

Rotor-Gene[®] 6000 real-time rotary analyzer

corbett

THE TIME HAS COME

discover

Rotor-Gene[™] 6000

real-time rotary analyzer

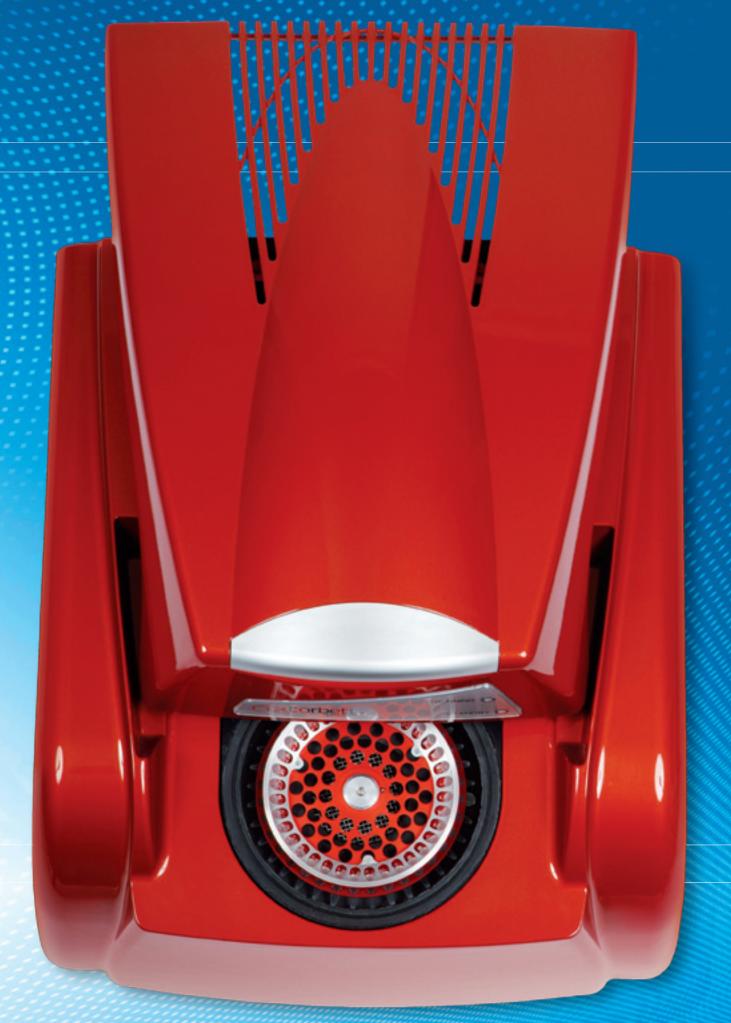
define

the future of real-time genetic analysis starts **here**.

The Rotor-Gene 6000 is the first of its kind. A real-time analyzer with performance so advanced it unlocks new research possibilities.

Fully equipped for real-time amplification, end-point analysis, high-resolution melt, autocall genotyping, and nucleic acid concentration measurement. However, this is only the beginning. Uniquely flexible hardware and software let you explore new ideas, chemistries, methods, and analysis options. With it you can embrace or invent the future of real-time and thermo-optical analysis.

<u>invent</u>



Rotor-Gene[™] 6000 real-time rotary analyzer



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Technology Innovation Award

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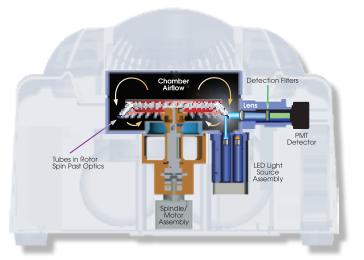
Think outside the Block

When generating publication data, confidence in your results is paramount. You must have a reliable instrument that always performs to specification. A tall order for any block-based system. Thermal and optical variation is unavoidable and worsens as lamps and Peltier devices age. Furthermore, the faster a block is heated or cooled the greater the sample-to-sample variation observed.

Rotary Design

The Rotor-Gene[™] is unlike any other instrument. It was designed from the ground-up for real-time thermo-optical analysis. The key difference is the unique centrifugal rotary design that ensures wellto-well variation is negligible—as it should be.

In the Rotor-Gene, every tube spins quickly in a chamber of moving air. Thus there is no positional temperature variation such as the recognized "edge effect" observed in block-based instruments. Optically, the Rotor-Gene is similarly uniform because every tube moves past the identical excitation and detection optics.



Cross-section of the reaction chamber

Diagram shows how sample tubes are illuminated and signals detected from within the reaction chamber. All tubes pass the detector every revolution (150 milliseconds), enabling high-speed data capture. Up to six separate LED light sources can be used in combination with six different detection filters. For maximum sensitivity, a photomultiplier (PMT) captures each optical signal.



Convenient

The design simplicity and robustness of the Rotor-Gene has many welcome benefits. For example, there's no block to clean and maintain, no alignment or optical calibration needed and there are no lamps to change. You also don't need a reference dye like ROX™. The centrifugal force on each sample ensures there are no condensation issues and air bubbles are automatically removed. You can swap rotors on-the-fly to change tube format (the equivalent to swapping a whole block) and even write on individual tube caps! All this adds up to maximum convenience and minimum maintenance.

Temperature

Well-to-well thermal uniformity, equilibration time uniformity (the time for each well to reach a set temperature) and accuracy (how close set temperature is to actual) are the thermal variables important to real-time analysis. The rotary design gives the Rotor-Gene the best thermal and equilibration time uniformity of any instrument. Thermal accuracy, on the other hand, relies on proper instrument calibration and here the Rotor-Gene also shines:

To ensure validated protocols are repeatable and transferable, many laboratories now require routine verification testing for thermal accuracy. To ensure accuracy, the Rotor-Gene uses an Optical Temperature Verification (OTV^{III}) Rotor that automates verification testing. A printable report documents each test and, in the unlikely event the instrument requires re-calibration, this is also automatically adjusted and reported. Each test takes only minutes and can be repeated at any time and as often as required.

Optics

The Rotor-Gene uses a separate high-power light-emitting diode (LED) as an excitation source for each channel. Each LED maintains a uniform output and has a lifetime guarantee. Compare this to other systems using incandescent projector lamps or lasers. Lamps fade continually, burn out unpredictably, and need regular replacement. Lasers are expensive to repair and have only a single excitation wavelength—meaning they properly excite a very limited range of dyes.

The complex optical mechanics used by other systems (such as X-Y scanning heads and fiberoptic bundles) can be fragile, expensive to repair and cumbersome to calibrate and clean. Further, they attenuate signal down a long path to the detector. By contrast, the Rotor-Gene has the fewest moving parts and the shortest optic path of any system. Simple, robust, ideal.

Optical calibration is a topic few vendors like to discuss. The Rotor-Gene doesn't need optical calibration because the identical optical path reaches all samples. Other systems require elaborate optical alignment and calibration. Furthermore, the Rotor-Gene doesn't need a reference dye (such as ROX) for the same reasons. For performance verification, the OTV Rotor (described above) checks the optical system every time it's used. Again, peace of mind that your system is always performing at its peak.

Security

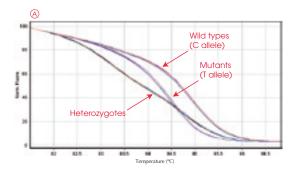
Data security is often overlooked, but vital to many laboratories. Corbett Life Science takes data integrity and security seriously. Each Rotor-Gene result file is given a digital signature that, when valid, ensures experiment data has not been manually altered or otherwise affected. You also have the option of identifying individual users as either an Analyzer, Operator or Administrator, each with different access privileges. Privileges are integrated with core Windows[®] security modules making it easy to administer and integrate with your current operating procedures. In addition, audit trails are stored along with run data to track changes made to experiment files, when they were made, and who made them.

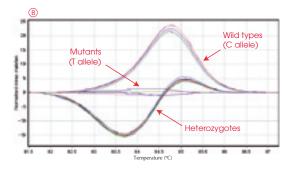


High Resolution Melt is a recent development that can greatly extend the utility of traditional DNA melting analysis. HRM is made possible by the combination of more advanced instrument design and changes to the type of dye used.

The Rotor-Gene 6000 is engineered for HRM. It incorporates a specially tuned high-intensity optical channel, high-speed data capture (up to 1000 data collection points per °C transition), extreme thermal resolution (0.02°C) and dedicated HRM analysis software. Dyes such as SYTO® 9, EvaGreen[™] and LC Green[®] provide the best results since they can be used at higher concentrations to provide increased resolution over traditional dyes like SYBR® Green 1.

HRM characterizes nucleic acid samples based on their disassociation (melting) behavior. Samples can be discriminated according to their sequence, length, GC content or strand complementarity.





SNP genotyping by High Resolution Melt (HRM)

Discrimination of human ACTN3 (R577X) SNP genotypes (C to T substitution) using SYTO[®] 9 intercalction dye (no probes). Homozygous wild type, mutation and heterozygote samples are shown on a standard normalized melt curve (A) and a difference plot normalized to T allele mutant samples (B). Amplification and HRM analysis was done using a Rotor-Gene 6000 instrument and genotypes were automatically assigned by the Rotor-Gene software. The fragment was pre-amplified using a 40-cycle fast protocol (46 min. run time). Even single base changes such as SNPs (single nucleotide polymorphisms) can be readily identified. An example of SNP genotyping by HRM is shown below left.

HRM Applications

HRM has renewed interest in the utility of DNA melting for a wide range of uses, including:

- Mutation discovery (gene scanning)
- Screening for loss of heterozygosity
- DNA fingerprinting
- SNP genotyping
- Characterization of haplotype blocks
- DNA methylation analysis
- DNA mapping
- Species identification
- Somatic acquired mutation ratios
- HLA compatibility typing
- Association (case/control) studies
- Allelic prevalence in a population
- Identification of candidate predisposition genes

With HRM, these and other applications are done using low-cost generic dyes where previously custom labeled probes such as TaqMan® or fluorescence resonance energy transfer (FRET) probes were required. HRM is thus a simpler and much more cost-effective way to characterize samples.

Recently, HRM was the subject of a detailed and independent Technology Assessment report from the National Genetics Reference Laboratory (Wessex, UK). A wide range of sample types were tested, including examples of challenging G to C and A to T single base substitutions. The full report is available for download at:

http://www.ngrl.org.uk/Wessex/downloads/Word/NGRL_HRM_Web.doc

Quantitative real-time DNA amplification

BCL-2 human gene target (68 bp amplicon) amplified from total genomic DNA template (Promega Corp., Madison WI). Two-fold dilutions shown in triplicate, from ~256,000 copies (920 ng) down to ~500 copies (1.8 ng) assuming 3.59 pg/haploid genome. Primer concentration 300 nM, dual-labelled probe 60 nM, 40 cycle amplification completed in 46 mins using standard Platinum[®] aPCR SuperMix-UDG commercial master mix (Invitrogen Corp., Carlsbad, CA). Semi-log amplification plots shown of normalized flourescence vs. cycle number with no smoothing applied and without ROX[™] normalization.

Real-Time Quantification

New applications, new dyes, new analysis methods —there's always something around the corner for real-time analysis. Don't let your instrument hold you back. The all-new Rotor-Gene 6000 is the most versatile real-time analyzer ever developed. With it you can work with dyes covering the entire spectrum, from infra-red to UV and up to 6-plex capability.

If throughput is important, the new Gene-Disc[™] 100 supports 96 sample workflow plus extra space for controls. To maximize throughput, try a high speed run—a 40 cycle amplification can be completed in about 40 minutes without the need for special fast reagents, consumables, or hardware modifications.

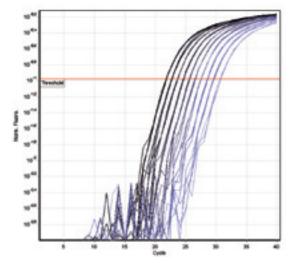
Results tell the story

So what can the most thermally and optically sophisticated instrument ever developed do? **Plenty.**

Shown below is data you won't see elsewhere. We simultaneously challenged the Rotor-Gene 6000 with:

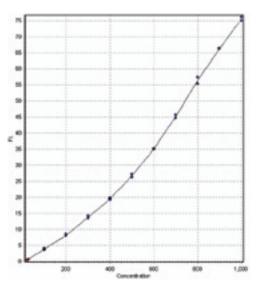
- 2-fold discrimination (1 cycle)
- 10 separate serial dilutions, each in triplicate
- Fast cycling
- Low probe concentration
- Standard commercial master-mix chemistry
- No passive reference (ROX) normalization
- Single-copy gene target amplification from a whole human genome

Notice how tight the replicates are, amplified in a third the time using a fraction of costly probe. And all achieved with standard chemistry!



Concentration Analysis

The Rotor-Gene is fully equipped to do DNA concentration measurement using fluorescent dyes (see below). Comprising a standard run protocol and integrated analysis software, the concentration of unknown samples is easily determined from a standard curve.

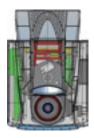


DNA concentration measurement

A DNA standard curve with replicates is shown for concentrations of 1000, 900, 800, 700, 600, 500, 400, 300, 200 and 100 pg/µL. Red data points at origin are negative controls. Curve interpolated using a spline curve fit (Rotor-Gene analysis software). Data was obtained using reagents in the Quant-IT[™] PicoGreen[®] dsDNA Kit (Invitrogen Corp., Carlsbad CA). Standard Rotor-Gene concentration analysis run protocol was used. 10 µL PicoGreen[®] (diluted1/200 in 1 × TE buffer). Final volume 20 µL.



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INSTRUMENT CONFIGURATIONS

			KOTOK CONTOORATIONS	
6200	2-Plex (Green, Yellow)	30 µL x 100-wells	Gene-Disc™ 100 (heat-sealed plate)	
62H0 6500	2-Plex (Green, Yellow) + HRM™ 5-Plex (Green, Yellow, Orange, Red, Crimson)	0.1 mL x 72-wells	Gene-Disc [™] 72 (heat-sealed plate) 0.1 mL strip tubes (strips of 4, matching caps) 0.2 mL tube (attached cap, domed or flat)	
65H0	5-Plex (Green, Yellow, Orange, Red, Crimson) + HRM™			
6600	6-Plex (Blue, Green, Yellow, Orange, Red, Crimson)			

ROTOR CONFIGURATIONS

SPECIFICATIONS

Thermal Performance:	Uniformity ±0.01°C; Resolution 0.02°C (smallest programmable and reported thermal increment);
	Range ambient to 99°C; Peak Ramp Rate (air) >15°C/sec heating, >20°C/sec cooling;
	Accuracy ±0.25°C, measured 30 seconds after clock start
Optical System:	Fixed path length, separate high intensity light-emitting diode (LED) excitation source for each channel,
	separate emission filter for each channel
Detector:	Photomultiplier (PMT) detector with variable or automatic gain setting (sensitivity control), user selected
Dimensions & Weight:	370 mm (14.6") wide, 420 mm (16.5") deep, 560 mm (22") deep door open, 275 mm (10.8") high, 14 kg (31 lbs)
Minimum Computer:	Pentium™ IV, 2.6 GHz (Desktop), Pentium M, 1.6 GHz (Laptop) or equivalents
	256 Mb RAM, Windows XP®, USB or RS232 Serial Port connection
Electrical:	100-120VAC @ 60 Hz, 200-240VAC @ 50 Hz; power consumption 8VA (standby), 560VA (peak)
Software:	Extensive analysis, graphing and statistical functions built-in. Unlimited use software licence included,
	free upgrades (by web download), Windows XP, Pentium IV (2 GHz) or higher PC, USB or Serial Port required
40 Cycle Run Time:	Typically 40 minutes to 1.5 hours (rotor and protocol dependent)
Supported Volumes:	5 μL to 100 μL (rotor and protocol dependent), typical reaction volume 20 μL
Warranty:	1 year on instrument; lifetime guarantee on LED light source; manufacturer's warranty on computer and monitor
Instrument Color:	Outback Red or Bondi Blue

CHANNEL INFORMATION

Channel	Excite nm	Detect nm	Example fluorophores detected
Blue	365±20	460±15	Biosearch Blue™, Marina Blue®, Edans, Bothell Blue®, Alexa Fluor® 350
Green	470±10	510±5	FAM™, SYBR® Green 1, Fluorescein, EvaGreen™, Alexa Fluor® 488
Yellow	530±5	555±5	JOE [™] , VIC [™] , HEX [™] , TET [™] , CAL Fluor [®] Gold 540, Yakima Yellow [®]
Orange	585±5	610±5	ROX™, CAL Fluor™ Red 610, Cy3.5™, Texas Red®, Alexa Fluor® 568
Red	625±10	660±10	Cy5™, Quasar 670™, LightCycler Red640®, Alexa Fluor® 633
Crimson	680±5	712 long pass	Quasar705™, LightCycler Red705®, Alexa Fluor® 680
HRM	460±15	510±5	SYTO® 9, LC Green®, LC Green ^{® Plus+} , EvaGreen™

HRM (HIGH RESOLUTION MELT)

New HRM capability is optional and comprises a dedicated high-performance optical subsystem, additional hardware and specific HRM analysis software (fully integrated). Thermal uniformity ±0.01°C, Resolution 0.02°C, Range ambient to 99°C HRM data acquisition (read) rate of 20 reads for each 0.02°C increment (=1000 reads/°C) NOTE: Conventional DNA Melt/Anneal capability and analysis software (including auto-call genotyping) is standard on all models

DNA CONCENTRATION MEASUREMENT

For direct measurement of nucleic acid concentration using fluorescent dyes (e.g. PicoGreen®, RiboGreen® etc) Comprises dedicated analysis software (standard on all models)

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