

Next Generation DNA Sequencing For Research

High throughput long and short read sequencing solutions to accelerate your experimental goals



Beckman Coulter Genomics is pleased to offer comprehensive Next Generation sequencing services designed to meet the evolving DNA sequencing needs of academic, biotechnology and pharmaceutical researchers worldwide. A complete suite of the most advanced DNA sequencing technologies has been implemented to offer clients a wide array of services to support a broad scope of sequencing needs. This multi-platform Next Generation suite allows Beckman Coulter Genomics to address the data requirements of each individual research goal.

Next Generation Sequencing Platforms

- 454 Life Sciences* Genome Sequencer* FLX (GS FLX) Titanium
- Applied Biosystems SOLiD* v3
- Illumina* Genome Analyzer Ix (GAIIx)

Next Generation Sequencing Capabilities

- Long-read or short-read sequencing
- *De novo* sequencing or resequencing
- Single, paired-end and mate paired sequencing
- Finished genome sequencing incorporating Sanger primer walking

Next Generation Sequencing Applications

- Whole genome *de novo* and resequencing
- SNP sequencing including rare mutation detection
- Transcriptome sequencing for cDNA and smallRNAs
- ChIP-SEQ
- Metagenomics
- Targeted resequencing

Maintaining Quality on the Cutting Edge

Next Generation sequencing technologies are new sequencing technologies. Beckman Coulter Genomics recognizes that characteristics distinguishing different Next Generation approaches may be subtle yet critical to your experimental outcome and has made it a priority to understand these nuances.

Responsible Strategies - Most projects are discussed in terms of achieving the data required rather than the number of runs to be purchased. By anchoring a strategy around your research objective rather than the per run throughput we can provide the best path for you to achieve the results you need.

Reliable Services - Next Generation sequencing platforms are maintained current to the latest upgraded specifications from the vendors. New applications, upgraded equipment and improved protocols are carefully validated prior to release to ensure the same data quality and provider integrity long associated with Beckman Coulter Genomics award winning Sanger sequencing services.

Project Support - Beckman Coulter Genomics sequencing experts consult with clients on Next Generation sequencing needs to ensure the most appropriate technology and experimental approach are combined with sufficient sequencing depth to achieve the desired goals. Clients are assigned a dedicated Project Manager who becomes a technical contact available for communication with the client throughout the project lifecycle.

Data Management - Every measure is taken to be certain that Next Generation clients understand and are able to take full advantage of the data generated by the new technologies. Standard deliverables include consensus genome assemblies, individual reads with associated quality scores¹ and SNP calling. Depending upon the project scope data can be accessed via secure FTP site or is received on a portable hard-drive.

Using validated methods to produce high-quality data
Transform high-quality raw data into biologically meaningful information

We Get It.

454 Life Sciences GS FLX Titanium Sequencing

The 454 GS FLX sequencing platform run with Titanium reagents yields read lengths yet unmatched by other Next Generation sequencers. 454 sequencing has established utility in a variety of published applications from *de novo* whole genome sequencing to ultra-deep sequencing of PCR[†] amplicons for rare mutation detection.

About 454 Titanium Sequencing and Your Experiment

- Improved accuracy through homopolymers over GS FLX standard reagents.
- Long read lengths uniquely suited to *de novo* sequencing.
- Mate paired libraries with 3 kb inserts for improved genome assemblies.
- Overnight run times for fast turn around times.
- Multiplexing capabilities for flexible project design.

Read lengths - Averaging >350 - 400 bp suitable for *de novo* sequencing projects

Throughput (reads) - ~1 million reads per run

Single read accuracy - 99% at the 400th base and higher for preceding bases

Consensus accuracy - >99.99%

Quality scores - Phred equivalent quality scores

NCBI SRA Data Formats - SFF data accepted by NCBI since 2005

Applied Biosystems SOLiD v3 Sequencing

Di-base interrogation of DNA templates unique to SOLiD sequencing results in high confidence outcomes for variation detection. Beckman Coulter Genomics initiated the development of the AB SOLiD sequencer and is now a certified provider of SOLiD sequencing services. Beckman Coulter Genomics experience with the SOLiD sequencing platform surpasses that of any other sequencing provider.

About SOLiD v3 Sequencing and Your Experiment

- Ability to run up to 8 samples in physically separated segments.
- Mate paired libraries with 3 kb inserts for improved genome assemblies.
- Ultra-high per run throughput of version 3 valuable for counting applications such as Digital Gene Expression.
- Color space analysis with AB proprietary software for high confidence SNP calls.

Read lengths - 50 bp fragment, 25 bp and 35 bp paired

Throughput (reads) - >160 million reads per slide, fragment

System accuracy - >99.94%

Consensus accuracy - 99.999% at 15x coverage

Quality scores - NA

NCBI SRA Data Formats - SOLiD Native or SRF

Illumina GAllx Sequencing

With the highest per day throughput of the new technologies and a simple template amplification process simplifying multi-sample runs the Illumina GAllx platform is well-suited for many research projects. Beckman Coulter Genomics is a CPro certified provider of Illumina sequencing.



About Illumina Sequencing and Your Experiment

- Ability to run up to 7 samples per experiment in physically separated channels.
- Paired end and mate paired sequencing approaches.
- Mate paired libraries with 3 kb inserts for improved genome assemblies.
- Active community of Illumina users publishing advances in top journals and developing analysis tools.

Read lengths - 36 bp, 50 bp or 75 bp for fragment or paired sequencing

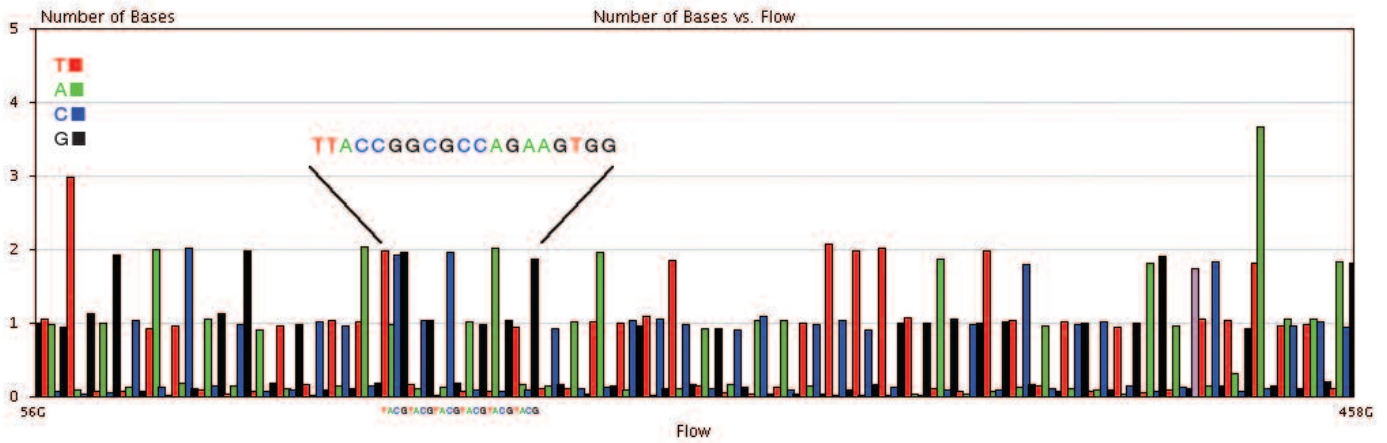
Throughput (reads) - >120 million reads per run, fragment

Single read accuracy - >98.5% per base at 2x 50 bp yielding ≥80% perfect reads

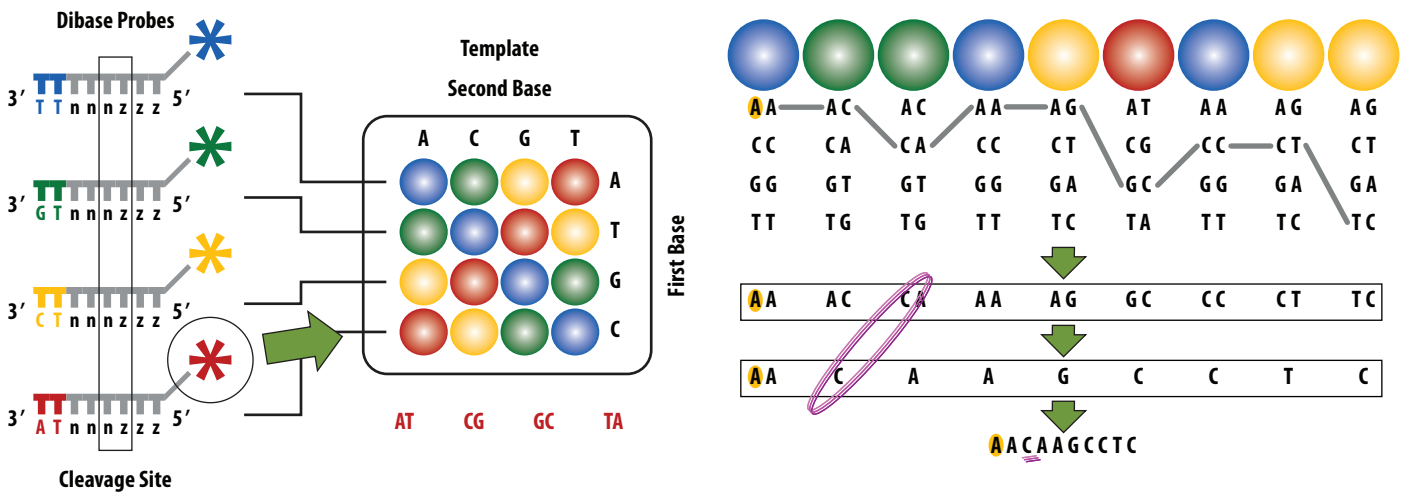
Consensus accuracy - >99.99% at 3x genome coverage

Quality scores - Phred equivalent quality scores, 70-85% of base calls score Q ≥30 at 50 bp

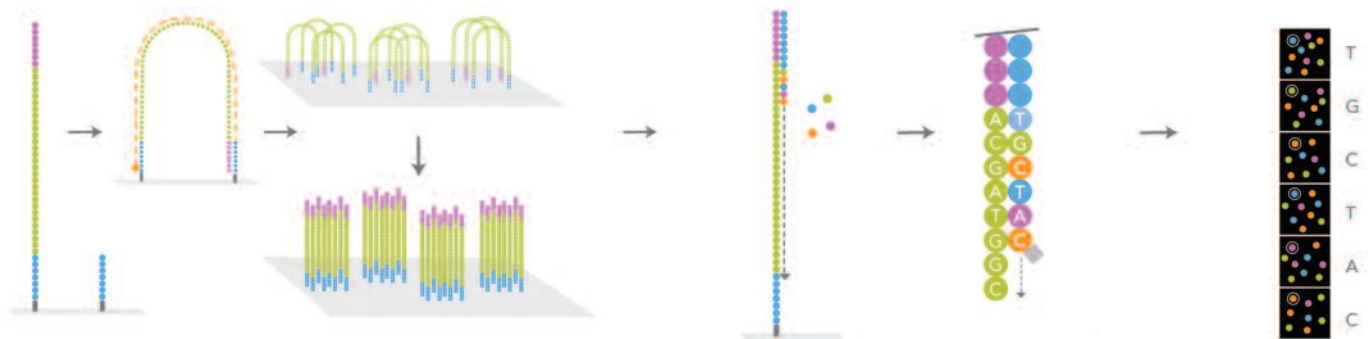
NCBI SRA Data Formats - Illumina Native or SRF



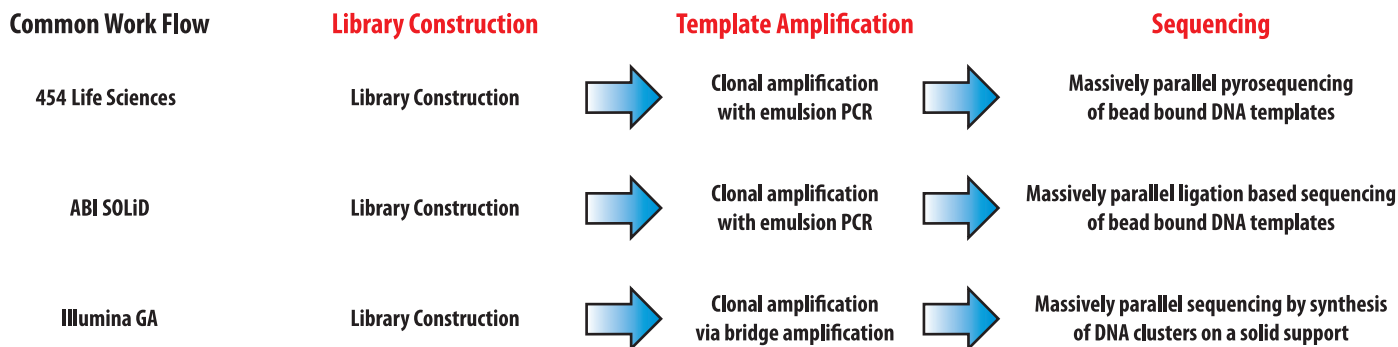
Flowgrams visually depict the signal intensity associated with base calls made for each nucleotide flow in a 454 GS FLX sequencing run. Relative peak heights distinguish single base calls from homopolymers. Base calls shown above the flowgram illustrate the base calls in a sequencing read associated with six cycles of the four nucleotides in the order TACG. Shifts in flowgram patterns reflect high confidence SNP detection in single reads.



The AB SOLiD sequences DNA via a unique ligation-based interrogation of a single stranded template with fluorescently labeled probes. Each probe decodes two consecutive bases with each round of sequencing shifting the probes set one base at a time. Anchoring the sequence at a known first base, in this case an A, the color-coded pattern of a DNA sequence can only be properly translated to base space through one logical path. Analysis of SOLiD data is best performed in color space to leverage the power of the dual interrogation of each position in the template DNA strand.



Illumina sequencing depends upon an automated bridge amplification process unique to the GAllx technology. The bead-free "Cluster Generation" process is walk-away and user friendly enabling Beckman Coulter Genomics to easily prepare multiple templates for a single machine run. During sequencing on the Illumina GAllx clusters are exposed to all four nucleotides per round of sequencing though reversible terminators limit strand incorporation to one nucleotide. Every sequencing read therefore grows uniformly to consistent read lengths directly dependent upon the number of sequencing cycles selected.



Next Generation sequencing technologies share a common work flow requiring Library Construction and Template Amplification followed by Sequencing. Adaptors for library construction and the combination of template amplification and sequencing approaches are unique to each platform. It is the distinguishing aspects of the Next Generation technical approaches that delineate their power relative to your individual research project.

Next Generation Sequencing 101

Next Generation technologies share a common work flow.

Library Construction - Samples are sheared and adapted with appropriate primers suited to the chosen technology.

Template Amplification - In preparation for sequencing, adapted templates, or libraries, undergo amplification resulting in single molecule templates being clonally amplified.

Sequencing - Clonal amplification results in millions of DNA strands that are sequenced in phase rendering the conglomerate light signal, whether from a fluor in SOLiD and Illumina sequencing or from chemiluminescence in 454 sequencing, detectable upon successful recognition of the next base in the DNA sequence.

Data Analysis - Base-calling and quality scoring, where applicable, is performed by proprietary Next Generation vendor software tools optimized for the individual platforms. All Next Generation sequencing data is eligible for submission to NCBI's Short Read Archive (SRA).

Applications of Next Generation Sequencing - Each of the new technologies offers fragment and paired sequencing approaches. Depending upon the nature of your research question the unprecedented high-throughput of Next Generation technologies can be devoted to horizontal genomic coverage or to vertical coverage such as deep sampling of metagenomic samples, PCR products or small RNAs. Beckman Coulter Genomics has applied Next Generation sequencing techniques to diverse templates from genomic DNA to cDNA to PCR amplicons derived from an assortment of organisms ranging from algae to pine, from bacteria to human.

Complete Solutions from Discovery to Validation

Combine DNA sequencing with other Beckman Coulter Genomics services for complete research solutions. Use a hybrid approach supplementing Next Generation whole genome shotgun sequencing with proven Sanger finishing strategies, including custom primer walking, to reach publication quality on your whole genome sequence. Apply your SNP discovery data to large scale genotyping studies. Use your newly sequenced reference transcriptome to design high-throughput microarray experiments. Initiate your experiment with DNA and RNA extraction services. Contact Beckman Coulter Genomics to discuss complete solutions for your research project.

¹ Availability of quality scores varies by technology.

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† The PCR process is covered by patents owned by Roche Molecular Systems, Inc., and F. Hoffman-La Roche, Ltd.

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For more information, please visit our website at www.beckmangenomics.com or contact your local sales representative.

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