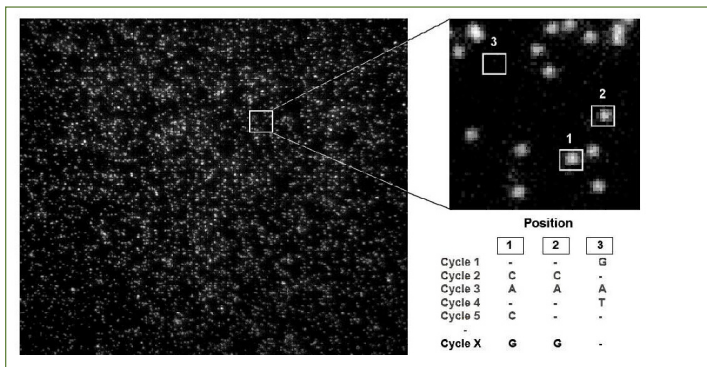


True Direct DNA Measurement

Helicos brings you the first True Single Molecule Sequencing (tSMS)[™] approach to genomic analysis – an advanced technology capable of directly measuring single DNA molecules, without amplification and biases, the cost and complexity that often accompany it. Offering unparalleled quantitative accuracy, simplicity and scale that no other genetic analysis technology can match, Helicos tSMS technology signals a new era of quantitative, functional genomics.

What is tSMS[™] Technology?

The tSMS technology is a powerful new method to accurately interrogate billions of single strands of DNA (or RNA) in parallel by directly detecting single nucleotide incorporations on each of the single strands. This unprecedented detection sensitivity is made possible by Helicos' proprietary ultra-low background surface chemistry, sequencing reagents and imaging technology.

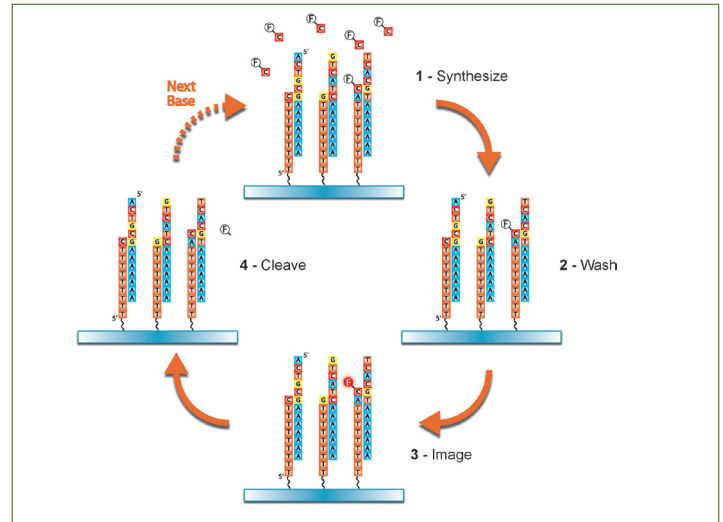


An image taken by the HeliScope Single Molecule Sequencer. Inset shows a close-up view of individual single molecules that incorporated a fluorescent "G" nucleotide in this cycle.

How tSMS Technology Works

Original DNA samples are first fragmented, the DNA double-helix is melted into single strands and a polyA tail is added to these DNA molecules. Billions of these single DNA molecules are captured on a proprietary surface within a flow cell and serve as templates for the sequencing-by-synthesis process.

Fluorescently-labeled nucleotides – the building blocks of DNA: C, G, A or T – are added one at a time and incorporated into the growing complementary strand by a DNA polymerase enzyme, based on the sequence of the template. Unused nucleotides are washed away. Upon illumination with a laser, the incorporated nucleotides emit light that is



After hybridization of modified genomic DNA to oligo dT capture primers inside the flow cell, acquisition of template positions, and cleaving the fluorescent templated label, the tSMS process is a cyclical process involving multiple rounds of (1) synthesis using labeled nucleotides, (2) washing, (3) imaging, and (4) cleaving the fluorescent label until the desired read length is achieved.

detected by the HeliScope[™] Single Molecule Sequencer. The HeliScope Sequencer captures thousands of images across the flow cell surface to record which strands incorporated which nucleotides. These images containing tens of thousands of single fluorescent molecules are akin to star fields, as pictured at right. Once the imaging of the flow cell is complete, the fluorescent label is removed before the next nucleotide is added to continue the cycle. Tracking nucleotide incorporation on each strand determines the exact sequence of each individual DNA molecule.

The Advantages of True Single Molecule Sequencing

Helicos tSMS technology is an entirely novel approach to DNA sequencing and genetic analysis and offers significant advantages over both traditional and "next generation" sequencing technologies. Helicos offers the first universal genetic analysis platform that does not require amplification. Pursuing a single molecule sequencing strategy simplifies the DNA sample preparation process, avoids PCR-induced bias and errors, simplifies data analysis, tolerates degraded samples.

	Sanger Sequencing	"Next Generation" Sequencing	Helicos True Single Molecule Sequencing
Information Capacity:	100's of reads per experiment	100,000,000's of reads per experiment	1,000,000,000's of reads per experiment
Scalability of Sample Preparation:	A few at a time	A few at a time	Hundreds at a time Easily automated
Amplification:	Required	Required	No amplification True direct DNA measurement
Accuracy:	Analog base calls Sequencing biases Not quantitative	Analog base calls Sequencing biases Not quantitative	Digital base call No amplification biases Digital quantitation

The Helicos® Genetic Analysis Platform

The Helicos® Genetic Analysis Platform harnesses advanced chemistry, engineering and data analysis power to perform True Single Molecule Sequencing. The Platform consists of the complete Helicos® Genetic Analysis System – which includes the HeliScope™ Single Molecule Sequencer, the HeliScope™ Sample Loader and the HeliScope™ Analysis Engine – as well as Single Molecule Sequencing (SMS) Grade™ reagents, precision flow cells and bioinformatics software, to support genetic analysis applications such as whole genome resequencing, targeted resequencing and digital gene expression.

The Helicos® Genetic Analysis System

As the heart of the Helicos Genetic Analysis System, the high-throughput **HeliScope Single Molecule Sequencer – the world's first DNA Microscope** – performs

tSMS chemistry and captures images to observe single molecule sequencing reactions for billions of molecules at once. The HeliScope Analysis Engine simultaneously processes the images to produce accurate sequence data for those molecules in near real time. This highly parallel and efficient workflow opens new research avenues and dramatically reduces the time needed to complete complex experiments.



SMS Grade™ Reagents and Precision Flow Cells

Helicos has developed SMS Grade reagents and buffers that meet strict purity and stability standards to achieve the highest level of performance and accuracy.

Now is the time to take those quantitative genome-wide experiments off of your wish list and perform them with the accuracy, simplicity and scale that only Helicos can offer.

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tSMS reagent kits are specially formulated for single molecule biochemistry imaging and consist of:

- Very bright fluorophores that allow single molecules to be detected
- A unique reagent cocktail that enhances and sustains fluorophore brightness
- A highly efficient and specific DNA polymerase, capable of incorporating modified nucleotides with high fidelity
- Virtual Terminator™ nucleotides to allow accurate sequencing of single nucleotide repeats (homopolymers)
- Precision flow cells with proprietary surface chemistry that is highly resistant to non-specific binding, providing extremely high signal to background ratios for single molecule imaging

Unbiased Genomics

Genomics research has entered a new age, in which deciphering the genome's effect on biology and medicine requires not only the detection of mutations and sequence variation, but also understanding the dynamic nature of genome biology. Accurately measuring the levels at which genes are expressed, promoters are methylated, and DNA-binding proteins interact with the genome and combining this information with sequence variation information has become a new paradigm for genome biology research. Nevertheless, the technologies used for such measurements have always relied on complex sample preparation techniques, such as amplification and ligation that alter the fundamental representation of nucleic acids in biological samples, resulting in unpredictable biases, and requiring large amounts of starting material.

As the world's first and only commercially available, highly-parallel single molecule sequencing technology, the Helicos Genetic Analysis System allows scientists to analyze the sequence and measure the abundance of nucleic acids directly for the first time. Researchers can finally explore genome regulation and function without the artifacts and biases introduced by amplification-based techniques. Furthermore, they can now perform these experiments on minute amounts of biological samples, without having to amplify.

These technical benefits open up new opportunities in functional and translational genomics and diagnostics by enabling breakthrough, integrative experiments with small numbers of cells - areas that stand to benefit include stem cell research, comprehensive tumor characterization and the analysis of circulating cells or nucleic acids for early detection of disease.