The Future is SMRT.....the PacBio RSII and Sequel Systems
RS TECHNOLOGY IMPROVEMENTS – LOOKING AHEAD
Average read length: 10,000 - 15,000 bp
Throughput / SMRT® Cell: 750 Mb – 1.25 Gb
Consensus accuracy: QV50 @30X
NEW FINDINGS REGARDING READ LENGTH LIMITATION

Immobilize the Polymerase/Template complex to bottom of ZMW using proprietary surface chemistry
The polymerase/template complex dissociates from bottom of ZMW thus shortening read length

- Looking at different approaches to solve this.
SAMPLE DATA FROM R&D

R&D Development mean = 32k

Current mean = 20k

Targeting 2016 Release
ACTIVE LOADING – TARGETING H12016

Increasing sequencing yield and reducing variability

- Increase in single loads 10-30% > Poisson
- Increase in read length of 20%
- Single loading over broader input ranges

- Up to 5kb amplicons (e.g., 16S, HLA)
- Implement first on PacBio RS II
  - New template prep, binding and sequencing kits

![Graph showing Single Loading vs Total Loading with Magbead and Active loading data points]
PACBIO RS II CONSUMABLES ROADMAP

- Q4 2015
- Q1 2016
- Q2 2016
- Q3 2016
- Q4 2016
- Q1 2017
- > Q2 2017…

- Active Loading <5kb amplicons
- Chemistry Update
- Active Loading Longer fragments
Sequel System
Introducing the Scalable Platform for SMRT® Sequencing
SEQUEL SYSTEM
THE SCALABLE PLATFORM FOR SMRT® SEQUENCING

Accelerate your research with the most comprehensive view of genomes, transcriptomes, and epigenomes from our higher throughput system. Reduce project costs and timelines as you create higher quality whole genome assemblies and explore the full size-spectrum of genetic variation.

- Based on proven SMRT Technology
- Increased capacity with 1 Million ZMWs/SMRT Cell
- Scalable throughput
- Reduced project time to results
- Reduced costs
- Decreased footprint and weight
SCALABILITY OF SEQUEL SYSTEM

4-8M ZMWs

1M ZMWs

150K ZMWs
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SEQUEL SYSTEM
TYPICAL PERFORMANCE

- Average read length: Comparable to PacBio RS II
- Consensus Accuracy: QV50
- Throughput per cell: ~5 – 10 Gb
- SMRT Cells per run: 1 – 16
- Movie lengths: 30 minutes – 6 hours
**SEQUEL SYSTEM**

Example Project: Coverage of a Human genome

10 Fold Coverage
- Total run time: 30 hours
- Number of SMRT Cells: 5
- Cost: €3,400

50 Fold Coverage
- Total run time: 150 hours
- Number of SMRT Cells: 25
- Cost: €17,000

PACIFIC BIOSCIENCES® CONFIDENTIAL
SEQUEL SYSTEM TOUCH POINTS

- Interactive touch screen
- Status light
- Sliding door
- Work deck
- Optics bench
- Primary analysis compute
- Environmentals
SEQUEL SYSTEM WORK DECK

- SMRT Cells
- Reagent plates
- Reagent tubes
- Tip boxes (3)
- Sample Plate
- Mixing Plate
- Trash
- Push-push loading
- SMRT Cells Prep
- Robot
- SMRT Cells Trays

PACIFIC BIOSCIENCES® CONFIDENTIAL
Sequel ICS Features:
- Select run designs from SMRT Link
- Guided work deck loading
- Obtain real-time run feedback & run metrics
- Guided post-run instrument clean-up
SMRT LINK
AN INTEGRATED END-TO-END WORKFLOW MANAGER
SMRT LINK
AN INTEGRATED END-TO-END WORKFLOW MANAGER

From sample setup to experimental results

- PacBio software tools accessed from single interface
- Workflow enables sample setup to experimental results
- Real-time monitoring across multiple instruments
- Modular design allows easy independent upgrades
- User permissions through pre-defined roles
SMRT LINK MODULES
SEQUENCING TOOLS

- Sample Setup
  - Guides template preparation for sequencing
  - Easy-to-use guided protocols
  - Save and retrieve sample calculations

- Run Design
  - Design runs for multiple instrument
  - Setup automated secondary analysis
  - Save your favorite run parameters for easy setup

- Run QC
  - Monitor instrument run status and metrics
  - Obtain key run metrics including
    - Read length and quality
    - Throughput
    - Loading
SMRT LINK MODULES
DATA MANAGEMENT AND ANALYSIS TOOLS

- Data Management
  - Create data sets from SMRT Cells, samples within SMRT Cell or runs
  - Generate data set reports including key QC metrics
  - Organize data sets in projects
  - Manage access permissions to projects by sharing the data with SMRT Link users

- SMRT Analysis
  - Perform de novo assembly for genomes of various sizes
  - Align reads to a reference sequence
  - Identify genome variants
  - Detect DNA methylation
SEQUEL SYSTEM
SITE PREPARATION

Site Preparation Guide
Sequel™ System
## SEQUEL SYSTEM SITE PREP

### Footprint

#### Sequel System*

- **Width:** 36.5 in (92.7 cm)
- **Depth:** 34 in (86.4 cm)

#### PacBio RS II System

- **Width:** 106 in (269.2 cm)
- **Depth:** 35.9 in (91.2 cm)

*PacBio RS II System*
Sequel System Consumables
SAME SIMPLE SCALABLE WORKFLOW

- SMRT® Sequencing workflow is the same for both PacBio® systems.
  - From amplicons to RNA to large genomes
  - Done in a day or two
WHAT IS COMMON BETWEEN SYSTEMS?

- Same exact kits with same part numbers
  - SMRTbell™ Template Preparation 1.0
  - Barcoding kits
  - SMRTbell DNA Damage Repair Kit
  - MagBead Binding Kit v2
WHAT IS SPECIFIC FOR THE SEQUEL™ SYSTEM?

- Same function
  - SMRT® Cell 1M (4 cells / tray)
  - Sequel Binding Kit 1.0
  - Sequel Sequencing Kit 1.0
  - Sequel Internal and SMRT Cell Controls

- New to the workflow
  - Loading Cleanup Bead Kit
    - For diffusion loading only
    - Used after polymerase binding
    - Removes excess polymerase
SMRT Analysis 3.0
in SMRT Link
SMRT ANALYSIS 3.0

Updated Algorithms

- Push-button *de novo* assembly
  - HGAP4 – *de novo* assembly for large genomes (Human, diploid aware); ~72 hrs of processing for 50X data on HPC infrastructure*

- Viral genomics, Minor variant detection, 16S
  - CCS2 – significantly higher consensus accuracy

- Targeted sequencing
  - LAA2 - chimera identification, efficient memory usage

*PACIFIC BIOSCIENCES® CONFIDENTIAL*
SMRT ANALYSIS 3.0

Faster Time to Results

- BAM - industry standard file format utilization
  - Increased adoption for PacBio data from 3rd party analysis tools
  - 20-40% faster time to results

- Easier implementation of new applications and algorithms
  - SMRT Analysis 3.0 developed in C, C++

- Better utilization of compute resources
  - Manage memory and CPU usage based on application needs

- Customer support and software maintenance
  - Shorter time for fixing issues and releasing improvements
  - Reusable code, easy to support and maintain
SMRT ANALYSIS 3.0 RELEASE PLANS

- November’2015 – limited release
  - Sequel customers

- Q1’2016 – broad release to Sequel and PacBio RS II customers
SEQUEL CORE CONSUMABLES PRODUCT ROADMAP

Q4 2015
Q1 2016
Q2 2016
Q3 2016
Q4 2016
Q1 2017
> Q2 2017...

Updated Chem/Pol
Updated Chem/Pol
Sequel 150K ZMW

Active Loading
## SEQUEL–2016 ROAD MAP

<table>
<thead>
<tr>
<th></th>
<th>Estimated per SMRT® Cell 1M Output</th>
<th>Read Length Avg</th>
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</thead>
<tbody>
<tr>
<td>Nov 2015</td>
<td>~5Gb</td>
<td>8-12 kb</td>
</tr>
<tr>
<td>Mid 2016 Read Length Improvements</td>
<td>~7Gb</td>
<td>10-15 kb</td>
</tr>
<tr>
<td>End 2016 Active Loading</td>
<td>~10Gb</td>
<td>10-15 kb</td>
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</table>
## ANALYSIS ROADMAP

<table>
<thead>
<tr>
<th>Architecture</th>
<th>Data Management</th>
<th>1H 2016</th>
<th>2H 2016</th>
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<tbody>
<tr>
<td>Analysis Pipelines</td>
<td>Iso-Seq performance optimization</td>
<td>Minor Variant Detection</td>
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</tr>
<tr>
<td></td>
<td>Iso-Seq Gene Fusion</td>
<td>Phasing</td>
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<tr>
<td></td>
<td>Base mods performance optimization</td>
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<td></td>
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<tr>
<td></td>
<td>SV Detection</td>
<td></td>
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</tr>
</tbody>
</table>
Consistent Throughput Improvements on the RS

- New Chemistries
- Improved Polymer
- Improvements with Sample Prep
- Better SW Algorithms
- Loading Improvements

RS to RS II – 75K to 150K ZMWs

Consistent Throughput Improvements on the RS
Sequel is a scalable platform
Sequel: Estimated Sequencing Cost
Human Genome at 50X Coverage

- 2015 / 2016: €17,000
- 2016 / 2017: €9,000
  - 1 million ZMWs
  - 65% Active Loading
  - Read Length Improvements
- 2017 / 2018: €3,000
  - 4 million ZMWs
Sequel: Estimated Sequencing Cost
Human Genome at 8X to 12X Coverage

- 2015 / 2016: €3,400
- 2016 / 2017: €2,000
  - 1 million ZMWs
  - 65% Active Loading
  - Read Length Improvements
- 2017 / 2018: €700
  - 4 million ZMWs
Sequel: Estimated Sequencing Cost
Genomes Per Year
Increasing to 4 million ZMWs

<table>
<thead>
<tr>
<th>Time Frame</th>
<th>50X Coverage</th>
<th>8X to 12X Coverage</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Cost</td>
<td>Genomes/Year</td>
</tr>
<tr>
<td>2015 / 2016</td>
<td>€17,000</td>
<td>50</td>
</tr>
<tr>
<td>2016 / 2017</td>
<td>€ 9,000</td>
<td>95</td>
</tr>
<tr>
<td>2017 / 2018</td>
<td>€ 3,000</td>
<td>300</td>
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</tbody>
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