

SLAS 2023

Automating the Optical Genome Mapping Workflow

February 28th

bionano™

Transforming the Way the World Sees the Genome



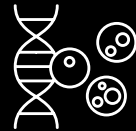
CYTOGENOMICS



**HEMATOLOGICAL
MALIGNANCIES**



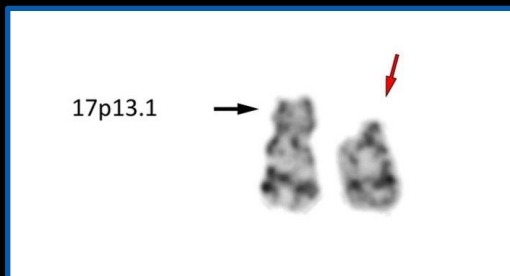
**MOLECULAR
GENETICS**



**CELL
BIOPROCESSING**

The Gap Between Karyotyping and Sequencing is Huge

Karyotyping (KT)



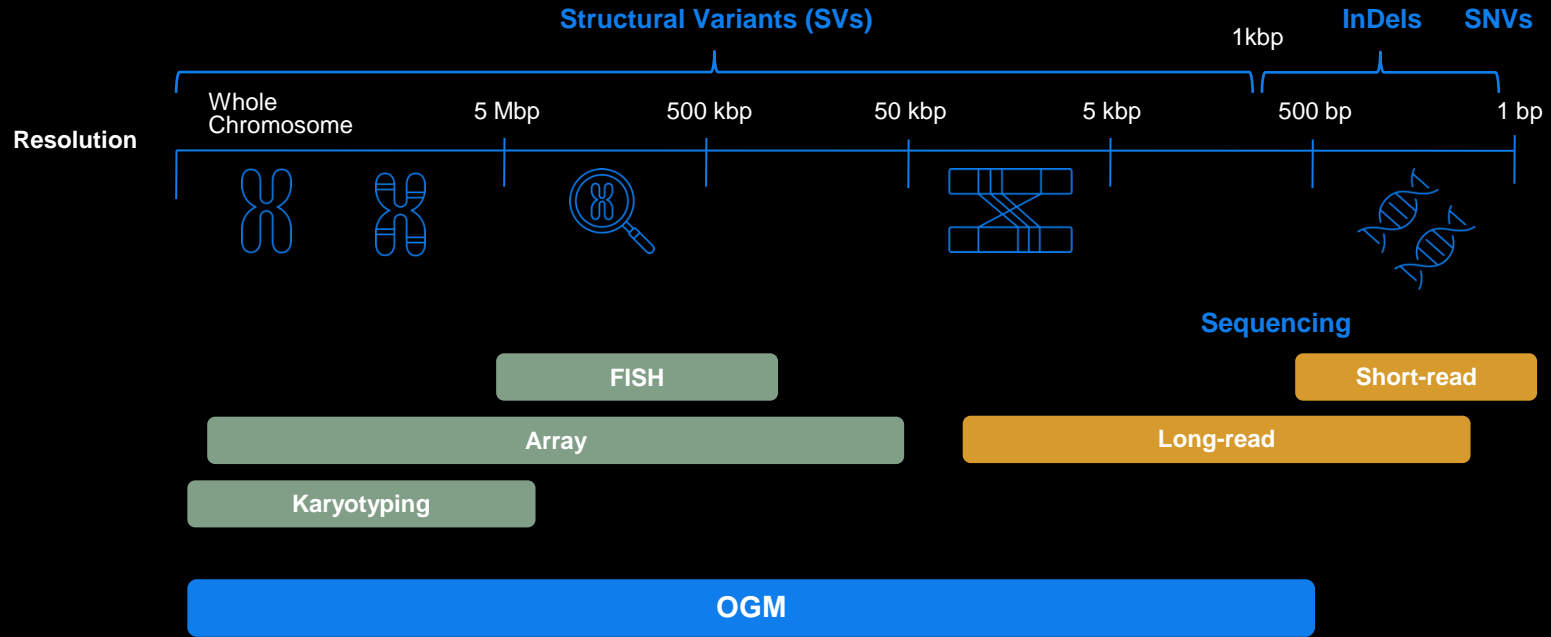
- First line test for blood cancers and solid tumors
- Hasn't changed in 50 years

NGS

```
AGGTCCTTTAGCATCTA
TCCTGTAGCATCTACGA
GGTCCTTTAGCAGCTACGATT
CCTTTAGCATCTCCG
TCCTTTACCATCTACGATT
```

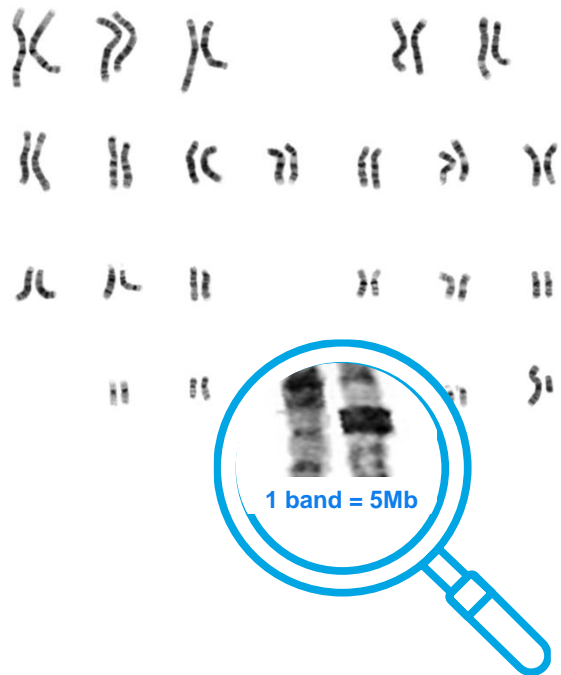
- First line test with KT for SNVs in blood cancers
- Best for SNVs and small in/dels

Genome Variation Unfolds Over An Incredibly Wide Spectrum



OGM is the only technology that detects all types of SVs without bias, and it has the highest resolution of any non-sequencing technology

Optical Genome Mapping as High-Resolution Digital Karyotyping

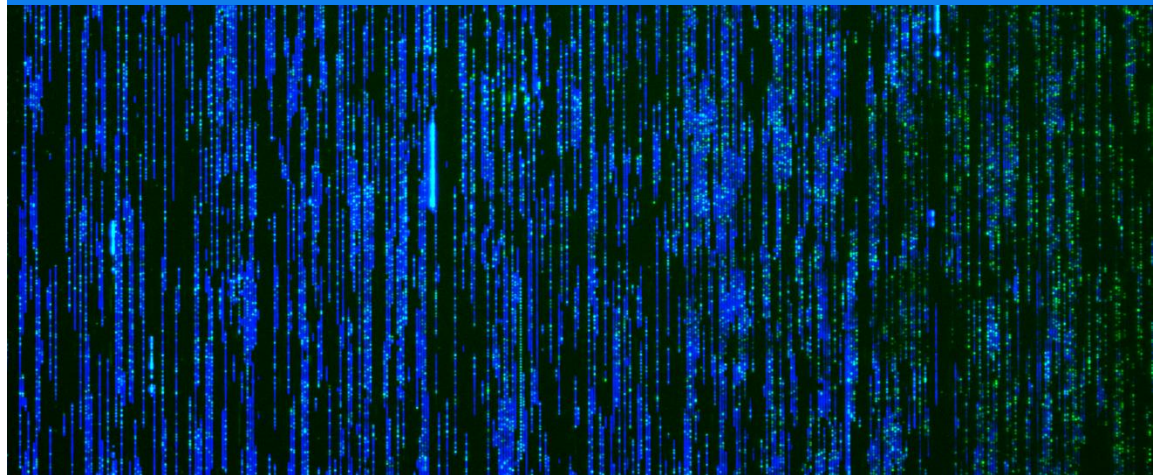


OGM provides

~1,000x times more “bands”
in the form of labels and can
detect chromosomal aberrations
as small as 500 bp



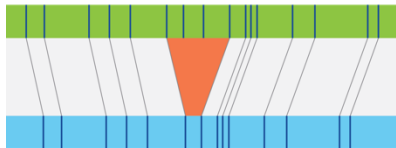
10,000x
resolution



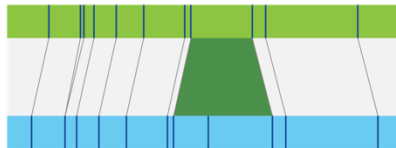
All Classes of Structural Variants Can Be Detected By OGM on the Saphyr® System

Gain/Loss

Deletion

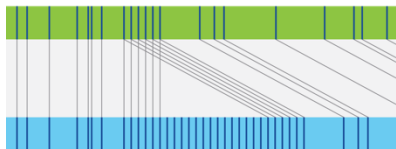


Insertion

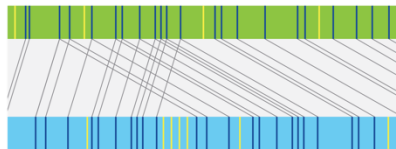


Copy Number Change

Repeat array expansion

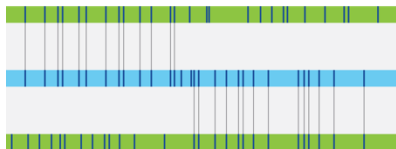


Tandem duplication

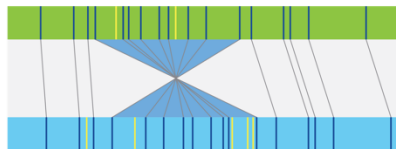


Balanced

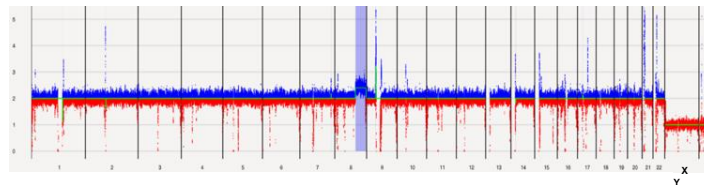
Translocation



Inversion



CNV



- Compared to karyotyping, OGM offers much higher resolution in a fully digitized analysis workflow.
- Compared to CMA, OGM closes the gap on balanced rearrangements, including translocations and inversions.

Laboratories are Facing Analytical and Operational Challenges

Market Drivers & Pressures



Strong demand for analysis of chromosomal aberrations

Multiple medical guidelines drive need for more comprehensive cytogenetic and molecular genetic testing across applications



Increasing test volume

Global demand for cytogenetic and genomics testing is growing



Growing test complexity

Discoveries in genomics and evolving guidelines have resulted in an increasing number of biomarkers and reflex pathways

Challenges Labs Face



Limited throughput

Traditional cytogenetic and genomic technologies have complex workflows analysis steps, limiting overall throughput



Resource constraints

The number of trained clinical cytogeneticists, bioinformaticians and med techs is expected to decline — creating challenges for meeting growing test demand



Technology limitations

Many genomic technologies are not well integrated making ultimate analysis increasingly complex - limiting the ability to meet the needs of growing test menus



**How is Bionano
Helping you Deal
with these
Challenges?**

bionano™

The Saphyr[®] System Delivers an Integrated Analysis Solution

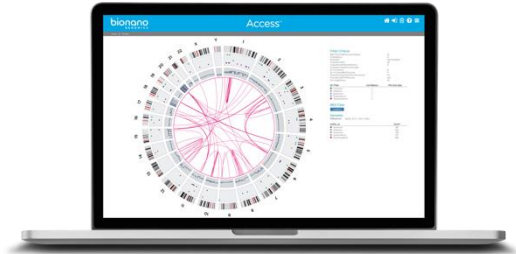
An end-to-end workflow that provides a package of reagents, consumables and software



Kits for Sample Extraction and Labeling

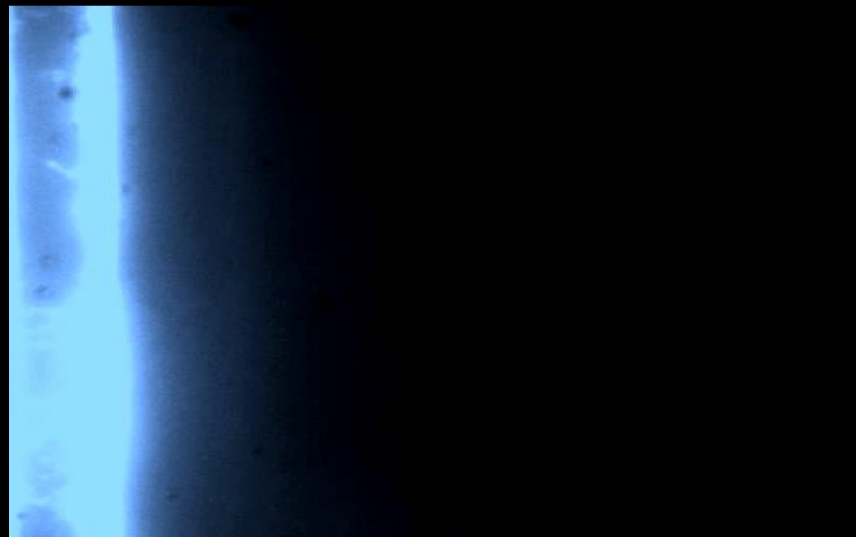
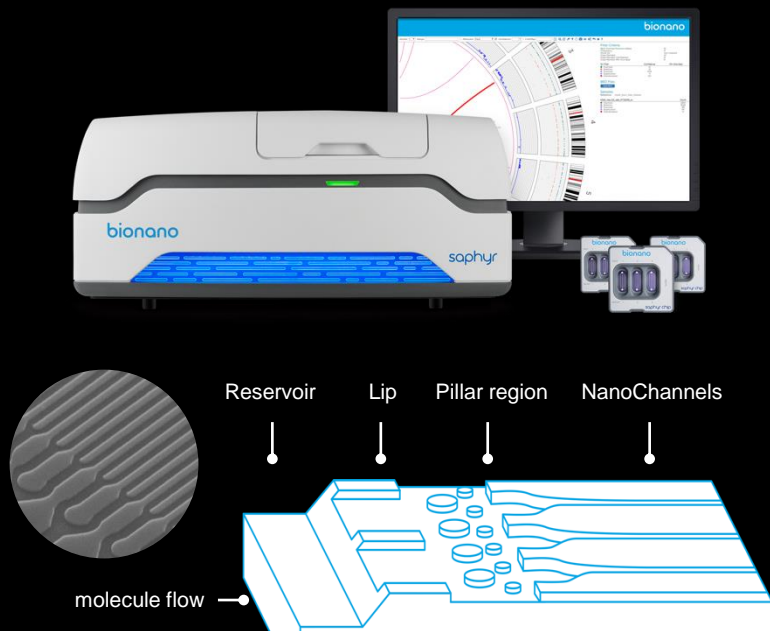


OGM Data Generation on the Saphyr System and Chips

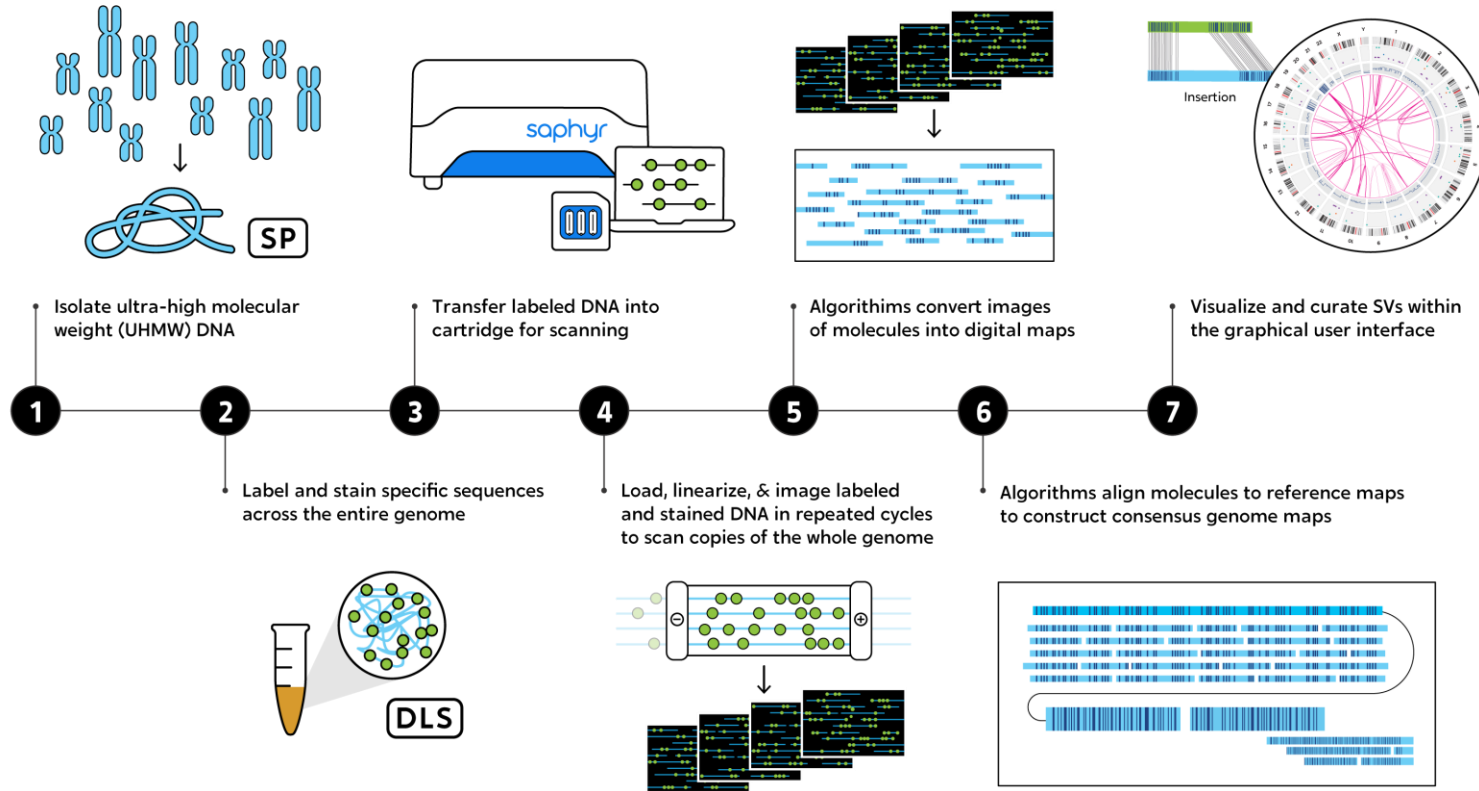


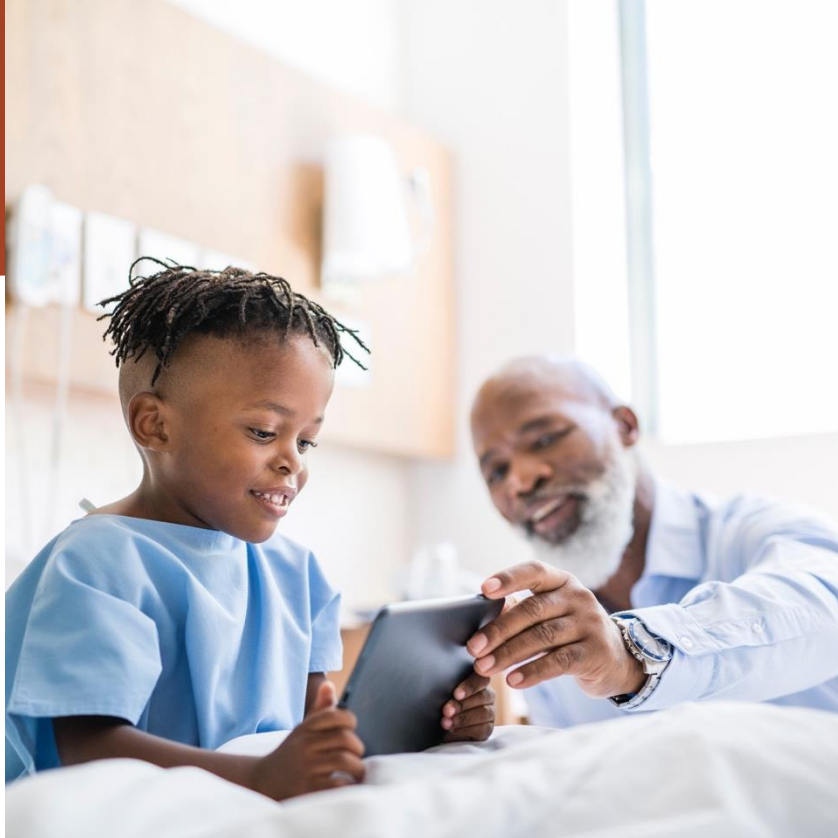
Data Analysis and Interpretation with Bionano Access[™] and Solve Software

OGM with Saphyr Uses Nanochannel Arrays to Linearize Ultra-High Molecular Weight DNA



Overview of the Saphyr[®] OGM Workflow





How do you perform
Optical Genome
Mapping and
Analysis?

bionano™

Second Generation Isolation of Ultra High Molecular Weight DNA

Robust sample preparation workflow with SP-G2 and DLS-G2 kits



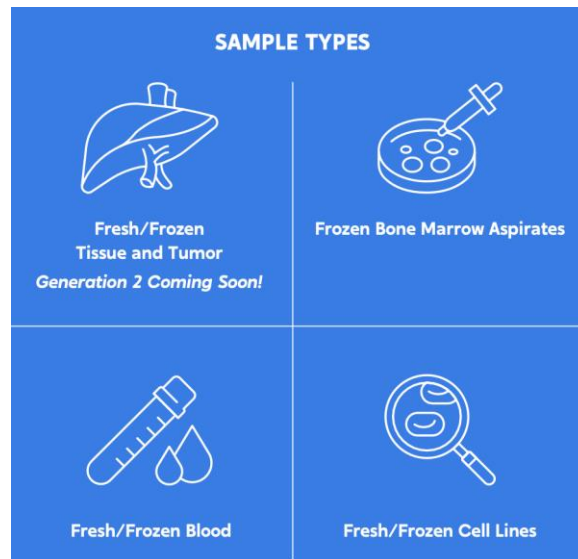
High gDNA quality for high sample success rates



Easy-to-Use SP and direct label and stain kits

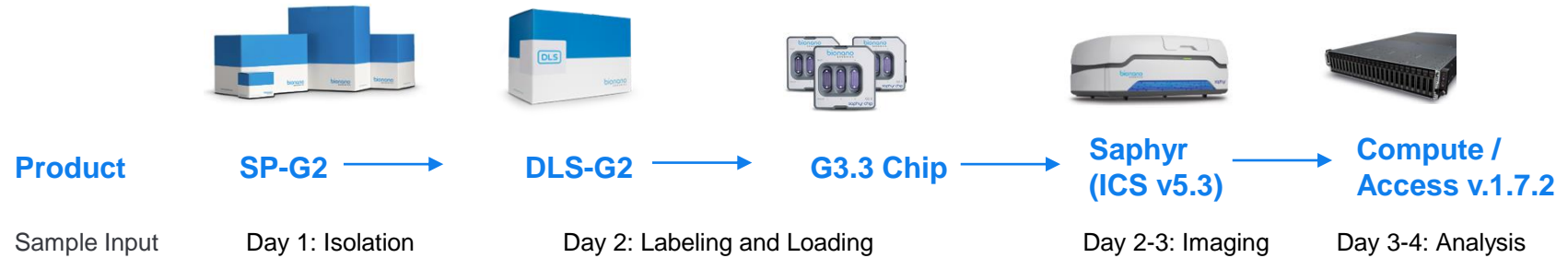


High DNA throughput for up to 40Gbp data generated per run



Second Generation (G2) Reagents for Better Results in Less Time

Achieve a sample-to-answer in as few as 3 days



Robustness in Sample Preparation workflow



Fast Turnaround Times for DNA labeling and imaging



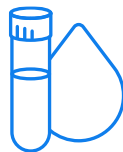
High success rates with high quality data

Hamilton's Long String + Bionano SP-G2 for UHMW DNA Isolation

Automation friendly kits to reduce hands-on time and increase samples per week



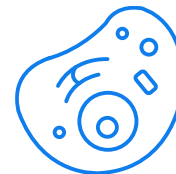
Sample Types (fresh or frozen)



Blood (650 μ l)



Bone marrow aspirate



Cultured cells

Automation optimized SP-G2.LS kits

- Pre-packaged and configured kits for automation

Isolate 24 DNA samples in a day

- Increase sample throughput routinely in your lab

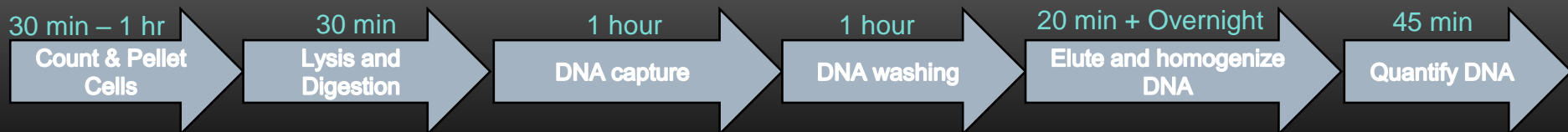
Optimize with Generation 2 Chemistry

- Improved DNA quality & throughput, length metrics

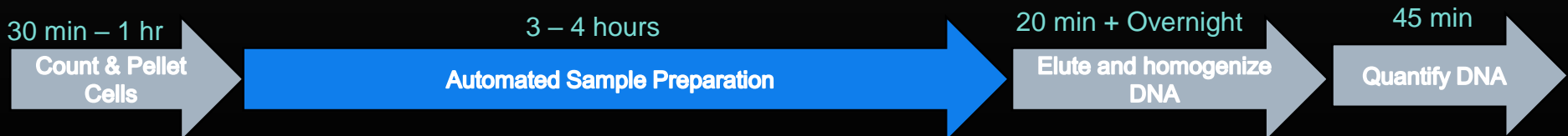
Automated vs. Manual SP-G2 Workflow

Large hands-on time savings with Long String and reduction of multiple experimental touchpoints

SP-G2 Manual Workflow



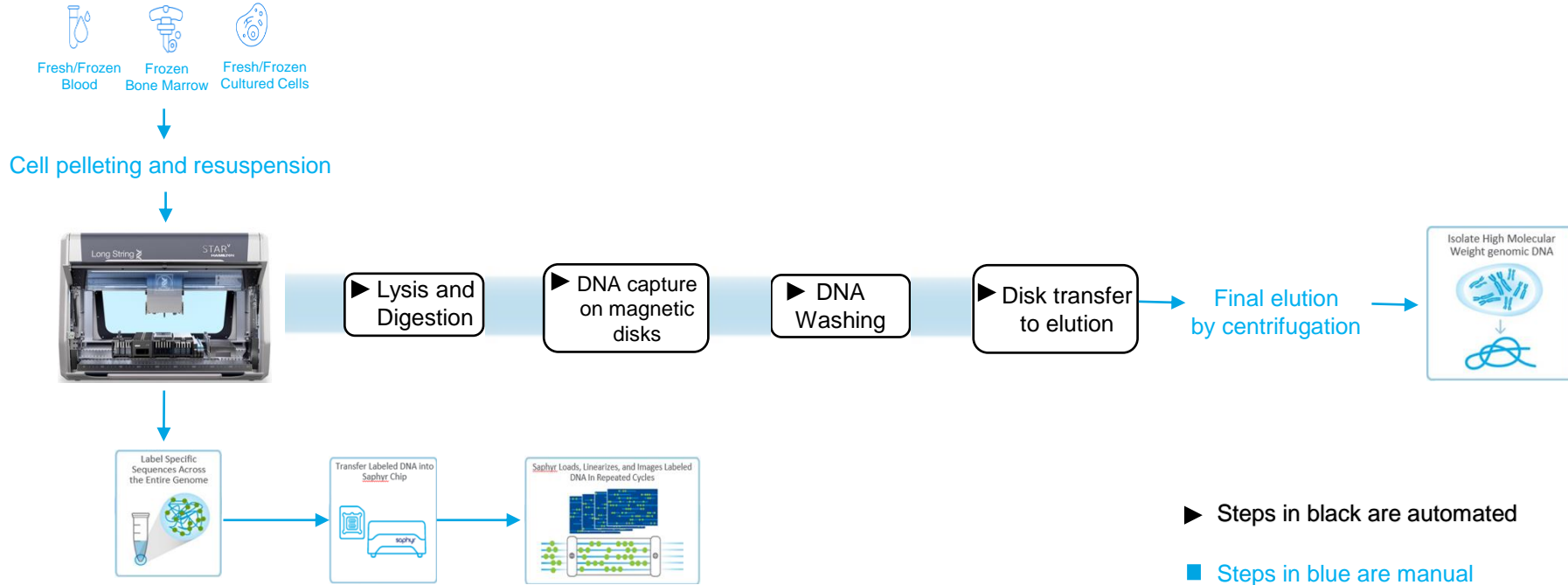
SP-G2 Automated Workflow



Increase your sample throughput up to 2x with automation

Introducing Automated UHMW DNA Extraction

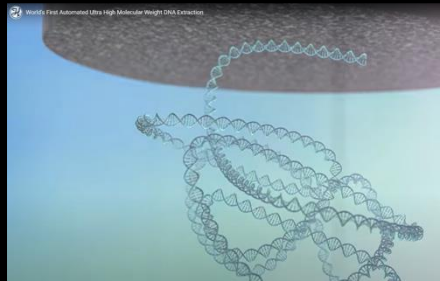
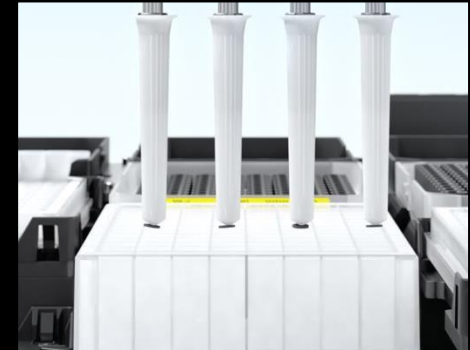
Workflow of SP-G2 on the Hamilton Long String Star V Instrument



Bionano captures DNA by a novel magnetic disk with gentle end over end agitation in the manual method

The automated solution for disk handling are these unique magnetic rods with disposable sleeves in the 5 mL channels of the Long String.

Each MagRod captures a magnetic disk and moves it through solution and from well to well.



Bionano Assay Development - Goals and Study Design

OGM Long String Development

- Develop and optimize the automation of Bionano Prep SP-G2 kits for extraction of UHMW DNA

Development Design

- Reagents:
 - Notebook and Development Lot (produced by manufacturing) of SP-G2.LS Kits
 - Notebook, Development, and Pilot Lots of DLS-G2 Kits
- Consumables:
 - Hamilton Development and Production level consumables
 - Bionano Commercial Saphyr G2.3 chips
- Sample types: Cultured Cells, Blood, and Bone Marrow Aspirate
- Four operators
- N = 208
- Tested Cell/WBC Input: 1.2M - 1.5M
- Quality Metric Thresholds:

QC Metric	Threshold
Average Molecule Length (filtered for ≥ 150 kbp)	≥ 230 kbp
Label Density	≥ 14 and ≤ 17 labels per 100 kbp
Map Rate (filtered for molecules ≥ 150 kbp)	$\geq 70\%$
Throughput	≥ 40 Gbp per scan

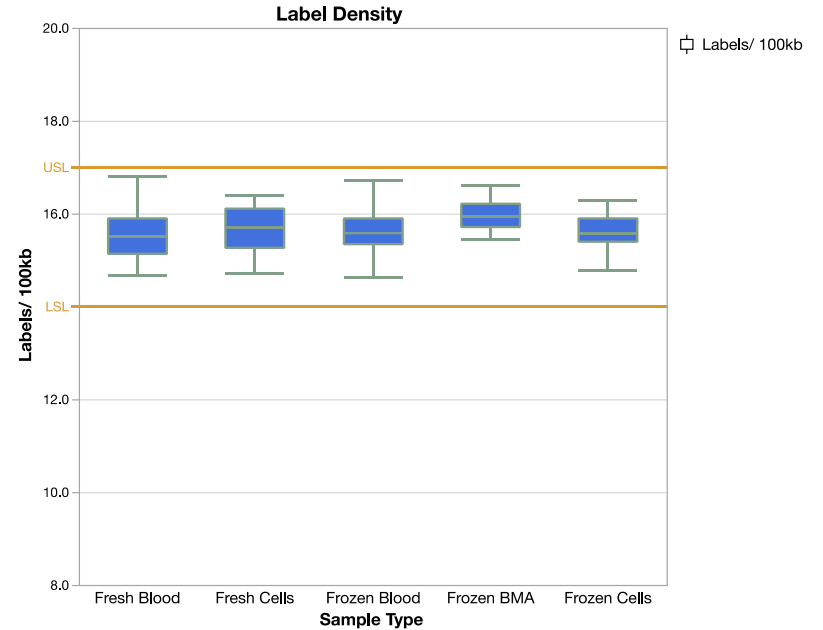
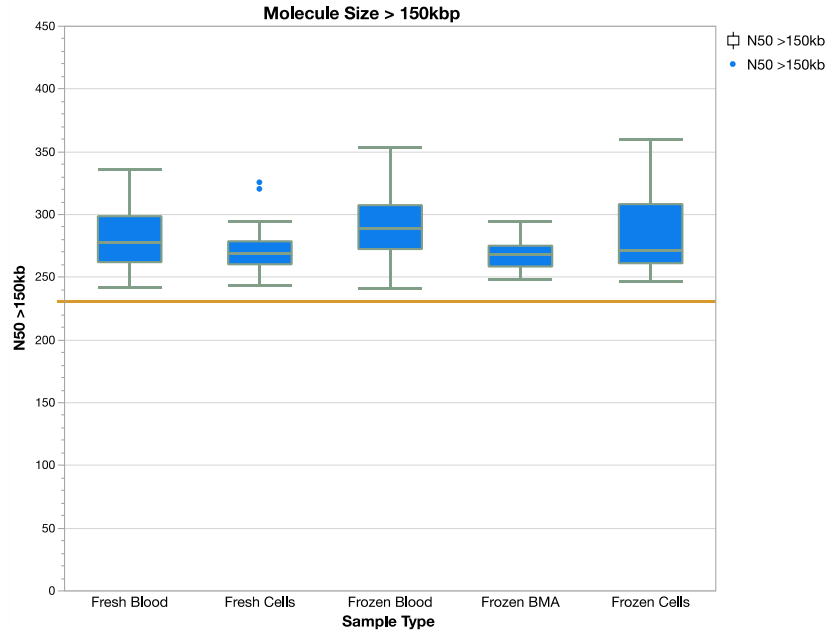
Sample Preparation Generation 2 on Long String Data

OGM Average QC Metrics by Sample Type

Sample Type	N	N50 (\geq 150kbp)	Label Density	Map Rate	Throughput (Gbp/scan)
Fresh Cells	30	271.3 \pm 19.2	15.7 \pm 0.5	92.8% \pm 1.4%	73.1 \pm 12.1
Frozen Cells	32	282.7 \pm 28.2	15.6 \pm 0.4	91.8% \pm 2.1%	65.0 \pm 14.0
Fresh Blood	39	282.5 \pm 25.1	15.6 \pm 0.5	90.9% \pm 2.2%	59.2 \pm 13.0
Frozen Blood	88	289.8 \pm 25.6	15.6 \pm 0.4	92.4% \pm 1.7%	61.3 \pm 16.9
Frozen BMA	19	267.7 \pm 12.5	15.9 \pm 0.3	90.5% \pm 1.8%	61.0 \pm 13.8

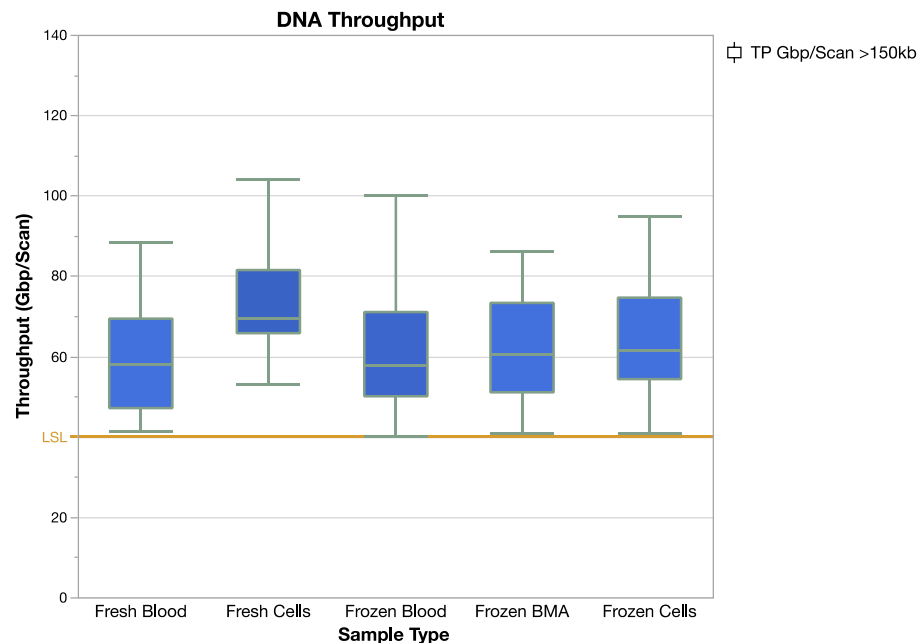
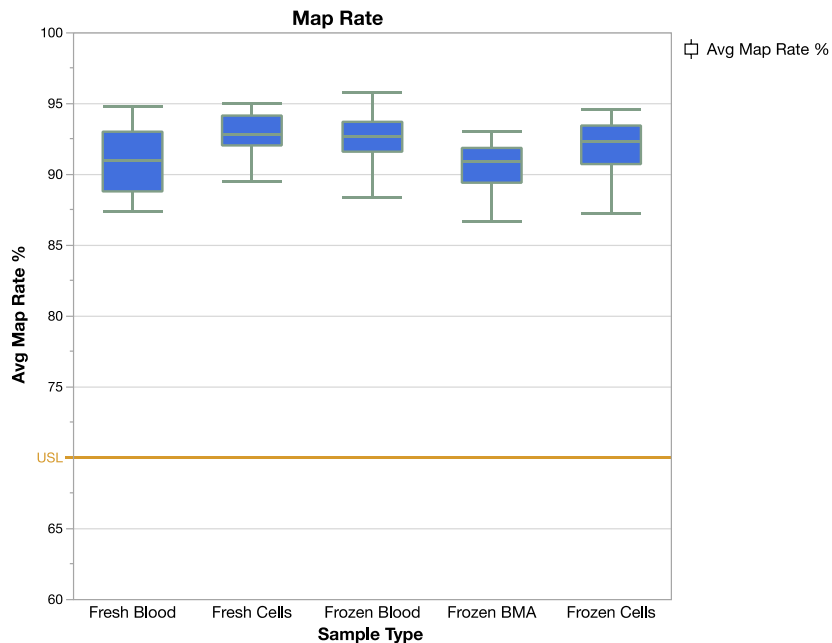
Sample Preparation Generation 2 on Long String Data

QC Metrics by Sample Type: Molecule Size and Label Density



Sample Preparation Generation 2 on Long String Data

QC Metrics by Sample Type: Map Rate and DNA Throughput



Future Improvements to the Optical Genome Mapping Workflow

End-to-end workflow optimized to deliver faster and higher quality results

Sample Preparation (SP and DLS reagent kits)



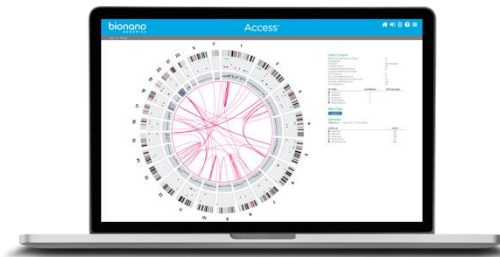
- ✓ Increased robustness
- ✓ Faster sample prep
- In progress More sample types

OGM Data Generation (the Saphyr® System)



- In progress Decreased processing time
- In progress Increased throughput

Data analysis and Interpretation (Access and Solve software)



- In progress Automated decision support
- In progress Facilitated variant interpretation
- In progress Integrated modality analyses

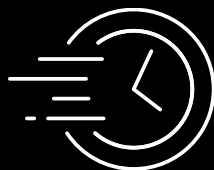
The Future of OGM Just Got Brighter!

Enhanced usability, speed, and reproducibility



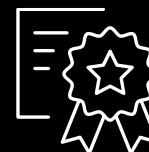
Workflow Automation

Automation friendly sample prep kits accelerates OGM workflow



Time to Result

Enhanced labeling kits + SW accelerates analysis



Improved Reproducibility

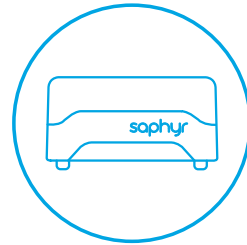
Enhanced sample prep kits and Saphyr® kits for cleaner DNA and on-board stability

How To Get Bionano OGM Data



Get the Consumables

Run samples in-house with Saphyr[®] reagent rental, which includes everything you need.



Get the Saphyr[®] System

Purchase the Saphyr[®] System, DNA isolation / labeling kits, Saphyr[®] Chips and Bionano Compute On Demand

“OGM reveals more of what matters: more clinically relevant SVs leading to higher success rates and resolution of unsolved cases.”

*Dr. Laïla El-Khattabi
Hôpitaux de Paris
(AP-HP)-Université de Paris*



Thank You.

bionano™