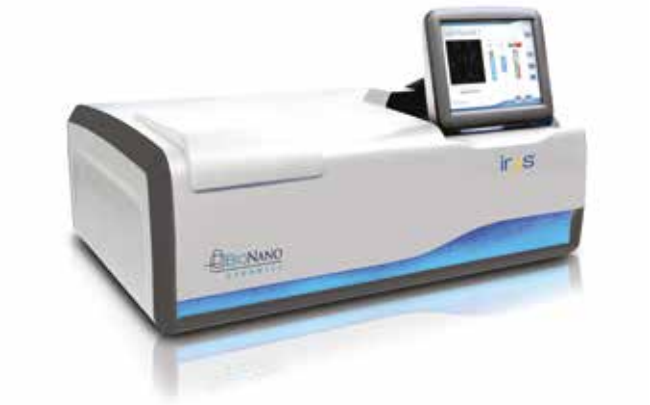
# Irys

## Single-molecule next-generation mapping

BIONANO GENOMICS



## Go beyond the genome you know

### More Understanding, Not Just More Data

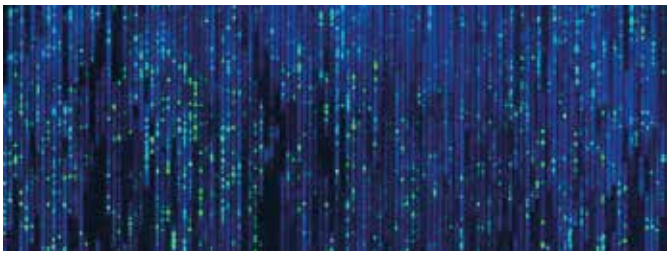
Despite remarkable access to massive amounts of relatively inexpensive short reads of sequence data, biologists still don't have sufficient tools to easily view the full context and architecture of the expansive genomic landscape. It is becoming increasingly clear that this long-range view of contiguity is essential for understanding structural variation.

### Long DNA Molecules

At the heart of the Irys System is a patented chip technology with micro- and nanostructures that unravel randomly coiled DNA and feed it into nano-scale channels. These NanoChannels prevent semi-flexible molecules from folding back or tangling so they can be directly imaged in a massively parallel array (Figure 1). IrysPrep reagent kits label long molecules of DNA at specific sequence motifs to generate signature patterns that uniquely identify the genomic region and surrounding context.

### The Genome in Context

Visualizing whole genomes at the single-molecule level eliminates bias induced by amplification and shearing, while overcoming the ambiguities and time investment that hinders large-scale assembly. A whole-genome physical map provides scaffolding to make sequencing experiments more efficient and complete. Long-range genome architecture is preserved in the maps to identify biologically significant structural variants.



**(Figure 1)** Single-molecule imaging of DNA up to megabase-length

**Long Molecules:** Intact DNA molecules, hundreds of kb long, span repeats and variants

**High-Quality Data:** Single-molecule, high-resolution imaging of uniformly stretched, linearized DNA

**Scalable Open Platform:** Automated multicolor IrysChip imager for use with IrysPrep kits or user-developed labeling scheme

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*Accelerate your biomedical research*

# Irys System—The Complete Solution

### Irys Instrument
Effortlessly linearize DNA and analyze genome data with automated, single-molecule imaging of extremely long DNA.

### IrysChip
The heart of the Irys System, proprietary NanoChannels uniformly stretch DNA for high-throughput analysis of genomic architecture.

### IrysReagents
Extract and label long DNA for use in Irys *de novo* assembly and structural variation detection.

### IrysView Software
Powerful analysis software for *de novo* assembly, structural variation detection, visualizing and exporting run results.

### IrysSolve Computational Solutions
IrysSolve is our streamlined data analysis pipeline implemented on a variety of computational solutions.

# Applications

## Structural Variation Analysis
Irys is particularly well suited for analyzing challenging structural variation, including inversions, that can have functional significance in essentially any species **(Figure 2).** NGS suffers when short reads collapse CNVs in addition to complications inherent to de novo assembly. Older methods, such as array-CGH, lack positional information and depend on probes limited only to model species reference sequence. Irys overcomes these limitations by creating, de novo, a genome-wide view of structural variation with read lengths long enough to capture the wide range of variant sizes. By visualizing the genome in its native state, positional information, such as balanced translocations and the localization of duplication insertion points, is readily apparent **(Figure 3).** Furthermore, using single-molecule detection, rather than aggregate measures in NGS and CGH, means subpopulations can be detected directly.

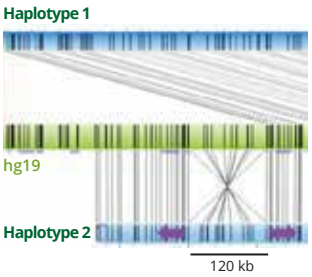
## NGS Anchoring and Scaffolding
Irys facilitates de novo assembly to higher levels of completion, in less time, by providing high-resolution genome maps to scaffold NGS data. Genome maps orient contigs and size gaps with long-range connectivity bridging across repeats and other complex elements that break NGS assemblies **(Figure 4).** Other restriction-based mapping methods do not use molecules long enough to capture complex repeats, whereas the proprietary Irys nicking and labeling chemistry retains very long molecules intact. These long molecules allow us to assemble contiguous maps and visualize inheritance of genes in a heterozygous individual who receives alleles from each parent with different copy number variations **(Figure 5).** Without the ability to capture very long molecules, repeats may collapse upon assembly just as in any short-read method.

## Assembly Validation
Irys genome maps represent a powerful orthogonal validation method for assembled genomes. In IrysView, discrepancies from imported NGS assemblies are readily visible in a graphical browser and listed in tabular form for deeper exploration to individual molecule images, allowing one

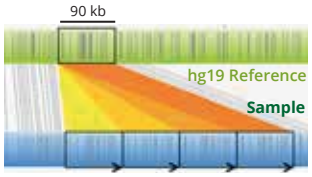
## System Performance

| Parameter | Value |
|---|---|
| Flowcells per IrysChip | 2 |
| Cycles per Flowcell | up to 26 |
| Runtime per Cycle | 55 min |
| Filtered Throughput per IrysChip (24 hrs)* | 96 Gbp |
| DNA labeling Input Amount* | 300 ng |
| DNA Labeling Time (total \| hands-on)* | 1.5 day \| 3 hr |
| Average Labeled Molecule Size (post filter)* | 225,000 bp |
| Consensus Label Error Rate (FP/FN)** | ~1% |
| Consensus Label Precision** | 150 bp |

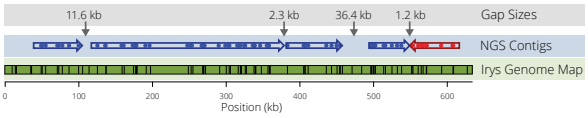
*for supported samples
**at 50X coverage, for consensus segments 25 kbp or less



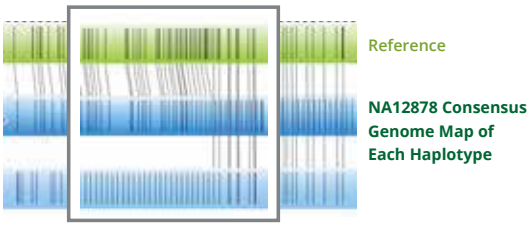

**(Figure 2) Genome-Wide CNVs.** CNVs of a wide range of sizes are automatically detected across the genome from consensus maps. Inversions and other complex rearrangements are identified based on distinct label patterns.




**(Figure 3) Tandem Amplification.** Copy number variation is readily detected with high resolution, including positional information to determine context and potential impact in the genome.




**(Figure 4) NGS Scaffolding.** The genome map provides anchoring information to order and orient five NGS contigs in the human MHC region, to generate a more complete scaffold and to accurately size gaps for finishing (Lam et al, Nature Biotech, 2012).




**(Figure 5) Directly View Repeats and CNVs.** Repetitive regions in the Lipoprotein(a) gene relate to health, where higher copy number is beneficial. Direct measurement of very long molecules helps to accurately assemble complex repeats such as the Lipoprotein(a) locus. Genome maps span the entire repeat region and identify the haplotype-specific repeat copy number while also showing that one heterozygous individual received 39 variants of the LPA locus from one parent but only 26 from the other.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