Irys System
A game-changing genomics platform

More Understanding, Not Just More Data

The past several years of genomics have been dominated by advances made in next-gen sequencing that enabled vastly higher throughput data generation. Despite remarkable access to massive amounts of relatively inexpensive short stretches 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. Further, genomic complexity in the form of repeats and structural variation limits the ability to accurately assembly genomes to interpret genes and functional elements correctly. The Irys™ System overcomes these problems with a new approach to capturing data in the form of single-molecule imaging of extremely long intact DNA.

Long DNA Molecules

At the heart of the Irys System is a patented chip technology with micro- and nano-structures 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. Integrated software interprets the resulting "dots on a string" images to identify sequences and build consensus genome maps. Following imaging, molecules are flushed from the nanochannel arrays and a new batch of molecules are brought in. This dynamic, multi-cycle feature of Irys allows for high-throughput linearization and imaging of several gigabases of DNA per hour.

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. Extremely long "reads" generated by Irys are essential for sufficient sequence-uniqueness to unambiguously map or connect functional elements, anchor contigs, size gaps, quantify repeats, identify copy number variants, inversions, and localize translocations.

Fully informing genome analysis

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 multi-color irysChip™ imager for use with irysPrep kits or user-developed labeling schemes
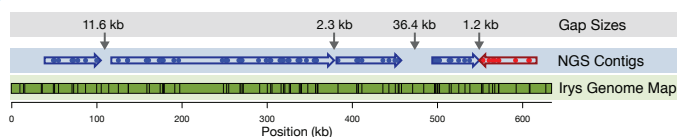
Figure 1: Single-molecule imaging of DNA up to megabase-length

100 kb

hg19 Reference

Sample
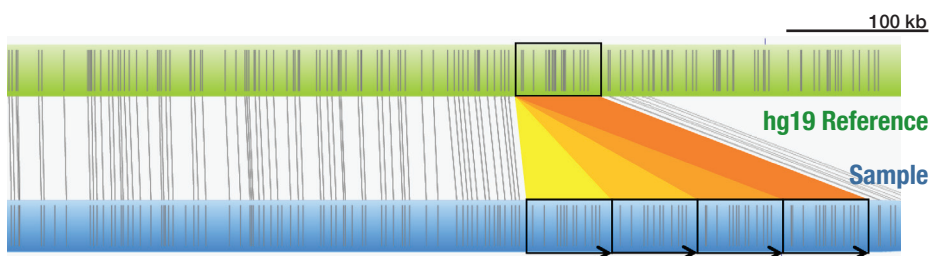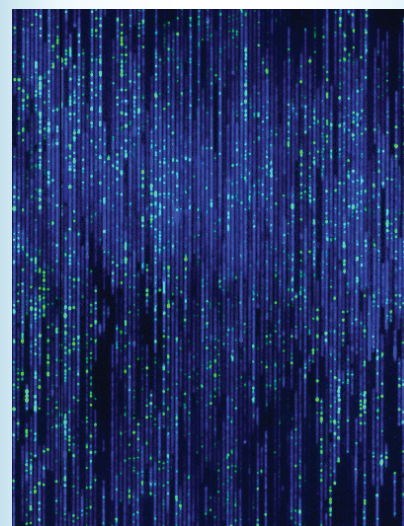
Figure 2: Tandem Amplification in Human *De Novo* Assembly
Copy number variation is readily detected with high resolution, including positional information to determine context and potential impact in the genome.

Figure 3: 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 accurately size gaps for finishing (Lam et al, Nature Biotech, 2012).

Figure 4: Reading Through Repeats to Size Gaps. Direct measurement of very long molecules is needed to accurately assemble complex repetitive regions such as the centromere of yeast, which was only partially assembled in the reference.

Applications

Irys empowers a host of applications that were previously too expensive, time consuming, or limited by short-read technologies. IrysPrep kits and IrysView™ analysis software support structural variation detection, assembly validation, and scaffolding of NGS data and enable virtually unlimited user-developed applications utilizing long-read single-molecule data.
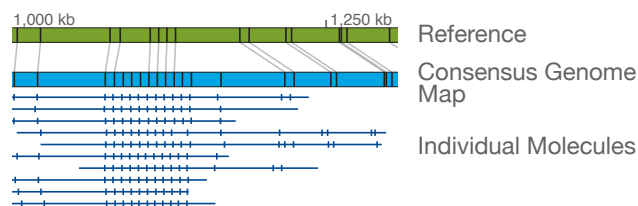
Structural Variation Analysis

Irys is particularly well suited for analyzing structural variation in essentially any species. 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 2). Furthermore, using single-molecule detection, rather than aggregate measures in NGS and CGH, means subpopulations can be detected directly.

NGS Anchoring

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 3).

Other restriction-based mapping methods lose small fragments (e.g., in repeats), whereas the proprietary Irys single-strand nicking and labeling chemistry retains long molecules intact (Figure 4). Without this ability, 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 to quickly design additional confirmation or sequencing experiments.

More Information

For more information about the system or to place an order, please contact sales@bionanogenomics.com or visit www.BioNanoGenomics.com.

Parameter	Value
Flowcells per chip	2
Cycles per flowcell	Up to 24
Runtime per cycle	33 min
DNA labeling time (total / hands-on)	1.5d / 2hr
DNA labeling input amount	300–635 ng
Raw throughput per IrysChip	50–100 Gb
Consensus error rate (FP/FN)*	< 1%
Label site precision* (< 25kb segment)	±150 bp

*at 50-fold depth

Table 1: System Performance

irysPrep *Reagents*   **irysChip** *Consumable*   **irys** *Instrument*   **irysView** *Software*

Figure 5: Irys is a Complete Solution. Proprietary labeling reagents and analysis software support unlimited applications.