PacBio

Next-level discovery

Setting a new standard for short reads with the Onso™ system

- Up to 15× higher accuracy than other benchtop sequencers
- Extraordinary sensitivity
- Reduced cost per sample
- Seamless workflow integration

What does Q40+ mean for you?

Powered by **sequencing by binding (SBB™) chemistry**, the Onso system delivers groundbreaking short-read sequencing performance with accuracy at 90% Q40+. This 15× improvement in accuracy translates to **increased sensitivity needed for rare variant detection, significantly reduced sequencing requirements, and overall increased throughput at lower cost per sample.**

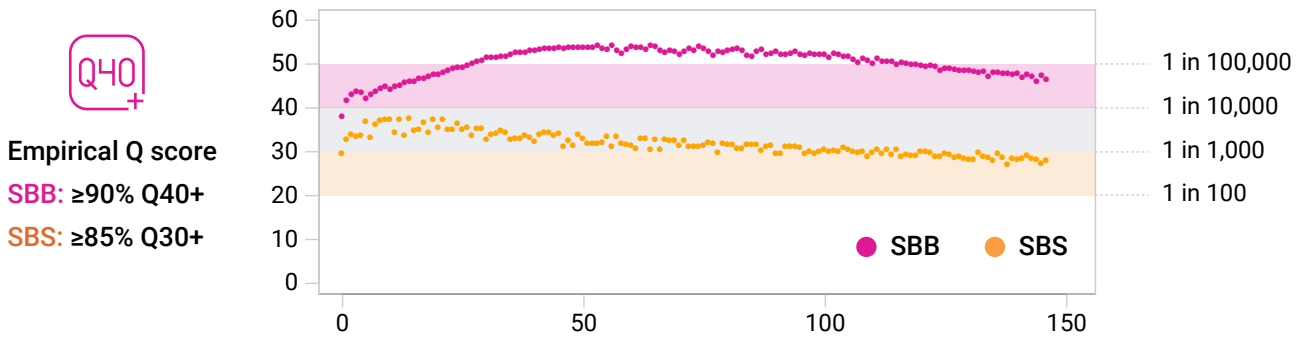


Figure 1. SBB consistently achieves Q40+ quality scores, relative to the diminishing scores of SBS to <Q30 after 100 cycles.

The heightened sensitivity enabled by the Q40+ accuracy of SBB technology allows for nearly twice the sensitivity for rare variant detection at equivalent sequencing depth compared to SBS (figure 2A) or better sensitivity with 4-fold less sequencing (figure 2B) compared to SBS.

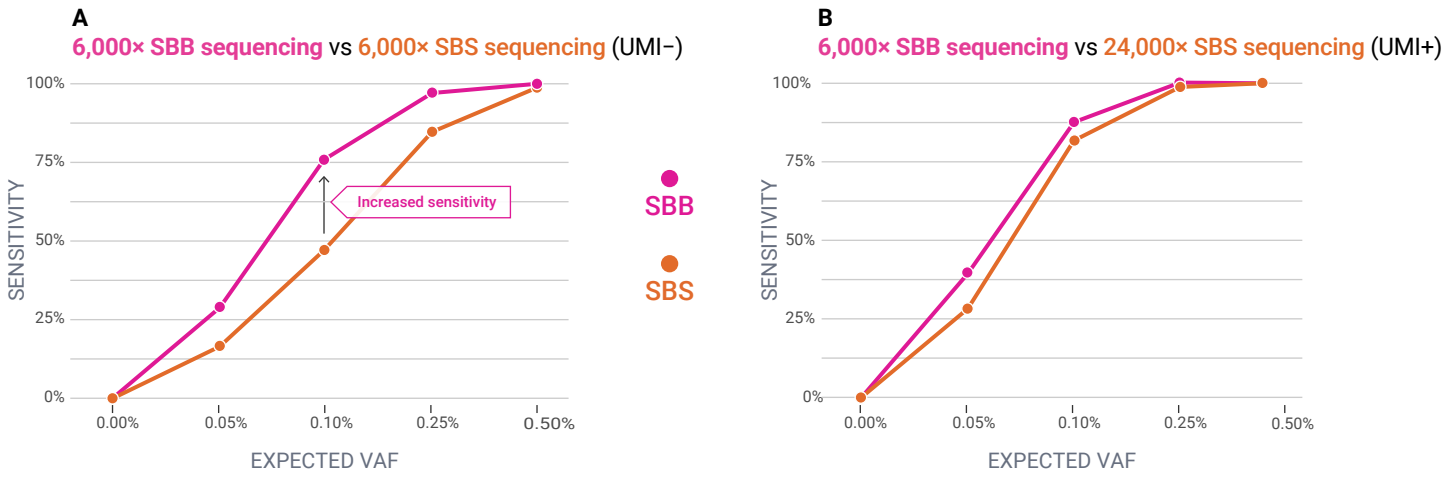


Figure 2. Variant detection performance was tested for SBB and SBS sequencing with known variants in ten genes across five variant allele frequencies. (A) 6,000× SBB UMI- vs 6,000× SBS UMI-, (B) 6,000× SBB UMI+ vs 24,000× SBS UMI+. Adding UMI-based deduplication increases Onso performance even further (SBB in panel A vs in panel B).

What can you do with the Onso system?

ctDNA detection for liquid biopsy research

Liquid biopsy, a noninvasive assay for circulating tumor DNA (ctDNA) in blood and other fluids, holds the promise to revolutionize research on cancer detection and monitoring. Because ctDNA variants often occur at very low frequencies, their detection requires ultrasensitive technology that can best be provided by SBB chemistry.

Distinguish the variant from the noise

Since higher Q scores mean a higher signal-to-noise ratio, the Q40+ accuracy of the Onso system enables confident variant detection with fewer confounding errors. Sequencing errors in SBS sequencing make it almost impossible to distinguish the variant from the noise (figure 3A), whereas sequencing on the Onso system makes the true variant clear (figure 3B).

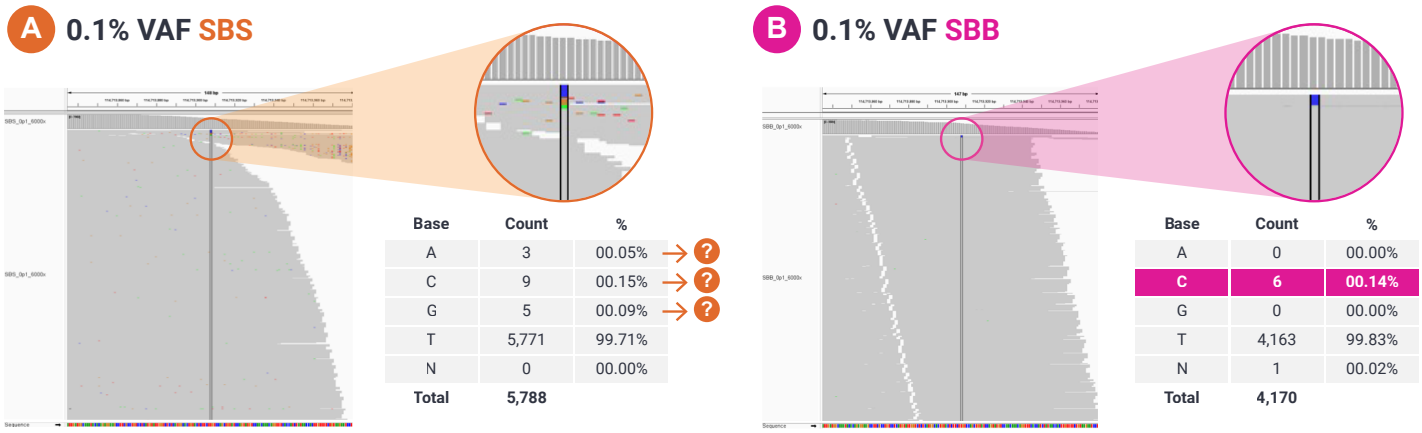


Figure 3. IGV output of SBS (A) and SBB (B) of example NRAS Q61R variant from the SeraCare ctDNA complete mutation mix at 6,000 coverage.

What will you discover?

Cancer research

Detect low-frequency mutations in cancer research applications, including in difficult-to-sequence regions

Infectious disease

Discover low-level drug-resistance mutations

Gene editing research

Identify novel biomarkers and confirm editing outcomes

Single cell

Understand cell heterogeneity with compatible 10x single cell DNA and RNA libraries

The difference is in the chemistry

Unlike traditional SBS technology, SBB uses optimized conditions for each phase of the sequencing cycle, nearly eliminating raw read errors. It is this difference in chemistry that constitutes a breakthrough in sequencing accuracy.

How does SBB technology work?

SBB consists of four primary steps: ***initiation***, ***interrogation***, ***activation***, and ***incorporation***. In a critical departure from SBS, SBB chemistry separates the binding and subsequent extension steps of the sequencing process which eliminates the errors introduced by molecular artifacts.

In a crucial difference from SBS, this tagged base is not incorporated into the DNA string, but is washed away after the signal is captured

Initiate

Sequencing is initiated with a reversible blocker on the 3' end to prevent additional bases from incorporating.

Interrogate

Fluorescently tagged bases flood the flow cell. Once the appropriate base binds, a signal is emitted and measured with the powerful optics of the Onso system.

Activate

Next, the 3' end of the nucleotide is activated via the removal of the reversible blocker.

Incorporate

Finally, the complementary base is incorporated from unlabeled, blocked nucleotides that flood the flow cell. This blocks additional incorporation.

SBB features

No molecular scarring
No residual linker arms left during incorporation

Minimal duplication
Fewer redundant sequences means more useful reads

7× less sample input
Use fewer of your valuable samples

Neglible index hopping
Avoids library misassignments and increases usable reads

These aspects of SBB chemistry make Q40+ accuracy possible

Q40+ accuracy
Extraordinary error rate of only 1 in 10,000 bases or less

Library prep

The Onso library prep kits are used to create libraries that are optimized to support the Q40+ sequencing accuracy of the Onso system. These kits benefit from streamlined workflows, including the conversion of existing P5/P7 libraries, that generate complete libraries in as little as three hours.

Workflow

Workflows are available for high-molecular weight (HMW) DNA (figure 4A), and pre-fragmented or degraded DNA (figure 4B).

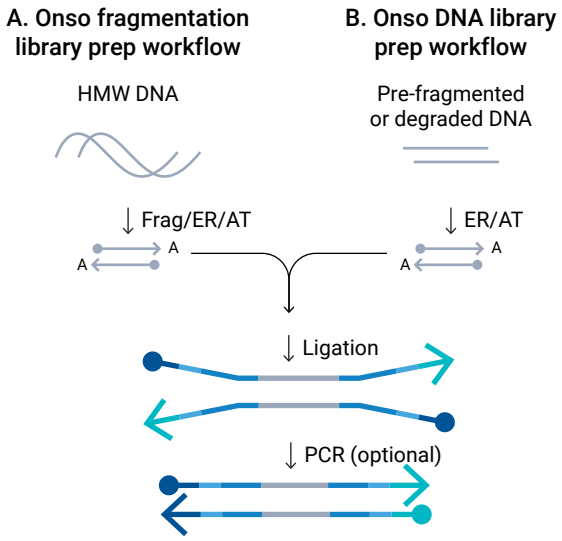


Figure 4. Workflows for the Onso fragmentation library prep kit and the DNA library prep kit.

Key benefits

Performance

- Libraries optimized for Q40+ sequencing accuracy
- Higher conversion efficiency than ligation-based approaches

Ease of use

- Optimized workflow for complete library prep with a single kit in as few as three hours

Flexibility

- Accommodates a wide range of sample types (e.g., fragmented or HMW DNA) and input amounts (10–1,000 ng)

Compatibility

- Supports major short-read applications
- Library conversion kit enables existing P5/P7 libraries to be sequenced on the Onso system
- Seamless integration of Onso libraries with *PacBio Compatible* partners across the sequencing workflow

Libraries optimized for Q40+ accuracy

Sequencing reads generated from Onso library prep kits benefit from greater accuracy than those generated through standard short-read library prep methods (figure 5).

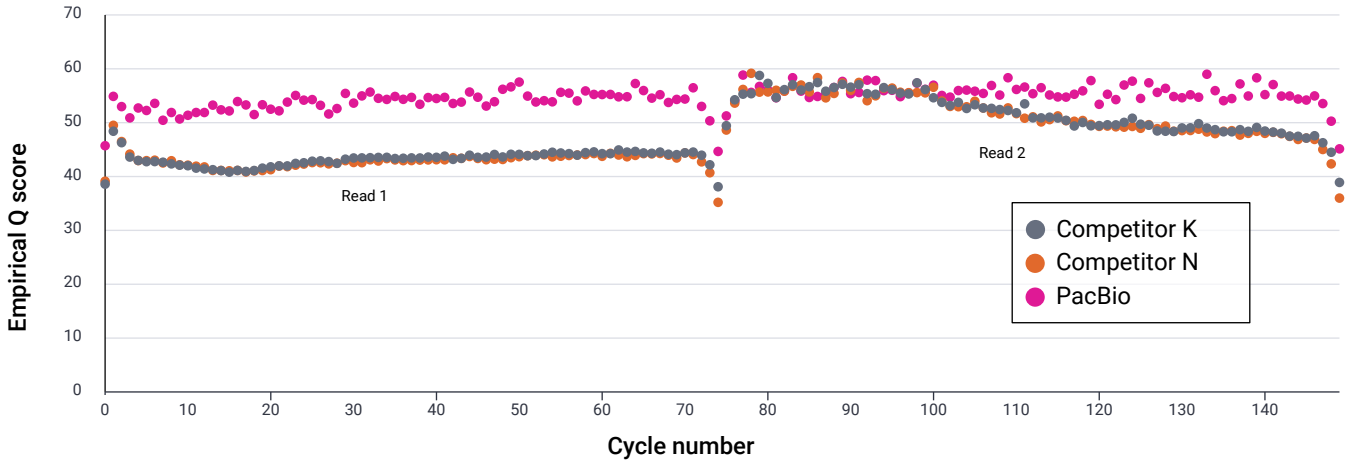
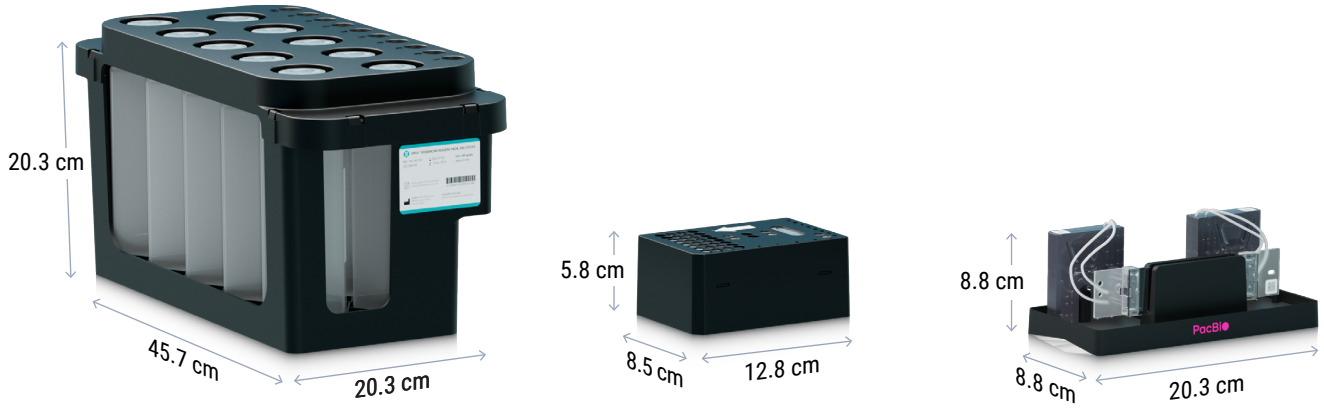


Figure 5. Improved read accuracy with Onso library prep vs competitor kits (competitors K and N).

Fits into your workflow

Onso sequencing consumables and ancillary kits enable a seamless workflow for today's NGS laboratories.



Onso reagent pack, flow cell, and clustering plate.

Three-step loading process

1. Load flow cell into cluster generator
2. Insert reagent pack into sequencer
3. Insert flow cell into sequencer

Minimal hands-on time required for setup

Intuitive user interface allows step-by-step guidance through workflow

Individually accessible flow cell lanes for added loading flexibility

Application specifications

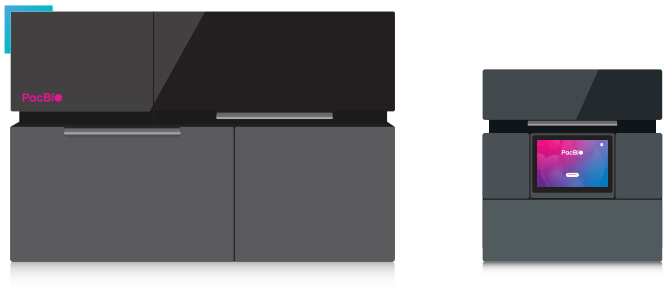
The Onso system is a mid-range short-read sequencer capable of supporting a wide range of applications required for most laboratories.

Sample	Read format	Number of samples/run†
Target enrichment panel (1 Mb, 6,000× mean depth)	2 × 150	20–25
Single-cell RNA-Seq (10K cells, 20K reads/cell)	2 × 100*	2–3
Targeted amplicon panel (160 genes/500× mean depth)	2 × 150	48–60

* Application-specific read format varies; supported by Onso 200-cycle sequencing kit
† Numbers shown are estimates based on expected output per kit. Actual number of samples will vary depending on sample type, quality, and experimental objectives.

The Onso system

The Onso system and cluster generator offer a scalable and flexible benchtop platform that gives you remarkable accuracy and the capability to integrate with existing short-read tools.



Sequencing specifications

Onso reagents	Read length	Reads	Output (Gb)	Run time	Quality score
200 cycle sequencing kit	1 × 200 bp 2 × 100 bp	400–500M (SE) 800–1000M (PE)	80–100	32 hours	≥90% Q40
300 cycle sequencing kit	2 × 150 bp	800–1000M (PE)	120–150	48 hours	≥90% Q40

Ordering information

Product	Part number
Onso fragmentation DNA library prep kit	102-499-100
Onso DNA library prep kit	102-431-400
Onso indexed adapter kit	102-431-700
Onso library amp kit	102-410-800
Onso library quant kit	102-431-800
Onso blocking oligo kit	102-431-600
Onso library conversion kit	102-529-500
Onso indexed library control kit	102-529-900
Onso system	102-837-000
Onso 200 cycle sequencing kit	102-860-100
Onso 300 cycle sequencing kit	102-860-300

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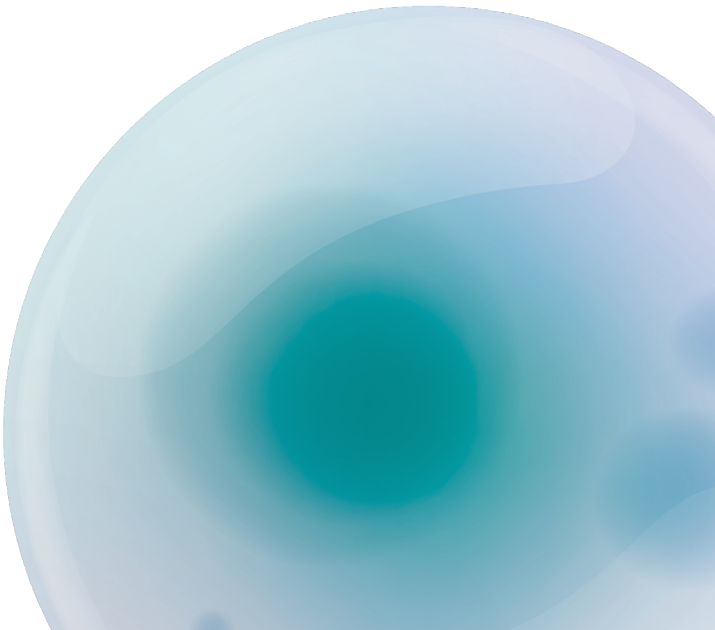

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