MONOCHROMATOR VS FILTER-BASED PLATE READERS

horses for courses, or a winning combination?

By Dr John Comley

This article is based around feedback obtained in HTStec's recent Multi-Mode Microplate Reader Trends 2007 Report. It highlights findings on what influences reader choice, current use of different plate reader detection modalities, main target types/classes investigated using plate readers, sources of assay reagents, and where different reader types (filter-based vs monochromator) are preferred. The survey found that sensitivity and flexibility in a multi-mode format were the key decision factors in the purchase of a new reader, however both these requirements are difficult to meet in the same machine. Filter-based readers provide maximum sensitivity, also best read speed and can accommodate particular read modes. Monochromator-based readers provide greatest flexibility, wavelength scanning capability and reduced running costs. Vendor updates reviewing their latest multi-mode plate reader developments are discussed together with comments on how their products attempt to address the competing challenges of sensitivity and flexibility. Of particular interest is the emergence of the first hybrid plate reader, ie one that has both monochromator and filter-based detection modules installed within the same instrument, and readers that make use of elements of both components. The report suggests that in the future, a greater proportion of labs will make use of both reader types, lending support to the suggestion that a significant market opportunity now exists for a hybrid plate reader.

Microplate readers, particularly those which are able to read multiple detection modes (multi-mode) are a very common sight in today's pharma, biotech and academic research laboratories and were the subject of detailed investigation in HTStec's recent Multi-Mode Microplate Reader Trends survey and market report (published May 2007).

Multi-mode microplate reader market

In this report the global market for multi-mode microplate readers was estimated to be around $140 million and growing at 6% annually. With a median price range of $65,000-$110,000, this is equivalent to sales in excess of 1,700 units a year. This market was segmented by sales value to approximately ¼ Large Pharma, ¼ Academic Research and ½ Small-Medium Pharma and All Biotech, with sales in the Academic Research segment predominantly in the price range $35,000-$65,000 (**Table 1**).

2007 market value ($ million)	142
Growth rate (CAGR)	6%
2007 volume (Units sales/year)	1,700
2007 median reader price range	$65,000-$110,000
MARKET SEGMENTATION:	
Large pharma	23%
Academic research	25%
Small-medium pharma and all biotech	52%

Table 1: Multi-mode microplate readers – global market estimate

Monochromator vs filter-based reader – sales and current use

Multi-mode microplate readers fall into two main categories: 1) filter-based, which use filters to select the wavelength – two filters are required per application, one for the excitation wavelength and the other for emission wavelength; and 2) monochromator-based, which use multiple (sometimes up to four per reader) diffraction gratings to create the desired excitation and emission wavelengths, with the wavelengths selected (tunable) through software. The current breakdown of multi-mode plate reader sales was estimated in the report to be 50% filter-based, 39% monochromator-based and 11% other (which includes multi-mode imagers and some speciality single mode readers) (**Figure 1**). The current lab use of different plate reader types, however, presents a different picture (**Figure 2**) and shows that the majority of labs still use only filter-based readers (39%) or mainly filter-based readers (29%) today. In comparison the current use of only monochromator-based readers (12%) or mainly monochromator-based readers (7%) is relatively small today. Only 13% of survey respondents claimed equal (50:50) use of filter-based and monochromator-based readers today.

Use of different detection modalities

The current use of different microplate reader detection modalities is shown in **Figure 3**. This shows that absorbance (23% share) and fluorescence intensity (22% share) were the main detection modalities used when the market as a whole

Figure 1: Current breakdown of multi-mode plate reader sales

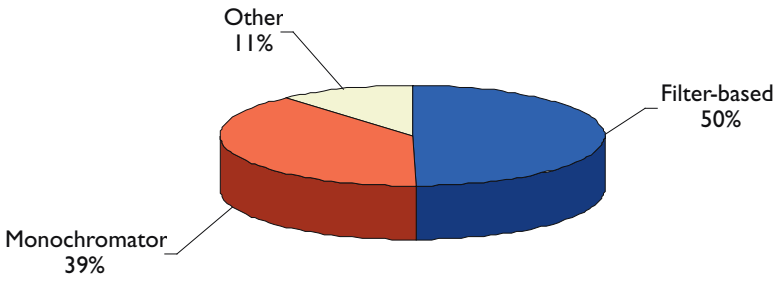


Figure 2: Current lab use of different plate reader types

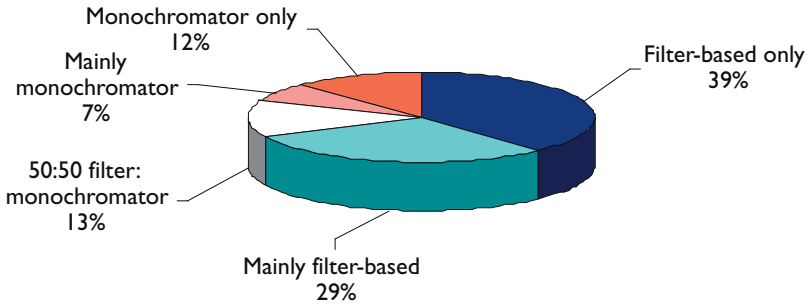


Figure 3: Current use of different microplate reader detection modalities

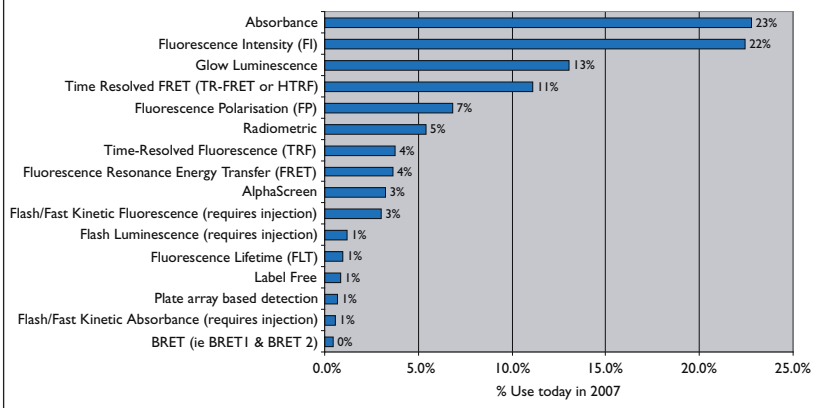


Figure 4: Main target types and classes investigated on plate readers

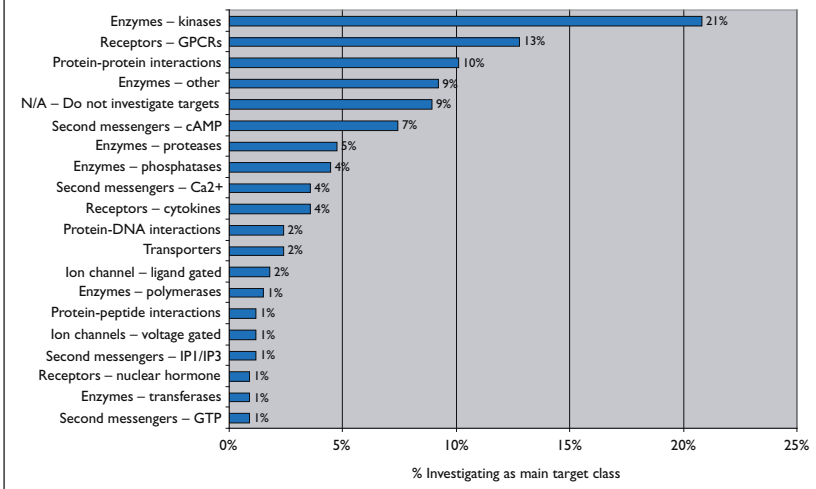
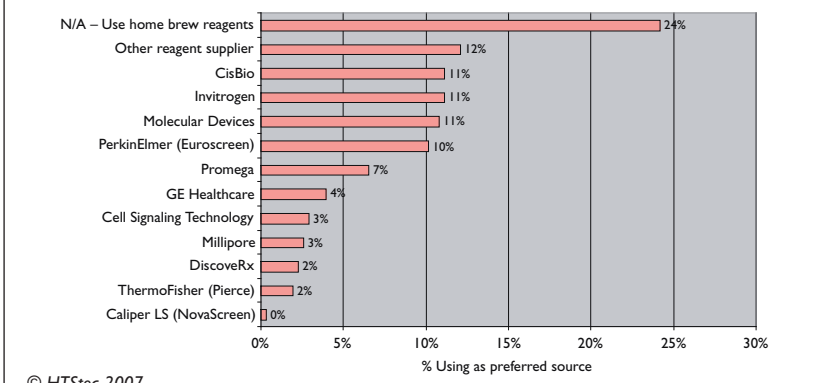


Figure 5: Preferred source of reagents in plate reader assays



was surveyed (ie including the academic segment). Glow luminescence (13% share) and time-resolved FRET (11% share) were then the next most commonly used detection modalities. A variety of other readouts (mainly fluorescent), each with a small percentage share, make up the remainder of use today. These other minority readouts also include AlphaScreen which is only available on some filter-based readers; radiometric, which is only rarely supported on multi-mode readers (eg Hidex Chameleon V); and label free which is only available as a single mode reader (eg Corning Epic). What **Figure 3** demonstrates is that users make use of a wide diversity of read modes and would prefer to see them offered in one instrument today. Those readouts whose use are expected to make the biggest growth over the coming years include time-resolved FRET, flash/fast kinetic fluorescence (requiring injection) and label free.

Target classes investigated using microplate readers

The main target types and classes investigated using plate readers alone are presented in **Figure 4**. This shows that enzymes (kinases) (21%) were the most popular target followed by receptors (GPCRs) (13%), protein-protein interactions (10%), enzymes (other) (9%), and then second messengers (cAMP) (7%). A further 9% of survey respondents indicated they did not investigate any targets using their plate readers. Overall most plate readers appear to be used to study multiple target types or classes and as such frequently need to access many different readout technologies. This is further reflected in **Figure 5** which shows the preferred source of reagents used in plate reader assays. The relative high use of home brew reagents suggests that many end users, particularly in the academic research segment, still design and develop their own assays. In comparison, the use of commercial reagent sources appears to show no strongly favoured vendor. Overall, these observations support the view that multiple assay technologies are used and there is a need for maximum flexibility in multi-mode plate readers to support this diversity of technologies.

Why microplate readers are chosen?

The technical factors that most influence the choice of a microplate reader are ranked in **Figure 6**. This shows that sensitivity and flexibility in a multi-mode format are the key decision factors, and these were ranked above instrument cost. However, these requirements tend to be difficult to meet in the same machine. **Figure 6** also highlights the fact

that add-ons such as a dispenser capability are nice to have options, but are relatively unimportant in purchasing decisions. Reader manufacturers lacking a reagent offering are also concerned about the effect this may have on their potential sales. However, data presented in **Figure 7** shows that overall it has little influence on the final decision to purchase a new plate reader.

Monochromator vs filter-based reader preference

Figure 8 attempts to explain under what circumstances a particular reader type (ie filter-based versus monochromator) is currently most preferred, as perceived by end users. It shows that based on capital (CapEx) cost, support for particular read modes (eg AlphaScreen), limits of detection (sensitivity) and read speed filter-based readers have the edge. While based on wavelength scanning capability (only supported by monochromators), ease of use, ability to run wide diversity of assay types (flexibility) and running (operational) costs, monochromators are preferred. Respondents were also asked about their experience with monochromator readers and whether these had proved limiting in their work. As shown in **Figure 9**, quite a high proportion of monochromator users have experienced some of the limitations described, particularly the lack of AlphaScreen, the read speed and some sensitivity issues. What this suggests is that although monochromators are the most flexible type of plate reader they are not necessarily the best choice for the routine reading of certain assay types if absolute sensitivity and maximum read speed are critical.

Hybrid plate reader

Survey respondents where then introduced to the concept of a hybrid plate reader (ie, one that has both monochromator and filter-based detection modules installed within the same instrument) and asked whether they would consider paying a price premium for such a reader. The results (**Figure 10**) suggests that the majority (70% of respondents surveyed) were interested in the concept and would consider paying a price premium to access a hybrid reader.

Vendor updates

In the following vendor updates we report the latest multi-mode plate reader developments and consider how these products attempt to address the competing challenges of sensitivity and flexibility. Please be aware that the updates present contrasting views and vendor biases on the usefulness and performance of monochromator versus filter-based detection, and the end-user should draw their own conclusions.

Figure 6: Technical factors influencing the choice of microplate reader

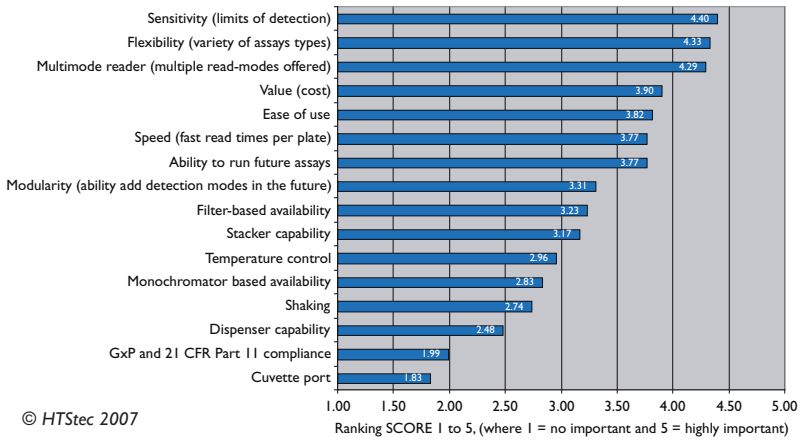


Figure 7: Influence of reagent provision by a specific vendor on the final decision to purchase a plate reader

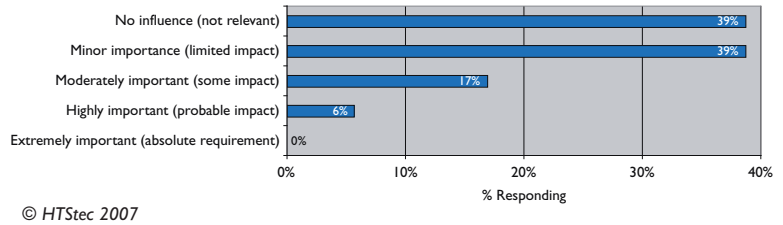


Figure 8: Where different plate reader types are preferred

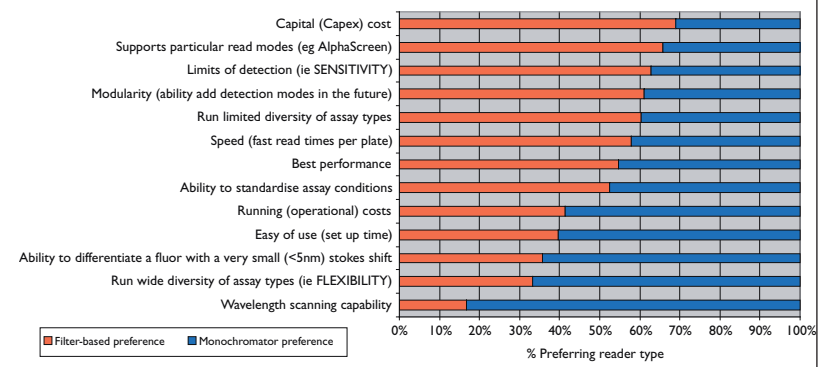


Figure 9: Areas where some monochromators have proved limiting

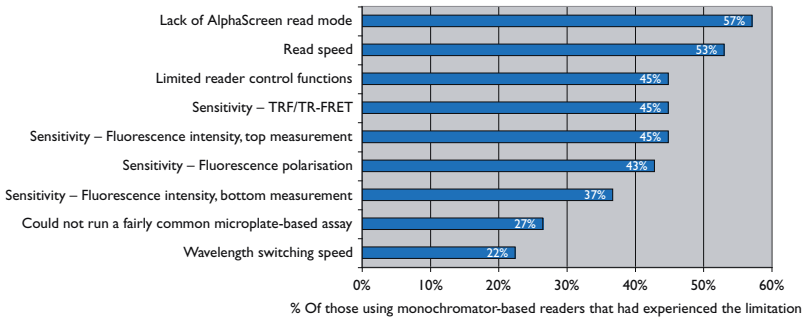
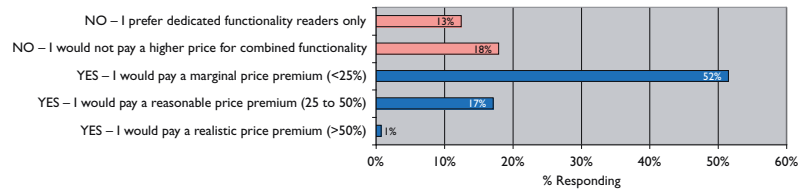


Figure 10: Interest in purchasing a hybrid plate reader



Earlier this year **Beckman Coulter** (www.beckman.com) introduced the PARADIGM™ Detection Platform, representing a significant advancement in addressing the delicate balance between sensitivity and flexibility by offering both filter and monochromator (currently only used for absorbance) in a single instrument. The PARADIGM features a selection of application-optimised, read-mode-centric detection cartridges that can be quickly interchanged to meet different assay needs, making this the first user-upgradable and user-configurable multimode reader. Each detection cartridge is designed to perform at the highest level when measuring fluorescence intensity, time-resolved fluorescence, fluorescence polarisation, FRET, TR-FRET, photometric, luminescence and dual luminescence measurements. Wavelength-tuned excitation source (flash lamp or LED), optics (filter and monochromator) and dedicated electronics in combination with dual photon counting PMTs make each detection cartridge a powerful measurement tool. PARADIGM gives users the flexibility to configure or change their system in less then five minutes to address all the necessary measurements for their applications. The upgradability makes it possible for users to maximise their return on investment by delivering a multimode reader that has the ability to grow as their needs grow. PARADIGM addresses six- to -1536-well microtiter plates and reads at speeds required for high-throughput screening. Currently fluorescence measurements are filter-based; however Beckman plans to add monochromator-based fluorescence scanning capabilities to the platform, so in the future existing customers can simply choose to add further functionality to their PARADIGM platform (**Figure 11**).

The unique idea behind the design of the **Berthold Technologies'** (www.bertholdtech.com) Mithras LB 940 multimode plate reader has been to have separate optical systems, each of them tailored to match the specific requirements of the individual reading technologies. This design is named

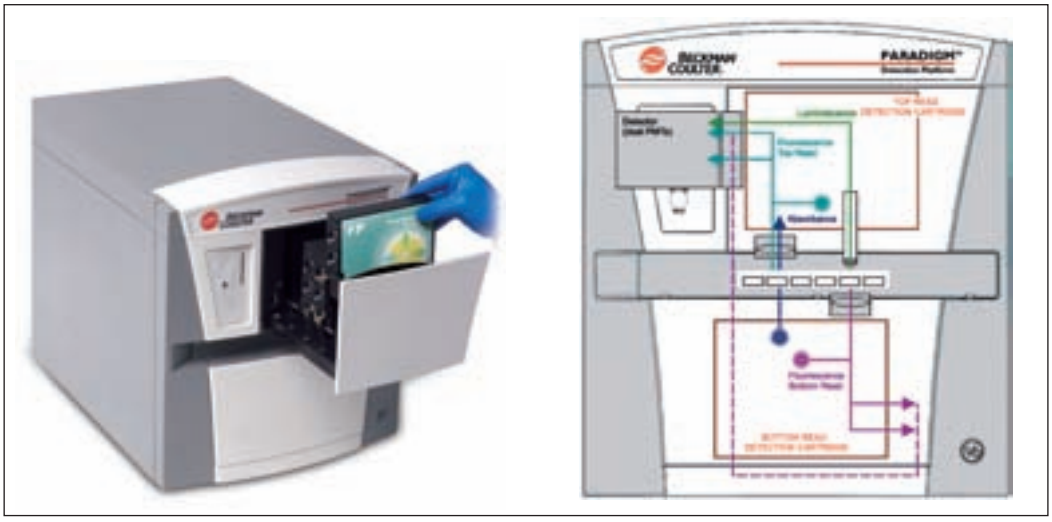


Figure 11
Beckman Coulter's new PARADIGM reader (left) and a schematic of the PARADIGM's optical setup (right) showing the detection cartridge locations highlighted by the red box. The reader is able to perform top and bottom read measurements and the specific optical paths are shown for fluorescence (teal and purple), luminescence (green) and absorbance (blue) measurements. Utilising the detection cartridge principle the PARADIGM is able to excite bottom read samples directly, removing the need for the typical optical fibre assembly

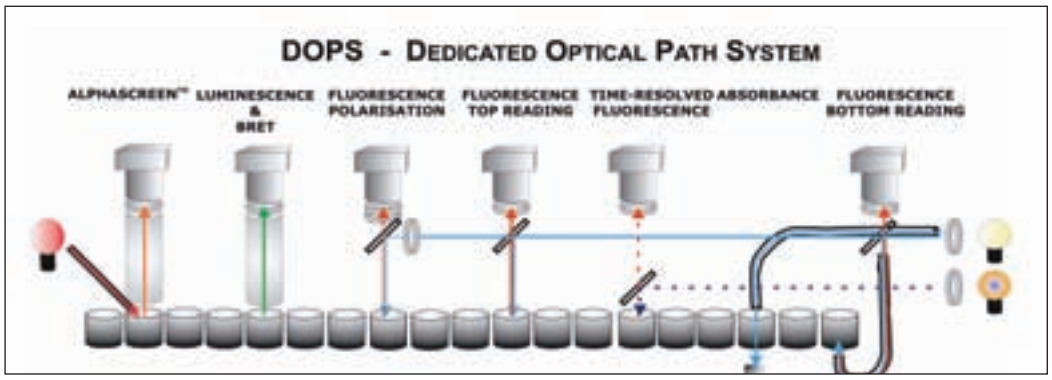


Figure 12
Berthold Technologies' Mithras LB 940 Dedicated Optical Path System (DOPS)

Dedicated Optical Path System (DOPS; see **Figure 12**) and has been applied to the recently introduced Time-Resolved Fluorescence reading technology as well. Luminescence applications including BRET require a highly efficient light collecting system to detect even lowest levels of light. Equally important are means to reduce crosstalk from adjacent wells to a non-detectable level. Fluorescence as well as absorbance applications work best when beams are parallelised by lenses as filters are designed for parallel rays of light. In this sense all non-radioactive technologies including Absorbance, Fluorescence, Time-Resolved Fluorescence, Fluorescence Polarisation, Luminescence, BRET and even AlphaScreen™ can be performed with sensitivities known from dedicated instruments: eg detection limit for Luminescence is as low as 6 attomole ATP and for Time-Resolved Fluorescence as low as 2 attomole Europium. Reagent injectors are another key feature contributing to the flexibility and versatility of a plate reader. At least some of the available reagent injectors need to have their tips at the measurement position to be able to perform fast flash reactions, eg Calcium flux detection with Aequorin or fluorescent dyes. For the Aequorin type receptor assays dispensing of receptor loaded cell suspensions into compound plates is required. The unique JET injectors used in the Mithras have been specifically designed with respect to suitable dispense speed, tubing diameters and materials compatible for cell dispensing.

BioTek's (www.biotek.com) new patent pending Synergy 4 with Hybrid Technology is the only multi-mode reader on the market combining monochromator-based detection with filter-based detection. This unique combination addresses the two key conflicting requirements that are flexibility and sensitivity in an affordable, upgradable platform. The most popular screening assay platforms (FRET, TR-FRET, fluorescence polarisation, luminescence) have been validated on the Synergy 4's filter-based system, for best performance. Its monochromator system can be used during research and assay development phases when exact assay conditions are still being investigated. In addition, the Synergy 4 incorporates exclusive features not found in other multi-mode readers, making it an extremely versatile instrument: it is equipped with two broad spectrum light sources (tungsten halogen and xenon flash) for fluorescence, to accommodate various assay requirements; its control software, Gen5, launched only a year ago, was developed with multi-mode functionalities in mind by software engineers experienced in microplate technologies, and provides

Figure 13
Simplified illustration of the BioTek's Synergy 4 hybrid optical system. The inset on right hand side shows the Synergy 4 reader

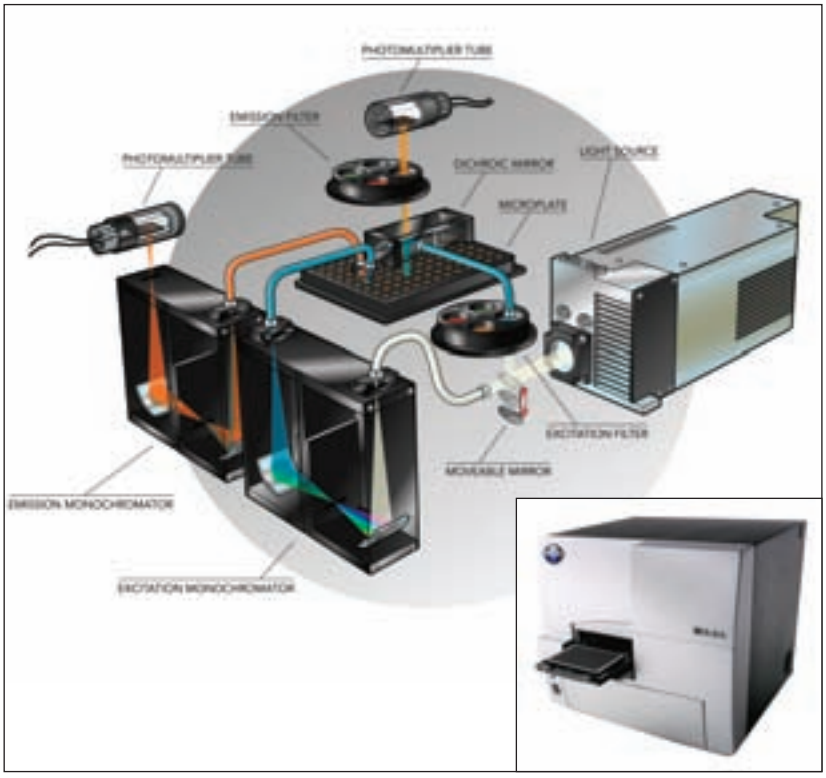


Figure 14
BMG Labtech's POLARstar Omega

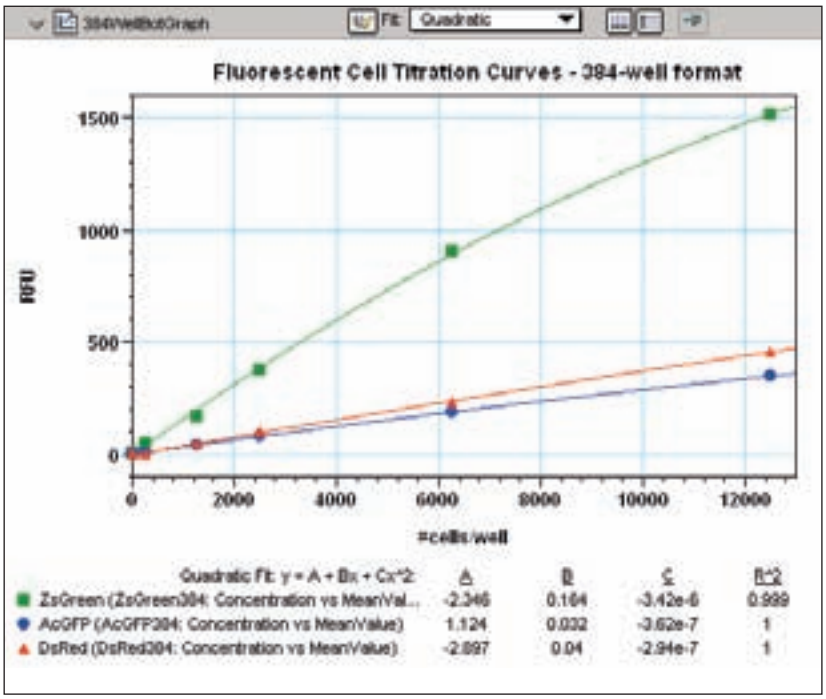
flexible and powerful programming tools for the instrument; its UV-visible absorbance measurement system does not share any optical components with the fluorescence detection system, making it totally dedicated to this detection mode. These unique features, in combination with more standard features such as a precise built-in temperature control system, shaker, automated reagent injection option, modularity or the compatibility with 6-well to 1536-well plates, make the Synergy 4 very well suited to the extreme diversity of assays found in the microplate format (**Figure 13**).

The two most popular systems of wavelength selection used in fluorescence microplate readers are optical filters (fluorescence microscopes always use filters for fluorescent imaging as they provide the greatest sensitivity with precise wavelength control) and monochromators (are most appropriate when characterising novel compounds or if a full fluorescence spectrum scan is required and sensitivity is not the first concern). Through many years of experience and research, **BMG Labtech** (www.bmglabtech.com) has chosen to use high quality optical filters for flexibility, reliability and the best fluorescence sensitivity. A survey of the top tier HTS microplate readers shows them to use filter-based detection. One of the many reasons for this is that the transmission efficiency of light through filters is usually more than 90%. Whereas monochromators need a complicated series of narrow light-apertures, gratings and mirrors to transmit light and select wavelength. This usually results in less than 50% of the source energy being transmitted to the sample, leading to lower excitation quanta for the fluorophore and can cause problems at low fluorophore concentration, in FRET or fluorescence polarisation experiments. Filters can be designed and manufactured to precise specifications, putting more light where it is useful and less where it is not wanted, thus giving more flexibility in assay design. In specific assays such as LanthaScreen™, AlphaScreen™ and HTRF®, filters offer the highest level of per-

Figure 15
Hidex's Plate Chameleon V with Laptop

formance in HTS laboratories. For users who need to capture full absorbance spectra, or who frequently measure at multiple wavelengths, BMG Labtech has incorporated a spectrometer into its new OMEGA series of modular and multifunctional readers. The spectrometer is not a monochromator and does not require tuning at all – it captures a full spectral scan (from 220nm-850nm) at resolutions as low as 1nm. A full absorbance spectrum can be measured in less than 1 second per well period. This system benefits from the sensitivity of filters for fluorescence and having the wavelength selection flexibility required by UV/Vis users (**Figure 14**).

Hidex (www.hidex.com) offers a reasonably priced multimode microplate reader called Plate CHAMELEON V. It accepts 6-384 well microplates and has a few unique features. Plate CHAMELEON V is the only microplate reader capable of reading radioactive labels and the most common non-radioactive labels, ie fluorescence, time-resolved fluorescence, fluorescence polarisation, luminescence and absorbance. Liquid scintillation counting for radioactive labels enables filtration based assays with cells, such as thymidine uptake. Because of liquid scintillation counting the CHAMELEON also has the absolutely most sensitive luminescence features. Normally multimode readers use fluorescence optics to read luminescent samples and this greatly reduces sensitivity. The CHAMELEON is also very flexible. A key point in the design has been the use of direct optics without optical fibres which limit sensitivity greatly. Another key feature is that no dichroic mirrors are used, this broadens the usable wavelength range and eases the operation as only filters for the excitation and emission need be selected. Plate CHAMELEON V has easily accessible filter slides and accepts common half inch and one inch filters that are available from variety of online sources. New applications are thus easy to adopt and inexpensive. Plate CHAMELEON V is available in different versions from a single luminometer to the full model incorporating all six technologies. The small foot print and size take up very little valuable lab bench space. One point often ignored when comparing filter-based instruments to monochromator-based readers is that the poor performance and slow speed of monochromators actually limit the number of applications that can be performed on scanning type of instruments. This in a sense does not support the general perception that monochromator instruments are more flexible (**Figure 15**).



SpectraMax® multimode readers, developed by **Molecular Devices**, now part of **MDS Analytical Technologies** (www.mdssciex.com) enables maximum light throughput compared to other tunable readers by integrating both monochromators and filters in the optical pathway. While monochromators facilitate wavelength and assay flexibility, filters allow for signal-to-noise discrimination, enabling superior performance for the widest range of assays. The SpectraMax platform also combines a series of proprietary technologies, such as SmartOptics™ design, AutoPMT™ technology and PathCheck® Sensor, allowing autocalibration of the multimode readers and standardised results. With these capabilities, researchers can compare results from multiple instruments, experiments and fluorophores during the course of a study. Conventional microplate fluorescence readers, which automatically adjust the gain of the PMT to accommodate the range of concentrations in a microplate, report a different relative fluorescence unit (RFU) for each sample depending on the concentrations of the surrounding wells. The AutoPMT capability solves this problem by normalising the RFUs to an internal reference. This standardisation of RFU means a particular sample concentration will always have the same reported RFU value regardless of the content in the surrounding wells, allowing the use of the instrument's wide dynamic range (**Figure 16**).

Figure 16
The graph shows titration curves for three colours of GFP transfected into HEK-293 cells. Measured on the SpectraMax M5e™ reader, AcGFP (jellyfish), ZsGreen (reef coral), DsRed (reef coral) fluorescent proteins expressing cells can be assayed on a single plate, down to approximately 30 cells per well (384-well format), highlighting the increased light throughput efficiency and sensitivity of the MDS Analytical Technologies SpectraMax M5e system

Figure 17
PerkinElmer's EnVision® Multilabel Plate Reader with TRF LASER™ option and dispensing module

Certain homogeneous time-resolved fluorescence (TRF) assays are difficult to optimise in generic multimode microplate readers, and are especially challenging in readers based on monochromator technology. These assays typically have a relatively weak assay window and/or a low energy transfer signal resulting in subdued Z'-values. In order to enable full optimisation of the TRF window time settings, such assays require a short and intense excitation pulse with a very sharp tailing edge. The TRF LASER™ option is a compact nitrogen laser module addition for **PerkinElmer**'s (www.perkinelmer.com) EnVision® Multilabel Plate Reader that provides improved performance for homogeneous time-resolved fluorescence (TRF) assays. The EnVision TRF LASER delivers an extremely sharp and short excitation pulse, which results in an enhanced signal-to-background ratio for optimum Z' values in

homogenous TRF assays, such as LANCE® Ultra and DELFIA®. A commonly used light source in TRF instrumentation is a Xenon flash lamp, in which the interfering tail generally lasts 50µs. With the nitrogen LASER, there is no tail and the excitation pulse duration is only 3ns at half height. In addition, assays showing wide emission spectra are best captured with optimised filter bandwidths. User-changeable label-specific optical mirror modules and filters in EnVision provide superior detection sensitivity and contribute to measurement speed. The EnVision features extremely fast filter switching and real time dispensing for kinetic dual excitation/emission ion channel applications (**Figure 17**).

The selection of a new microplate reader is related to some key questions, usually driven by application and budget. Although the majority of today's microplate readers are multimode readers, modularity and upgradability are of high importance. The decision to purchase a monochromator or filter-based instrument often depends on the type of application and the quantity of unknown substances or compounds to be screened (ie, throughput). **Tecan**'s (www.tecan.com) filter-based instruments are optimised for highest sensitivity and measurement speed that are beneficial for the most demanding applications. The recently introduced filter-based multimode Infinite™ F500 offers significantly improved performance for ratiometric assays such as TR-FRET (eg HTRF®). The integration of latest generation reagent injectors makes it a powerful and versatile research tool for cell-based assays. The patented filter slide with integrated flash counter enables continuous monitoring of filter exposure and hence quality control of the reader. With the invention of the quad4 monochromator technology, Tecan has been able to prove that monochromator systems can achieve sensitivity and speed levels comparable to high end filter-based instruments. The revolutionary performance obtained with Tecan's quad4 monochromator systems has several unique technology advantages: True wavelength flexibility, ie 4 monochromators for consistent performance over the whole wavelength spectrum; improved sensitivity by significant reduction of stray light (4 monochromators reduce stray light 10^6 times more than typical dual monochromator configurations). Furthermore, the user will obtain more accurate readings, ie 4 monochromators give a true spectral scan with no artificial peak shifts; and extremely fast scan times – Safire²'s 4 monochromators increase the speed of fluorescence scans by up to six times. In summary, Tecan's Infinite™ F500 and Safire²™ readers challenge the limits of filter and monochromator-based detection (**Figure 18**).

The **Thermo Scientific** (www.thermo.com) Varioskan Flash is a multitechnology reader with which photometry, fluorescence and TRF are performed using monochromator technology. Luminometry is measured either with a monochromator or dedicated lens optics. The instrument offers at least equal or better sensitivity performance than filter models, contrary to common understanding that monochromator-based instruments offer lower sensitivities. A special feature is the automatic elimination of the effects of instrument electronics

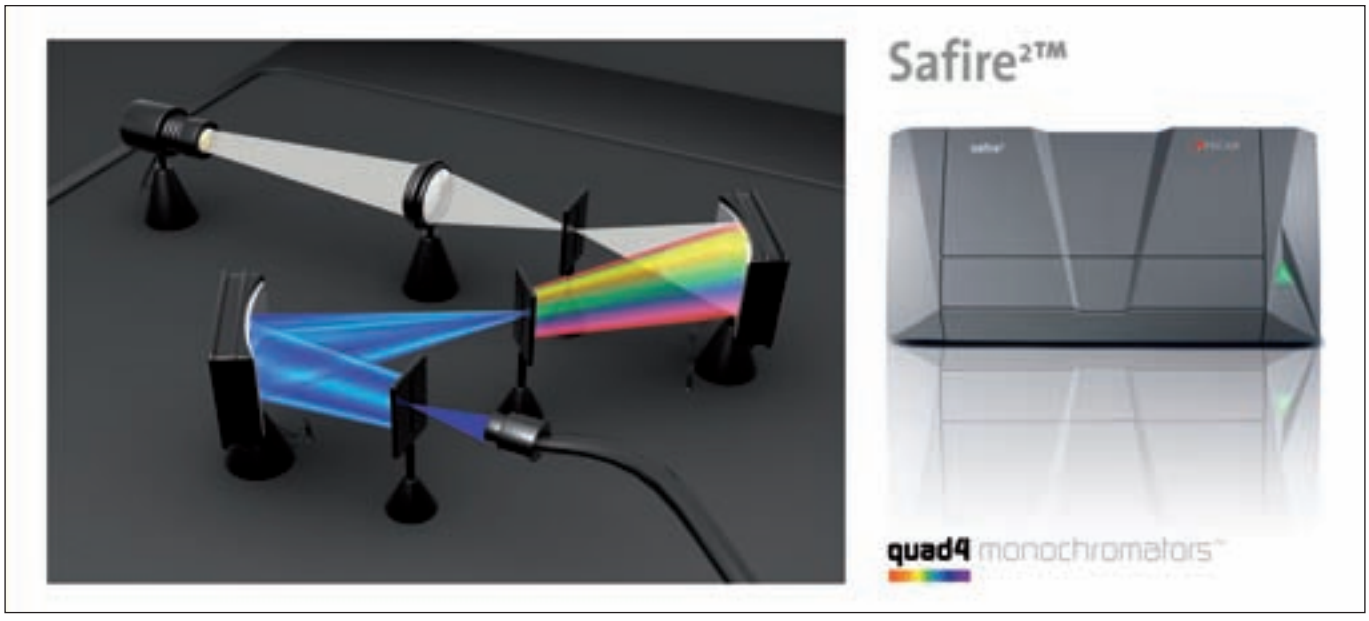


Figure 18
Tecan's Safire2™ plate reader with Quad4 monochromator technology – 4 monochromators for faster scan times and improved sensitivity. Visit: www.tecan.com/quad4/index2.htm for further details and an animation

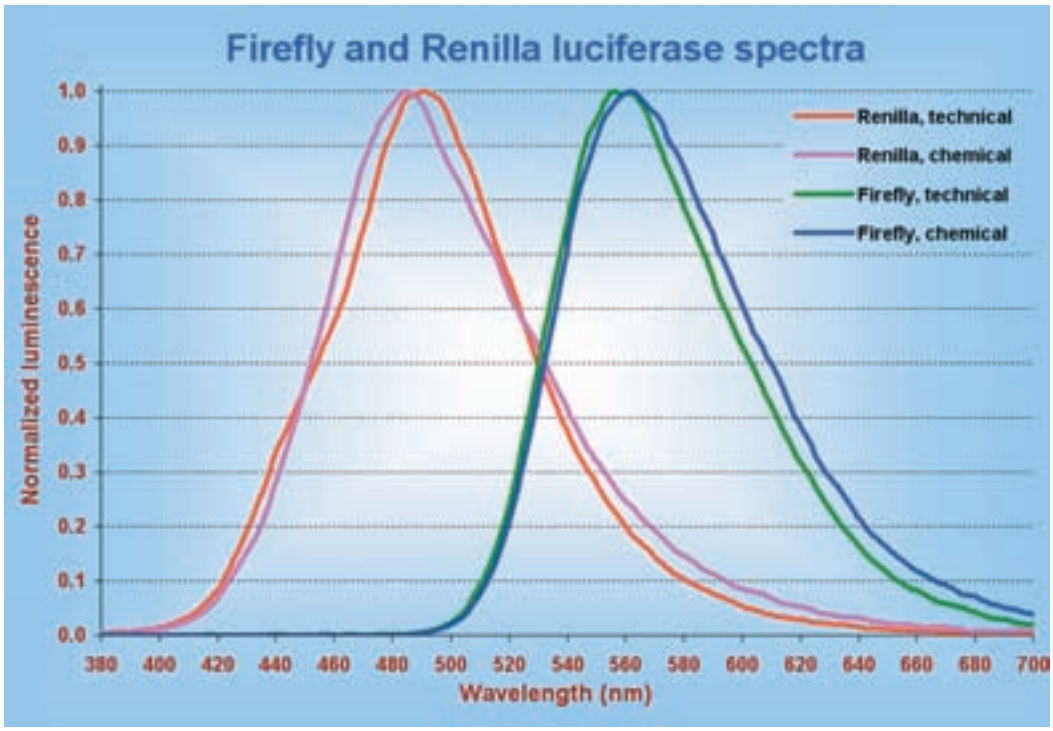


Figure 19
Example of the Thermo Scientific Varioskan Flash spectral correction function in luminometric spectral scanning. Spectra of firefly and Renilla luciferases were measured with and without spectral correction. A clear shift in spectral peak values is observed between instrument-dependent technical and the real chemical spectra

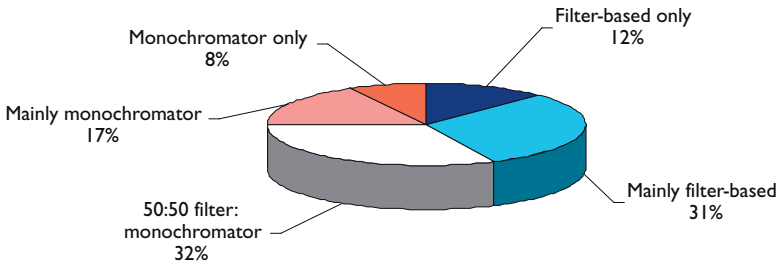
on fluorescent or luminometric spectra. As it is well-known, all electronic components, especially PMTs and monochromator gratings, have different relative sensitivities to different wavelengths. For example, the sensitivity of a typical PMT to red wavelengths is much lower than to green or blue wavelengths. These kinds of differences are normally transferred to the resulting technical spectra whose shapes are influenced by the instrument. This causes instrument-dependent variations in spectral scannings, and, for example, instrument-dependent peak values. The Varioskan Flash has an automatic spectral correction function that measures internally its own spectral sensitivity efficiencies and corrects the measured spectra by removing all effects of the instrument electronics. As a result, it produces real chemical spectra that would not be discovered with normal spectral scanning instruments (**Figure 19**). Another special feature of the Varioskan Flash is the incubator temperature control that makes it possible to measure even photometry with plates covered with lids. It is achieved by a special incubator system which keeps the lid constantly at a higher temperature than the samples. This elevated lid temperature prevents condensation efficiently and therefore guarantees reliable measurement through lids. This feature offers clear benefits in long kinetic applications at elevated temperatures.

Figure 20
Cosmo Bio USA's Artemis HTRF® Microplate Reader

In contrast to the multi-mode microplate readers discussed above, mega marine electronics manufacturer **Furuno Electric Co, Ltd** of Japan has entered the analytical microplate reader marketplace on a decidedly different tack, ie readout dedication. Utilising a high intensity xenon-flash lamp and high performance but non-interchangeable optical bandpass filters, Furuno's dual-wavelength TR-FRET reader, Artemis, is dedicated to this single detection mode, and currently to those only assays utilising Cisbio's patented HTRF® detection chemistry. Furuno's goals for the Artemis were to produce an easy to use, robust instrument providing top quality TR-FRET

data at the lowest possible price point, putting a reader on every desktop and simplifying assay development and optimisation by utilising reagents from a single compatible source. Towards these goals, Furuno's quoted sensitivities and CV%s for the Artemis compare very favourably to and in some cases exceed those of laser-based 'reference standard' instruments. Connected via USB cable to a Windows-based PC, the Artemis software provides flexible control of TR-FRET assay set-up parameters including flash, delay and integration times; plate mapping, data acquisition and data analysis. The Artemis is distributed exclusively by **Cosmo Bio USA** (www.cosmobiousa.com) and its affiliates. Time will tell if the marketplace is ready to trade assay mode flexibility for low cost specialisation (**Figure 20**).

Figure 21: Expected future lab use of different plate reader types



Summary

A comparison of the pros and cons of filter-based and monochromator readers are presented in **Table 2**. There is a broad consensus in the industry (not however shared by all vendors) that filter-based multi-mode plate readers are more sensitive, and as such have been traditionally favoured for routine assays by labs with limited budget and by the high end screening labs. In contrast, monochromator-based readers are generally recognised as being more flexible, are favoured for multiple applications, as shared piece of equipment have tended to be used more in assay development labs. However, nearly all users share the same aspirations to have both attributes (ie, sensitivity and flexibility) in the next reader they plan to purchase. So what is the likely future lab use and deployment of different plate reader types? If respondent feedback in HTStec's report is correct (**Figure 21**) we can expect to see significant declines in labs using only filter-based readers or only monochromator readers and general blurring in the current demarcation between labs using different reader types. The proportion of labs making use of both reader types looks set to increase, with the biggest shift towards those who plan to make equal (50:50) use of filter-based and monochromator-based readers. As lab benches become ever more cluttered with instruments and with the space for peripherals on robotic systems at a premium, the merits of a hybrid plate reader or readers that make use of elements of both components, begin to look very attractive, and it is predicted that such hybrid readers will emerge to take significant market share over the coming years. DDW

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FILTER-BASED	
PROS:	**CONS:**
High performance: can be designed for very high sensitivity and speed, especially in ratiometric or two wavelength assays in high density plates.	Higher operating costs: one filter set = one application. New applications require user to identify and purchase the appropriate filter set.
Cost-effective: can be designed to be inexpensive with good sensitivity.	No spectral scanning.
MONOCHROMATOR-BASED	
PROS:	**CONS:**
High flexibility and convenience: rapidly accommodates new applications.	Sensitivity: a lot of light is lost in the optical system. Usually less efficient than filter-based designs.
Spectral scanning: if more information on fluorescent molecule's spectral profile is required.	Cost/performance ratio: filter-based systems can be designed to provide the same level of sensitivity for less money.

Table 2: Comparison of monochromator and filter-based multi-mode plate readers