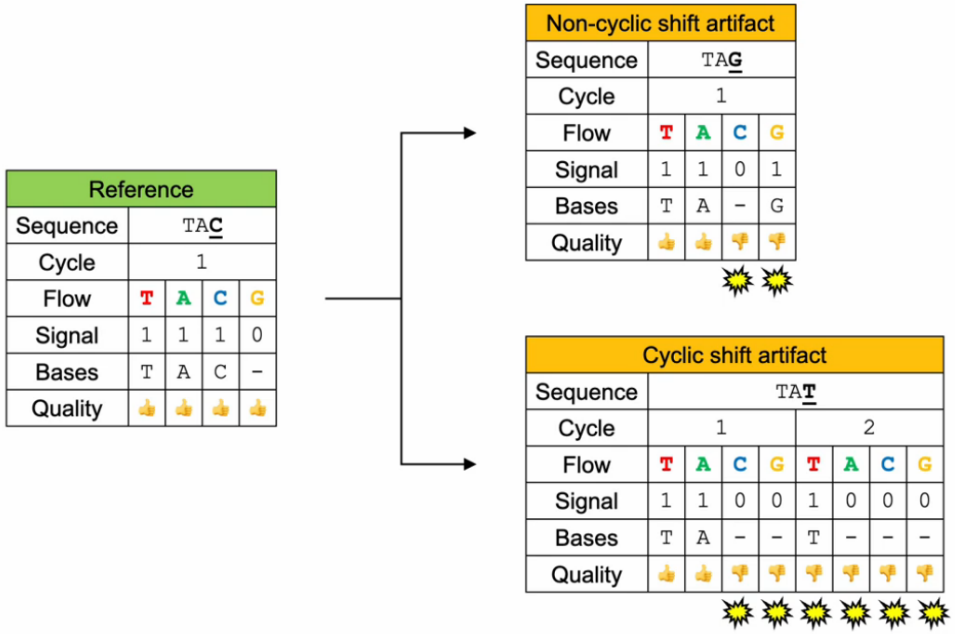
Ultima Genomics: flow based sequencing



Ultima Genomics: flow based sequencing

Cycle	1				2				3			
Flow	T	A	C	G	T	A	C	G	T	A	C	G
P(L=0)	–	1	–	1	1	–	–	1	1	1	–	–
P(L=1)	0.99	–	0.97	–	–	0.02	0.99	–	–	–	–	0.95
P(L=2)	0.01	–	0.02	–	–	0.96	0.01	–	–	–	0.01	0.05
P(L=3)	–	–	0.01	–	–	0.02	–	–	–	–	0.99	–
…	…	…	…	…	…	…	…	…	…	…	…	…
P(L=11)	–	–	–	–	–	–	–	–	–	–	–	–
P(L=12)	–	–	–	–	–	–	–	–	–	–	–	–
Signal	1	0	1	0	0	2	1	0	0	0	3	1
Bases	T	–	C	–	–	AA	C	–	–	–	CCC	G
Quality	37	40	31	40	40	29	35	40	40	40	35	32

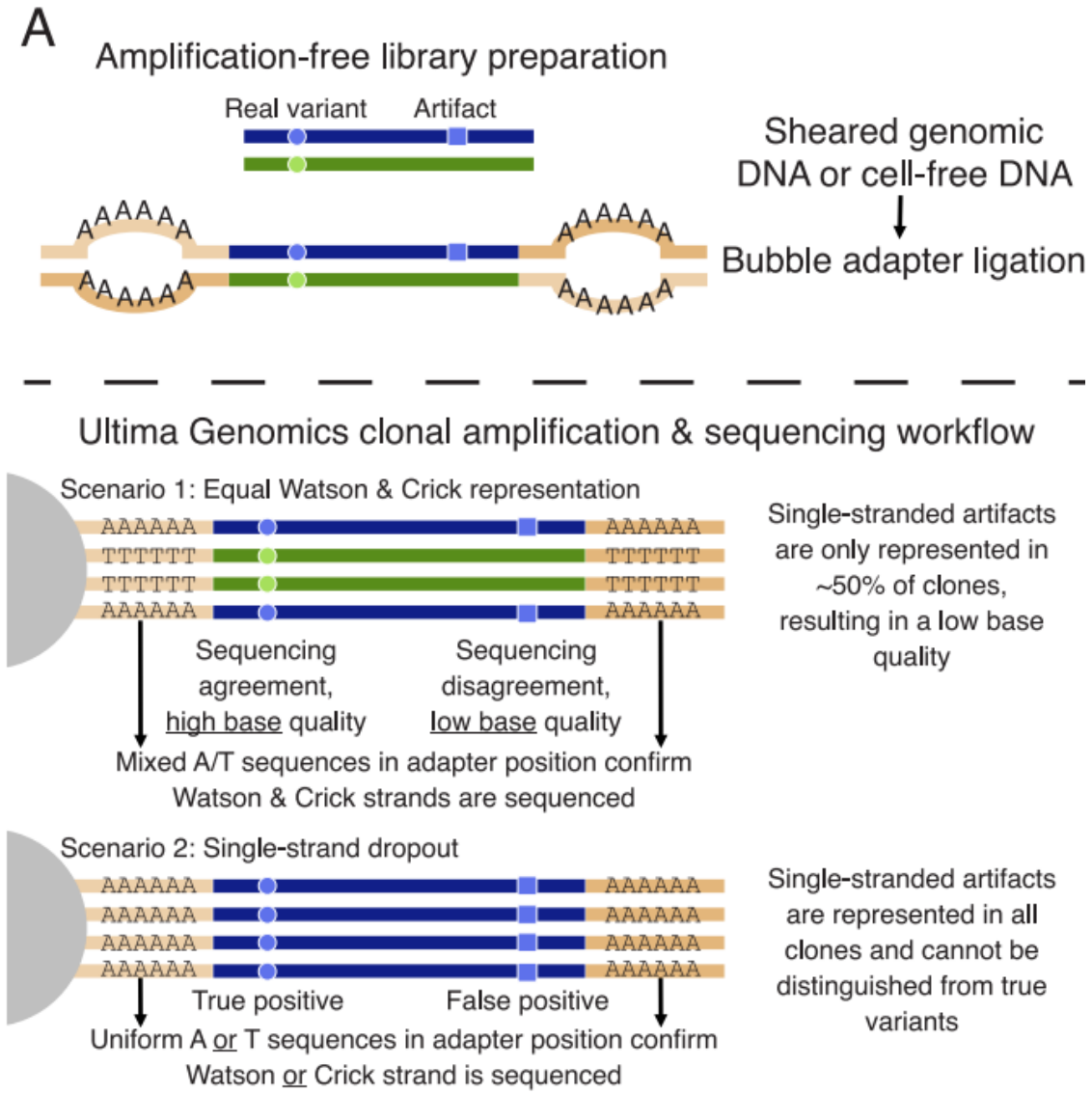
Ultima Genomics: Low substitution errors



	Indels			SNPs		
Sample	**Precision**	**Recall**	**F1**	**Precision**	**Recall**	**F1**
HG001	99.76%	99.43%	99.59%	99.95%	99.80%	99.87%
HG002	99.84%	99.56%	99.70%	99.99%	99.77%	99.88%
HG003	99.80%	99.47%	99.64%	99.96%	99.74%	99.85%
HG004	99.82%	99.53%	99.67%	99.98%	99.79%	99.89%
HG005*	99.82%	99.59%	99.71%	99.97%	99.81%	99.89%
Average	**99.81%**	**99.51%**	**99.66%**	**99.97%**	**99.78%**	**99.87%**

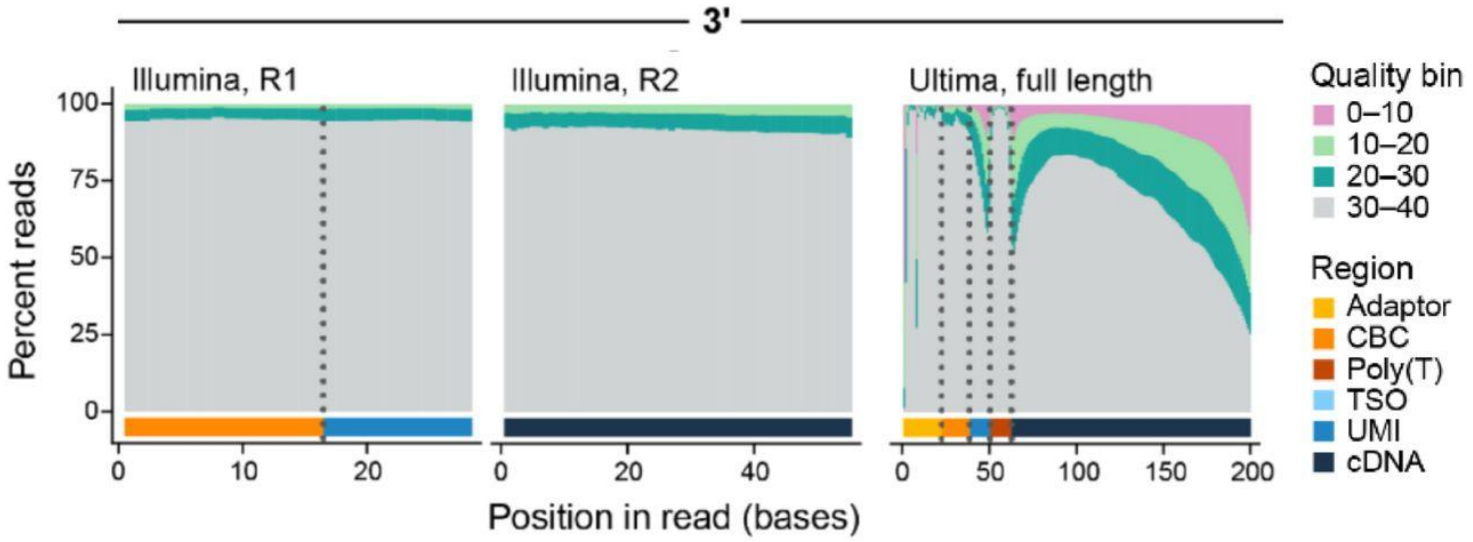
Table 1. Metrics and variant calling performance for GIAB reference samples, assessed in comparison to reference truth sets within the UG-HCR, which covers >99% of the GIAB v4.2.1 HCR and excludes genomic areas where UG performance is consistently of lower confidence, such as homopolymer regions of length >12 bp and limited regions of low complexity (see https://github.com/Ultimagen/healthomics-workflows/blob/main/docs/ug_hcr.md)

ppmSeq Paired Plus-Minus sequencing



Ultima Genomics

- High troughput
- 12B reads / flowcell
- 30000 genomes/year
- 0,7 euro/Gb
- Still high error rate
- Not yet fully available in Europe



Alternative / newer short read sequencers

Singular Genomics G4

multiomics

PacBio Onso

> acquired by Illumina on 30/1/2026

Alternative / newer short read sequencers

GeneMind

> Recently entered the European market

SURFSeq Q

Explore More

SURFSeq 5000

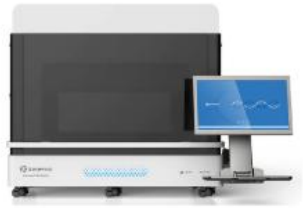
Explore More

GenoLab M

Explore More

FASTASeq 300

Explore More



MrLH-96

Explore More

FASTASeq S

Explore More

Next Generation Sequencing

Short read sequencing improvement 2

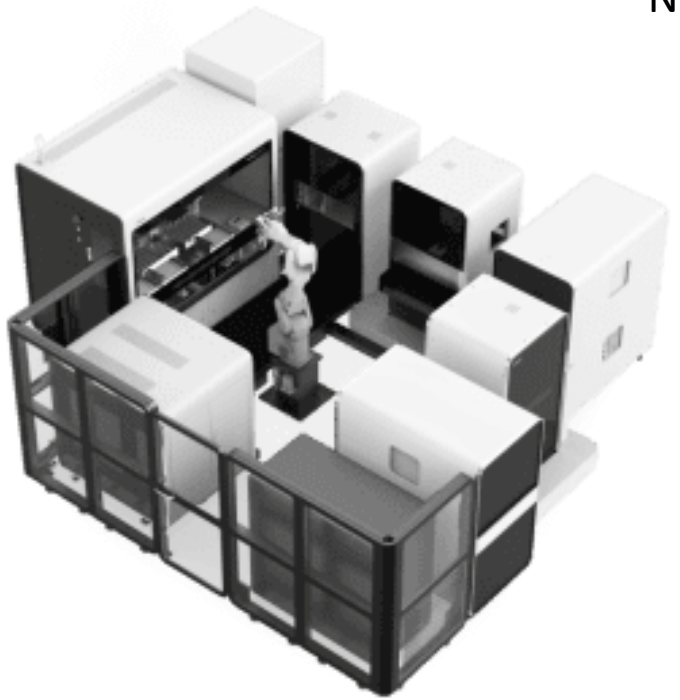
SCALE/COST

Increase in scale

ILLUMINA

ELEMENT BIOSCIENCES
NEW HT-SEQUENCER
ANNOUNCED

MGI



Increase in scale

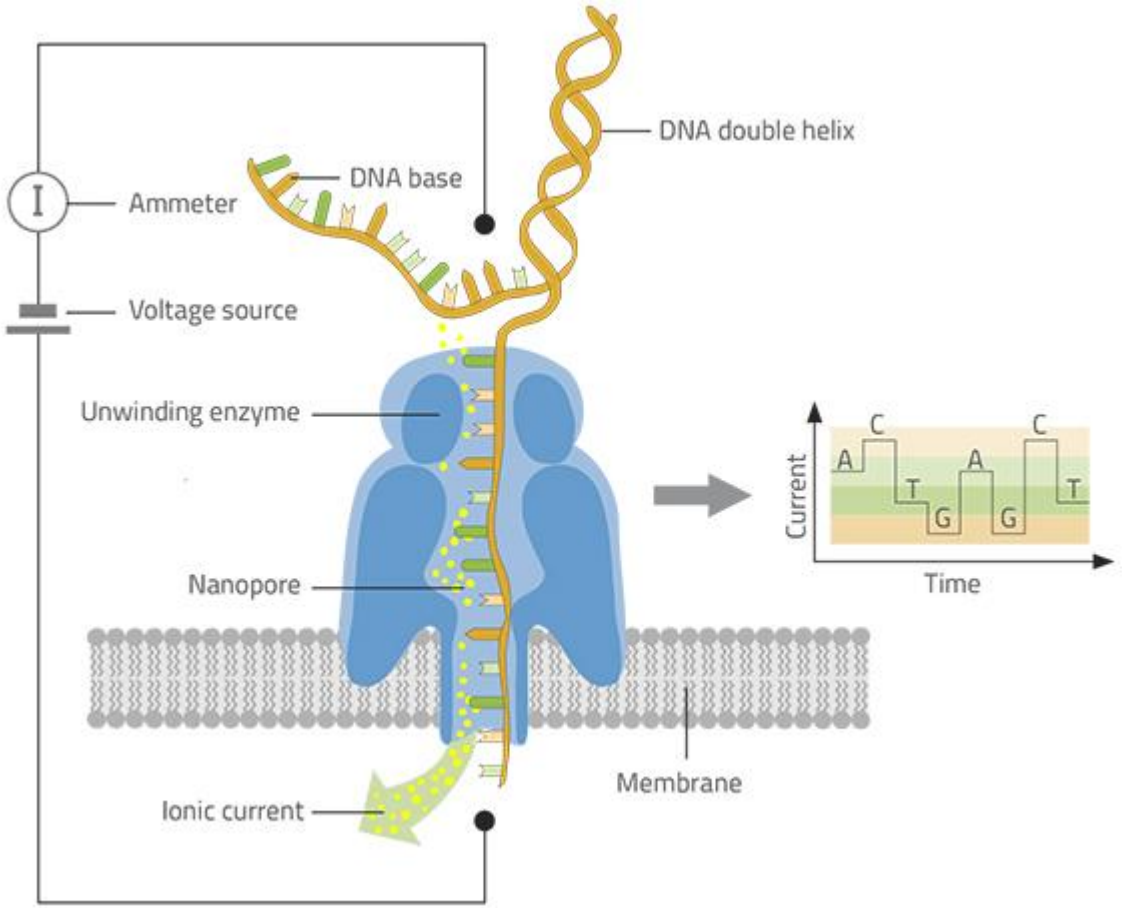
- Novaseq 6000: 5$/Gb
- New generation of sequencers are being released
  - Novaseq X (Illumina, released Q2 2023)
  - DNBSEQ-T7 (MGI, entered EU market in 2023)
- Cost drop to 2$/Gb
- WGS is cheaper in comparison to panel sequencing

Next Generation Sequencing

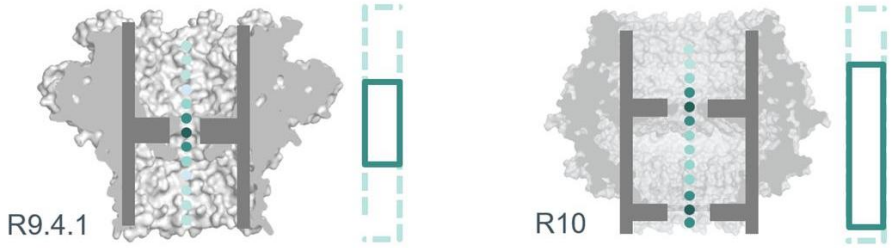
Long read sequencing

	Parallel session: Molecular Biology	Chair: Elke Boone	
11:45 - 12:15	Long read sequencing	Wouter Bossuyt (UZ Leuven)	006

Long read sequencing: Nanopore sequencing

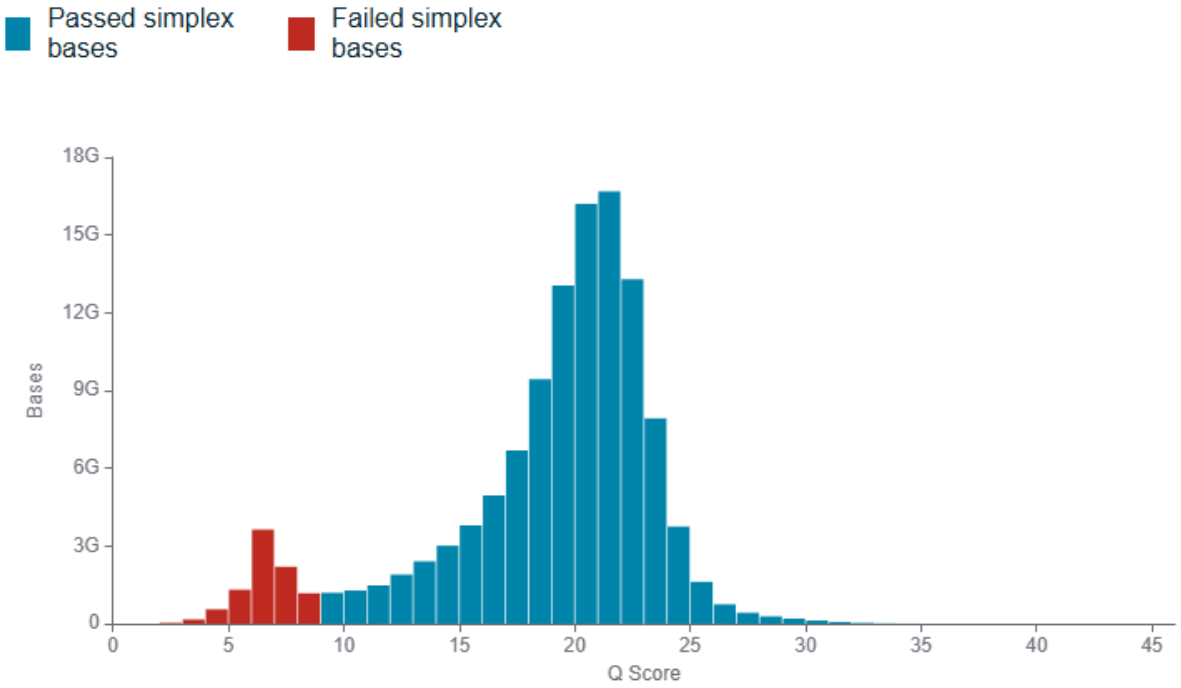


First Minion released in 2014 (!)



Current state

- 120 Gb run (40x human genome)



Phred Quality Score	Probability of incorrect base call	Base call accuracy
10	1 in 10	90%
20	1 in 100	99%
30	1 in 1000	99.9%

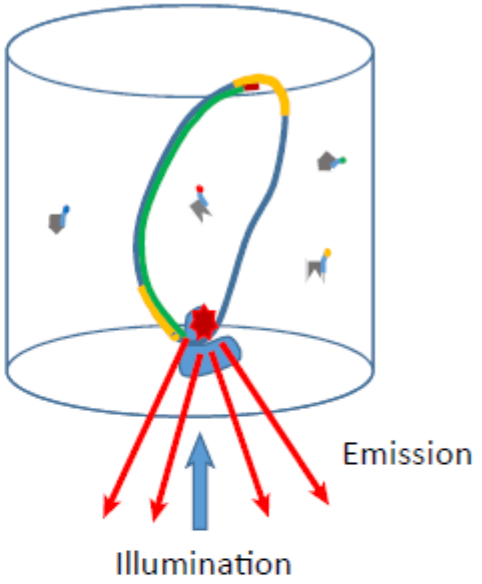
- Choice between output **or** long (>20kb) reads
- Accuracy still a problem
- Great for selected applicatons
  - de novo assembly
  - consensus sequencing
  - Structural variant confirmation

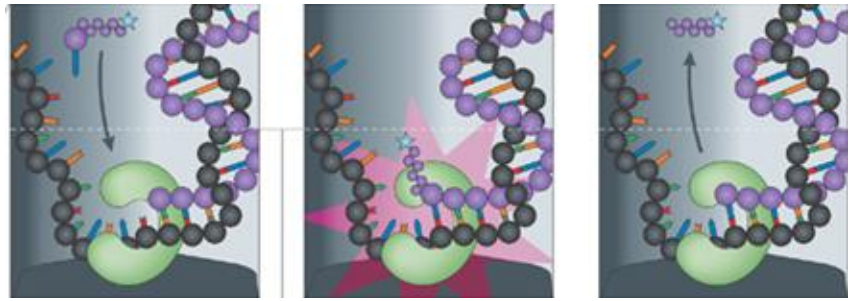
PacBio SMRT (Single-Molecule Real-Time) sequencing

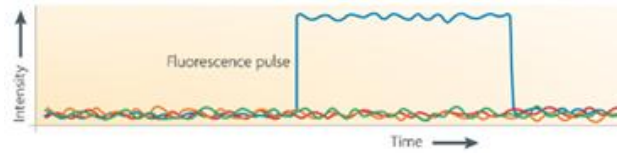
(A)

SMRTbell generation via hairpin adapters

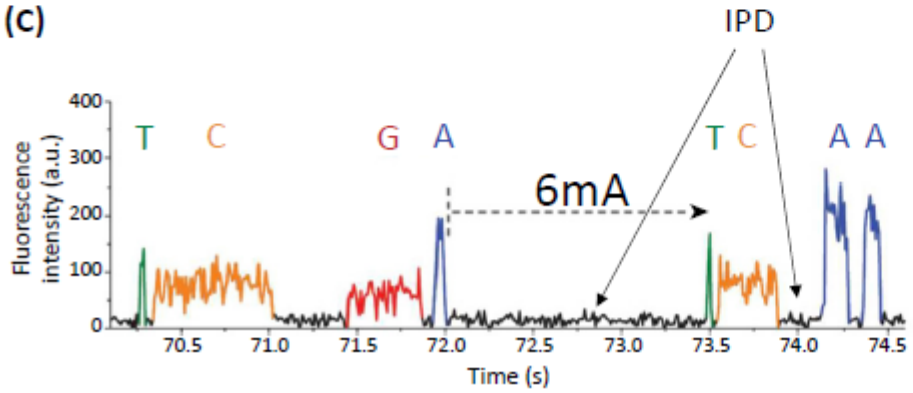
(B)







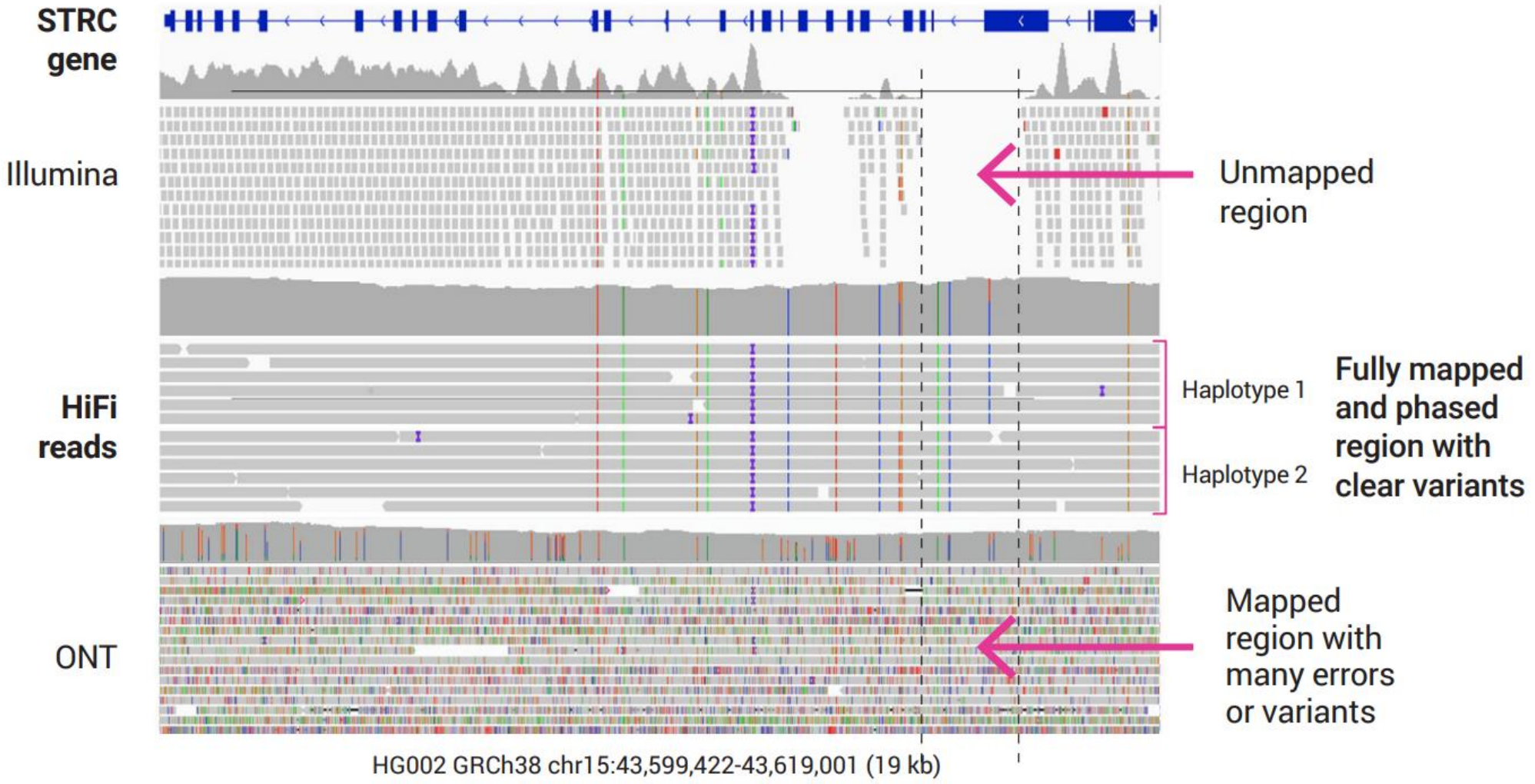
(C)



Every dNTP incorporation generates a signal
DNA modifications can be detected as well

- PacBio RS released in 2011 (!)
- High accuracy Hifi reads
- Output still limited
- Still expensive 1200 euro/genome

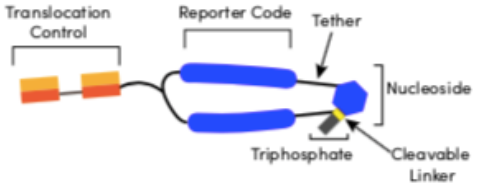
Long read sequencing



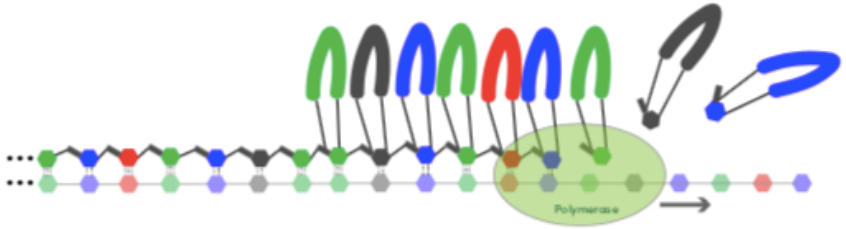
STRC gene alignments from *Genome in a Bottle* (GIAB), HG002_NA24385_son.

Roche Sequencing by expansion (SBX) technology

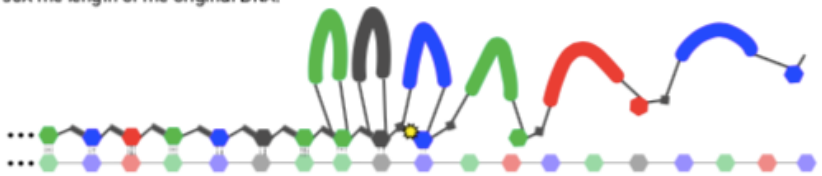
XNTP structure – Four XNTPs, one for each DNA base, are the building blocks for Xpandomer synthesis. Each XNTP is modified to include a long tether that contains a base-specific, high signal-to-noise reporter, a translocation control element that regulates transit through the nanopore during sequencing and a selectively cleavable linker engineered into the phosphate backbone.



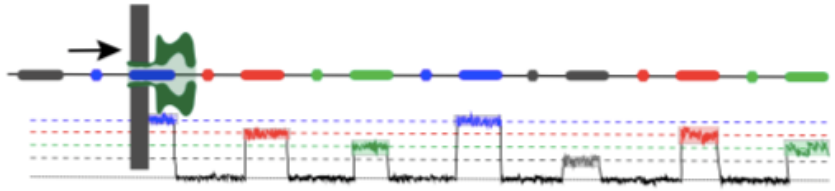
Synthesize Xpandomer – Template dependent Xpandomer synthesis is achieved using custom engineered polymerases to accurately incorporate expandable nucleotides. *Note: translocation controls have been excluded to simplify the graphics below.*

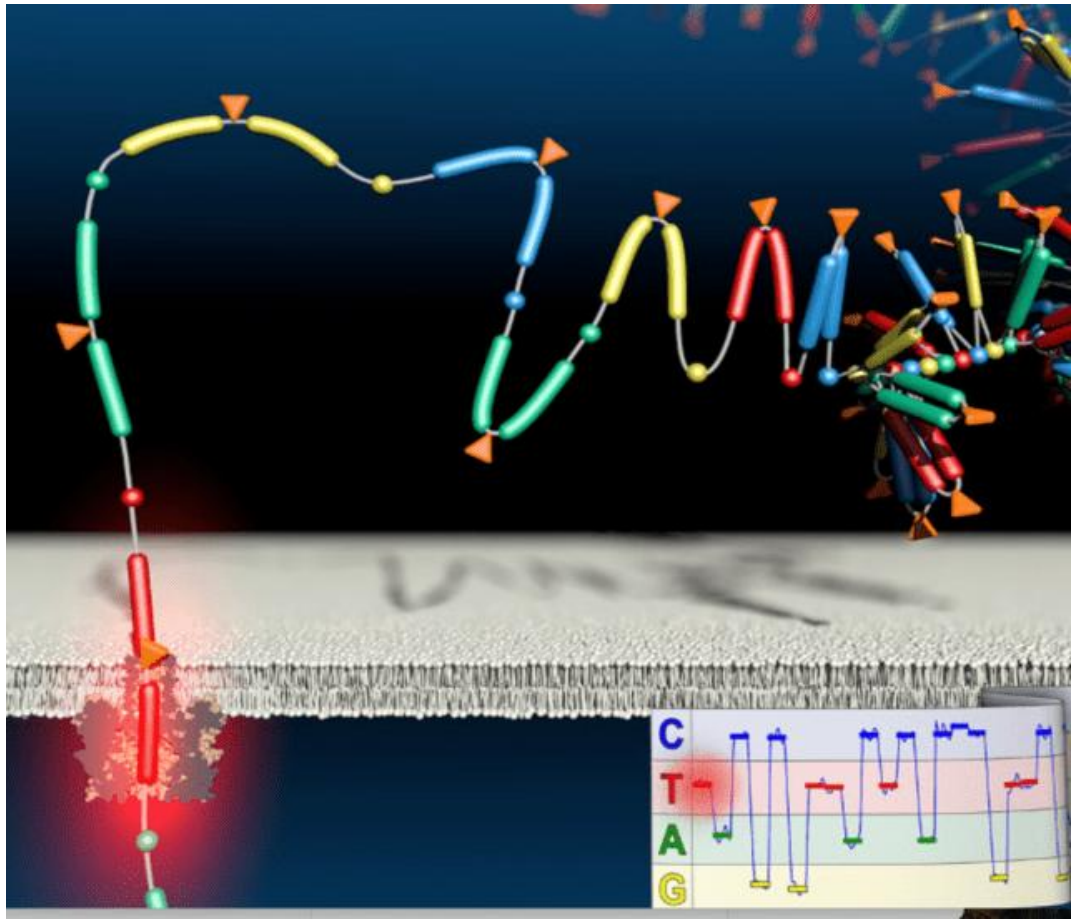


Cleave – Once the targeted DNA sequence is copied, the labile linker in each XNTP is cleaved to generate the full-length Xpandomer, expanding to 50X the length of the original DNA.



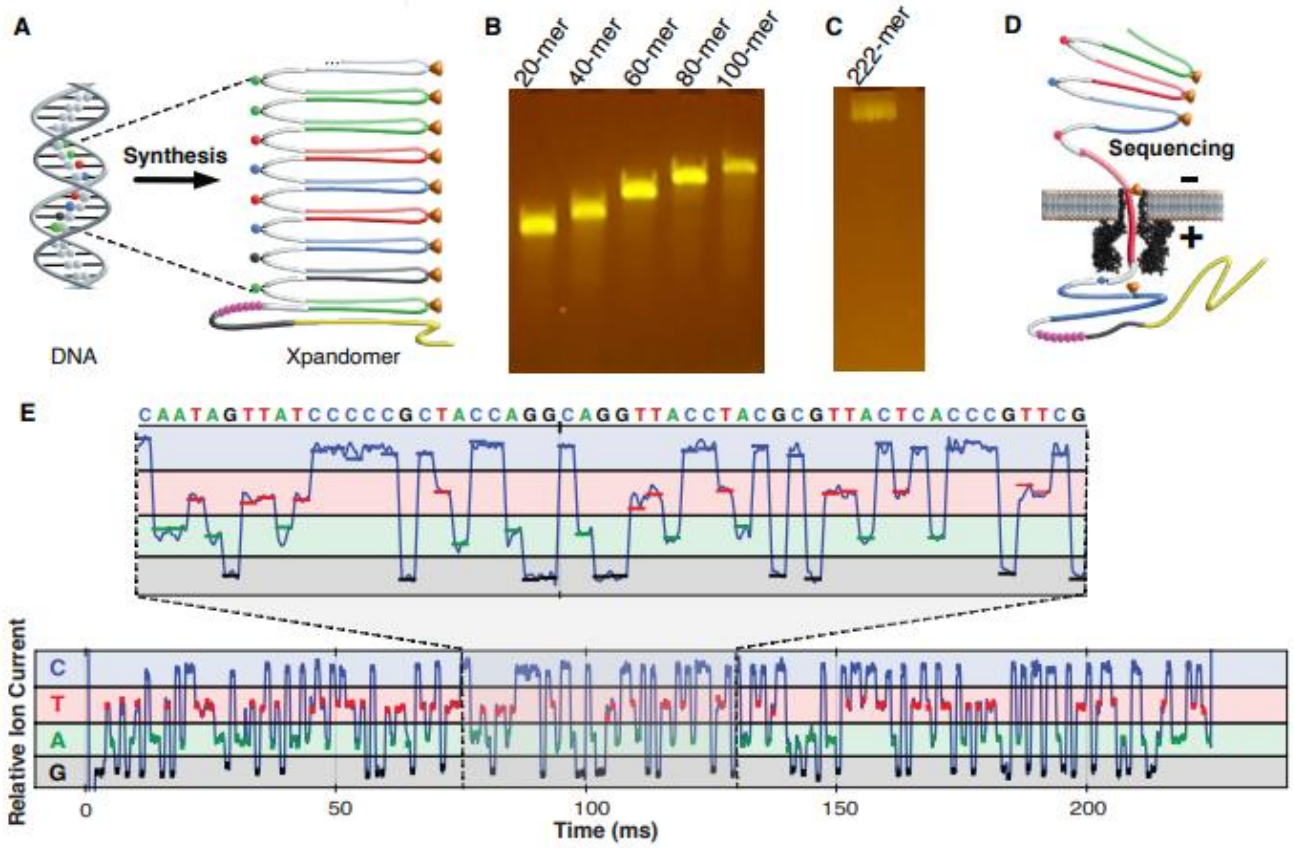
Sequence – Xpandomers are directly sequenced in real-time using a nanopore sequencing instrument. Nanopore sequencing relies on the change in electrical impedance as each reporter passes through a protein nanopore. Each of the four base-specific reporter codes displays a characteristic signal that is measured as the Xpandomer translocates through the nanopore.



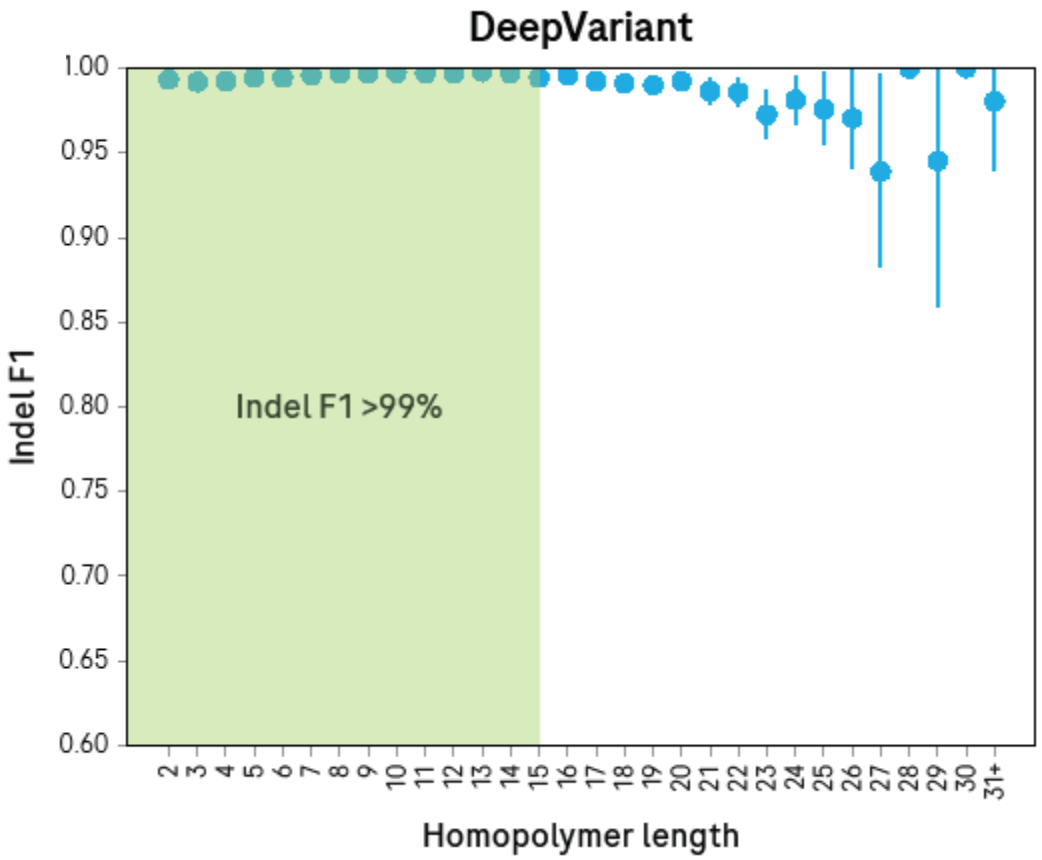


Roche SBX : a “high accuracy” nanopore sequencer

- Solves error rate of nanopore sequencing
- Removes the long reads (50-1000 bp)
- Pricing unknown, launch in Q2 2026



Advantages



Roche breaks world record for human genome sequencing

16 Oct 2025 | EMJ GOLD | View All News

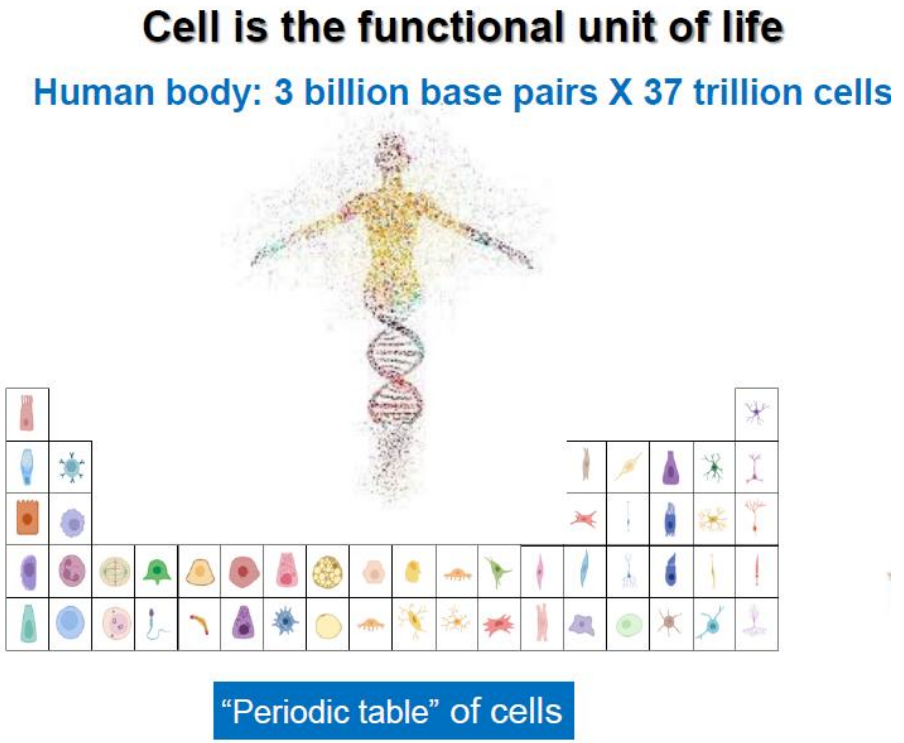
Sample	Total duplex reads (B)	Mean insert read length (bp)	Median coverage (x)	F1 score (GATK + Roche ML)[2]		F1 score (DeepVariant)[2]	
				SNV (%)	Indel (%)	SNV (%)	Indel (%)
HG001	0.79	235	38	99.77	99.54	99.80	99.56
HG002	0.71	233	34	99.69	99.44	99.75	99.46
HG003	0.76	231	37	99.66	99.46	99.70	99.47
HG004	0.80	231	38	99.70	99.56	99.73	99.56
HG005	0.79	230	38	99.69	99.56	99.74	99.60
HG006	0.71	233	35	99.68	99.59	99.74	99.58
HG007	0.73	229	34	99.63	99.54	99.71	99.50
Mean	0.76 ± 0.039	232 ± 2	36 ± 2	99.69 ± 0.04	99.53 ± 0.06	99.74 ± 0.03	99.53 ± 0.06

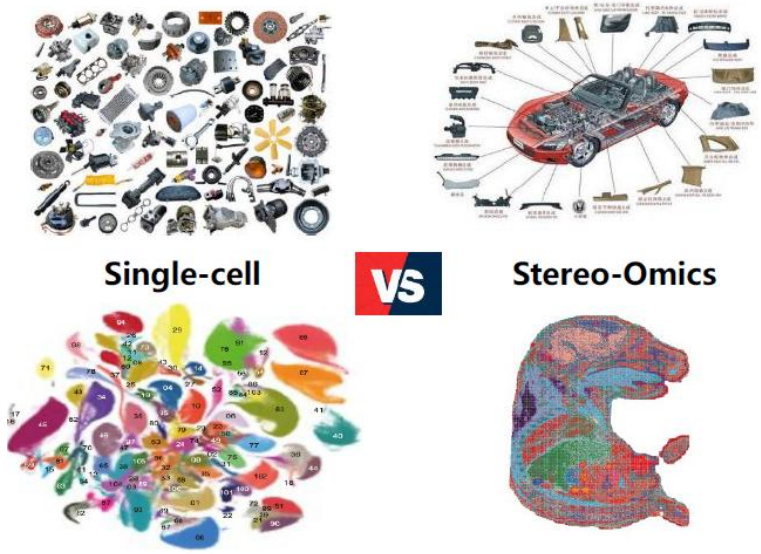
Next Generation Sequencing

Future

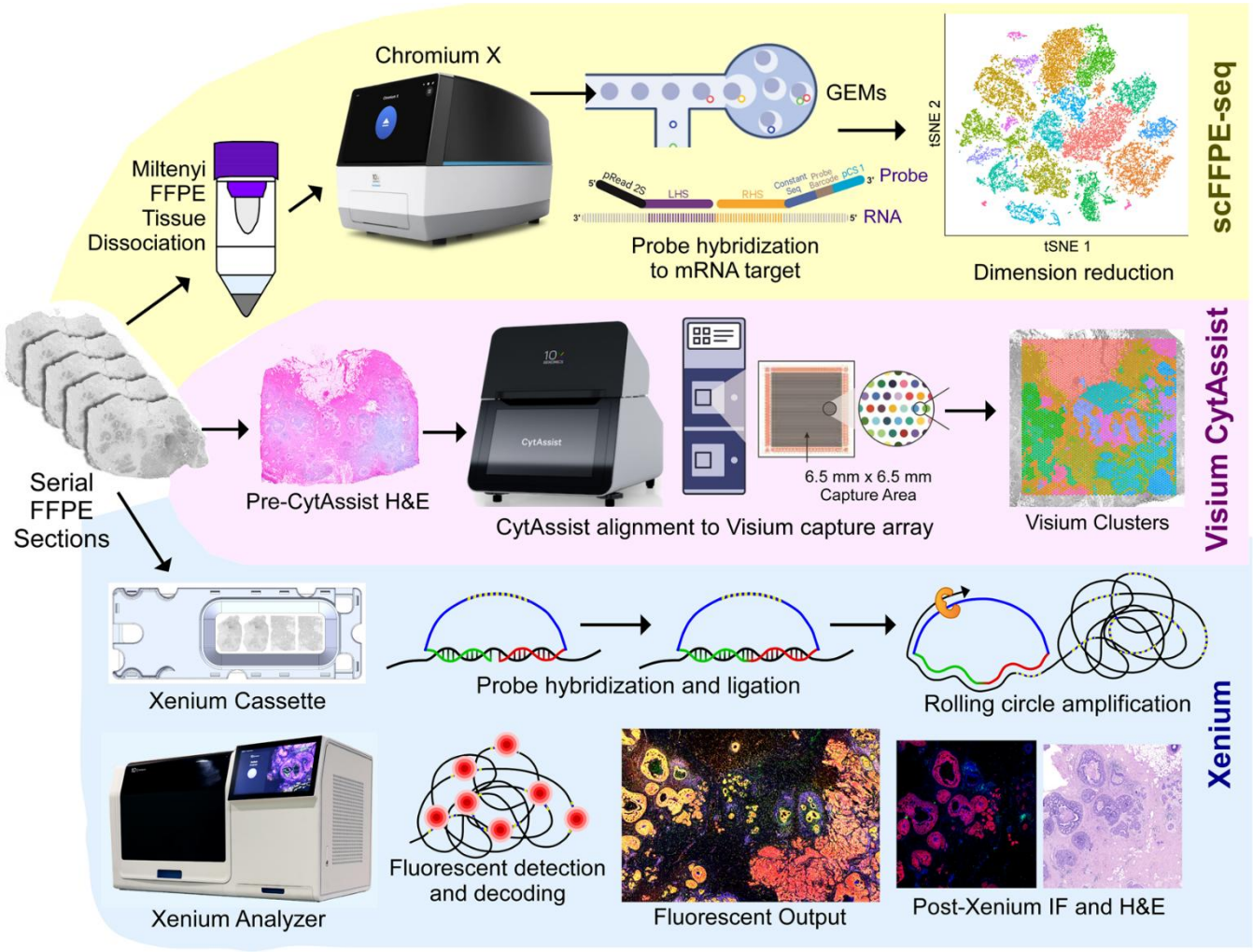
Big data

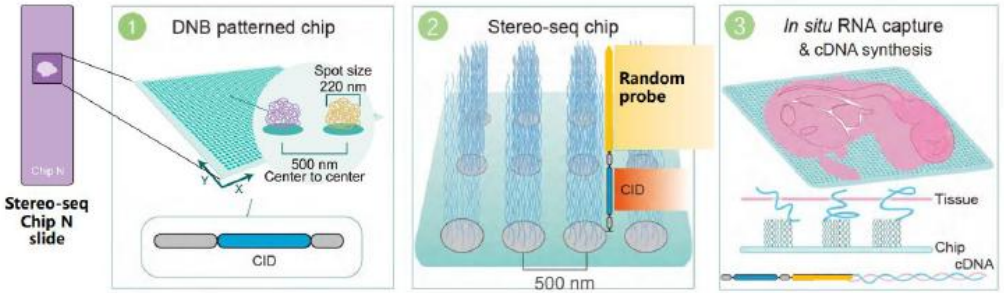
- Genomes are becoming mainstream
- Speed (TAT) is essential
  - Prenatal / perinatal care
- Transcriptome analyses are entering diagnostics
- Datasets are zooming in to single-cell/spatial level

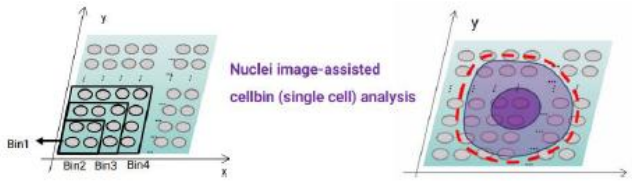




Single cell / spatial profiling







AI

- Need for better / faster / “smarter” tools to make sense of big data

	Plenary session	Chair: Barbara Dewaele (UZ Leuven)	
17:05 - 17:35	Artificial intelligence in the diagnostic laboratory workflow: from innovation to regulation	Glynis Frans (UZ Leuven)	005

Thanks!

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