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**T<sup>3</sup>**  
update

Tips, Tricks and Techniques for users of  
Beckman Coulter Automated Solutions  
for Drug Discovery

## He Wants to Play the Cello...

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The letter came home just prior to the start of middle school stating, "All 5th graders are required to either play a musical instrument or sing in the choir. Students will have music five days a week for the entire school year." This was a stunning turn of events for me because I had been eagerly anticipating my oldest son's entrance into the school's sports program. I had already begun to prepare him for his career in sports by signing him up for soccer, baseball and basketball since he's been able to walk.

Certain that some innocent mistake had been made I called the school. A very calm administrator assured me that my son's opportunities to participate in sports were on the horizon, 7th and 8th grade. This new program was intended to give the younger students a "more well-rounded" experience. To ease my concerns I was invited to an open house at the school where the students could try out a variety of musical instruments and we could get our questions about the program answered. A few days later my ever-patient wife informed me, "He wants to play the cello."

At Beckman Coulter™, we strive to continually improve our products and our client's processes. This can be accomplished in several ways. First, we can add new features and functionality to existing technologies. In this newsletter, you can read about the addition of 384-channel pipetting to our workhorse Multimek™ Pipettor system. Second, we can automate new applications on our systems. Again, herein you'll find information about new automated applications performed on the Biomek® 2000 using Promega MagneSil® technology.

Last, we attempt to break from convention by getting into new areas or

taking new approaches. Previously we announced our collaboration with Cellomics® in the area of High-Content Screening. In this issue, we will start listing some applications demonstrating the impact and utility of the discipline. We continue to extend into other areas like assay development with our SAGIAN™ Automated Assay Optimization. This product uses robotic liquid handling and design of experiments to dramatically improve assay performance, reduce costs, and cut development time. Those researchers who have worked with this new approach continue to be amazed.

One thing is certain: we can't become stagnant and be afraid to explore new ideas. The research environment where our products are used won't allow it. We at Beckman Coulter look forward to introducing you to more new developments in the coming years. We openly invite you to share your needs with us so that our products and services might have a positive impact.

Well we got the cello! One night a few weeks ago, I went upstairs to his room while he was practicing. He said, "Hey, Dad, listen to this," and proceeded to play the sound bite to the movie *Jaws*—you know the part right before the shark attacks. Now, I thought that was pretty cool! He then proceeded to teach me how to play "Mary Had a Little Lamb." I just happened to glance up in time to see my lovely wife grinning at me. I don't know if he'll grow up to be the next Michael Jordan or Yo-Yo Ma, but at least he is getting the chance to explore a variety of things to see where his true talents lie.

Best regards,

## SBS: A Meeting That Will Never Be Forgotten ...

**SHIRLEY WELSH**  
**BECKMAN COULTER, INC.**

The 7th Annual Conference for the Society of Biomolecular Screening (SBS) was held in Baltimore, Maryland, September 10-13, 2001. In preparation for the event, the usual planning took place: What products would we showcase? What graphics should be presented? What should we raffle to draw customers to the booth? It seemed like standard fare until the morning of September 11, which will forever change our lives.

Plasma screens, that elegantly showcased the Biomek® FX, switched to CNN reports. All of the attendees and exhibitors converged

upon the Beckman Coulter booth to witness the horrific events taking place at the World Trade Center and the Pentagon. Somehow, after witnessing such a tragic stream of events, to continue "business as usual" did not seem appropriate. For the safety of all participants, the city of Baltimore decided to close the Convention Center for the remainder of the day.

SBS continued on September 12. It was tough, but we knew we had to persevere to try and recover from the catastrophic events that happened just the day before. The exhibit hall opened promptly at 9:00 a.m. and we welcomed customers to our booth. This day, it seemed people were more cordial to

one another. Science and mankind were truly synergistically linked.

We showcased "Smart Solutions™ for Cell-Based Screening" by exhibiting the Cellomics ArrayScan® HCS System & KineticScan® HCS Reader, proudly distributed by Beckman Coulter. Other highlights were the NEW 384-Channel Head for the Multimek™ 96/384 Automated Pipettor and NEW 1536 capability on the Biomek FX.

The 7th Annual Conference for the Society of Biomolecular Screening will be forever etched in our minds. Even in times of tragedy, the scientific community demonstrated its commitment to move forward.



## 384-Well Pipetting Head Expands Multimek™ Liquid Handling Platform

**ROB DONOHO**  
**BECKMAN COULTER, INC.**

Beckman Coulter, Inc., recently introduced a new 384-channel pipetting head for its Multimek™ liquid handler. The Multimek 96/384-Channel Automated Pipettor extends this time-tested, rugged platform to applications requiring work in the 384-well format. With capacity from 1 to 30 µL, the new head delivers precise liquid transfers for the automation of higher-density assay formats and plate replication methods. The new pipettor uses air displacement pipetting technology and highly precise, proprietary pipette tips developed by Beckman Coulter.

The original Multimek 96 has a track record of reliability and accuracy, delivering longer run times with fewer breakdowns than other

liquid handlers. That same reliability and precision are retained with the new 384-channel functionality. The Multimek 96/384 automatically loads 384 tips, eliminating manual steps and tip loading errors that reduce



accuracy. Beckman Coulter's patented disposable tip technology eliminates liquid carry-over and contamination and includes built-in quality control information.

Existing Multimek 96 systems can be upgraded to accommodate the use of the 384-channel pipetting head.



## Beckman Coulter and Promega Develop New System for Automated DNA Extraction from Forensic Samples

SUSAN STONE  
BECKMAN COULTER, INC.

At the 12th International Symposium on Human Identity (ISHI) held in October in Biloxi, Mississippi, U.S.A., Promega Corporation and Beckman Coulter unveiled a new DNA purification system for automated extraction of DNA from virtually any type of forensic sample. The system pairs Promega's new DNA IQ<sup>®</sup> DNA Isolation System with the Biomek<sup>®</sup> 2000 Laboratory Automation Workstation from Beckman Coulter.

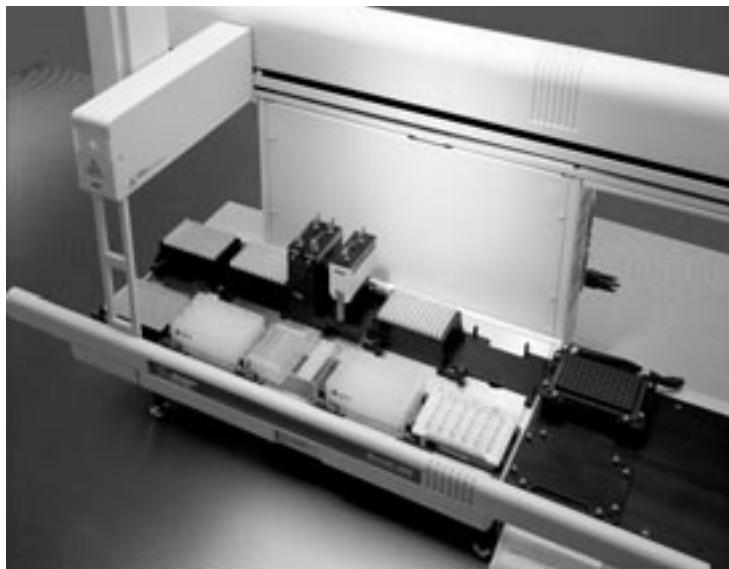
Promega's DNA IQ System uses a novel technology with paramagnetic particles to prepare clean samples for short tandem repeat (STR) analysis. Designed with the forensic community in mind to overcome the problems of current extraction and isolation protocols, the DNA IQ System simultaneously extracts, isolates, and quantitates DNA from various sources. The DNA IQ System can be used either to extract a constant 100 ng of DNA from database samples on a variety of supports (*i.e.*, bloodstain cards, buccal swabs, liquid blood) or to obtain purified DNA free of PCR<sup>®</sup> inhibitors from diverse casework sample types. The system is environmentally friendly and can be automated.

Beckman Coulter has developed a configuration of the Biomek 2000 Laboratory Automation Workstation specifically for the automation of the DNA IQ System. The Biomek 2000 automates the pipetting, magnetic separation, heating, and shaking/mixing steps of the DNA IQ protocol, improving performance and produc-

tivity. The amount of time saved by using the Biomek 2000 and DNA IQ System to extract forensic samples can be substantial. Manual extraction of a single sample can take

approximately five hours. In comparison, the automated system can extract DNA from 88 samples in about two hours, with only 15 minutes of hands-on time by the forensic examiner.

The Virginia Division of Forensic Science in Richmond, VA, one of the nation's leading crime laboratories, is among the first to use this powerful combination to perform DNA extractions. The division is known for being the first state laboratory to offer DNA analyses to law enforcement agencies and the first to create a DNA data bank of previously convicted sex offenders. Its DNA data bank was the first to identify an interstate "cold hit." As a result of its leading-edge practices, the division is widely recognized for its efficient and effective forensic laboratory system. The division expects that use of the Beckman Coulter and Promega solution will further reduce turnaround time for casework while simultaneously improving the quality of the analyses.



Dr. Susan Greenspoon, forensic molecular biologist at the Virginia Division of Forensic Science, presented results of the Virginia Forensic Laboratory's Biomek 2000 and DNA IQ alpha tests at the ISHI. Dr. Greenspoon's conclusions were that the Biomek 2000 and DNA IQ combination performed at least as well as, and outperformed in most instances, the manual extraction method when DNA quantities were limited.

Moving forward, Promega intends to expand its range of forensic sample preparation chemistries that are automated on the Biomek 2000. In December 2001, Promega will begin marketing the AluQuant<sup>®</sup> Human DNA Quantitation System for use on the Biomek 2000. Early in 2002, Promega intends to introduce improved protocols for automating differential extraction—a preliminary and time-consuming step prior to DNA isolation frequently performed on forensic casework samples.



## Announcing MagneSil<sup>®</sup>: A New Paramagnetic Technology in Automated DNA Purification

PETER LOUIE, PH.D.  
BECKMAN COULTER, INC.

Paramagnetic particles (PMPs) have become a revolutionary approach to bioseparations. They are generally small and will respond to a magnetic field but are not capable of becoming independently magnetic, which is an important property to be exploited for efficient separation and collection of the beads.

### PRINCIPLE OF MAGNESIL<sup>®</sup>

The working principle of magnetic separation is based on the affinity groups on the particle surface. When a suspension of these PMPs is mixed with the target molecules, the target will bind to the PMPs, then a powerful magnet is used to immobilize the particles with the bound molecules. After the unbound material is removed by aspiration, the targeted molecules can be eluted by specific reagents from the particles. Advantages of magnetic separations include: low cost, rapid, scalability, lesser stress to

the biomolecules, and, most often, absence of toxic reagents.

MagneSil from Promega represents a unique technology for purifying nucleic acids with the same bind, wash, and elute steps as the familiar silica membrane-based technology. The use of these PMPs allows flexibility in purifying nucleic acid from a variety of starting materials. The small particle size and high binding capacity enable reaction volumes compatible with a 96- or 384-well plate for complete automation of the purification process.


### THREE APPLICATIONS: ONE FORMAT

High-throughput DNA sequencing requires automated, economical, and robust plasmid preparations. The MagneSil Plasmid Purification System employs PMPs for lysate clearing as well as DNA capture, thereby eliminating the need for centrifugation or vacuum filtration for an ideal automation system. Plasmid DNA prepared by the MagneSil method has been tested to ensure optimal performance as templates in BigDye<sup>®</sup> Terminator cycle sequencing.

The Wizard<sup>®</sup> PCR<sup>®</sup> Clean-Up System enables researchers to purify PCR products away from contaminating nucleotides, primers, and small nontargeted amplification products in a complete, walk-away automation format while maintaining high yields. The purified DNA is suitable for microarray preparation, fluorescent sequencing, and many other molecular biological downstream applications. The system efficiently removes primers ( $\leq 50$  bp) and primer-dimers ( $\leq 100$  bp) with yields of  $\geq 80\%$  for PCR products  $\geq 500$  bp.

In fluorescent dye-terminator sequencing chemistry, failure of the removal of unincorporated dye-label terminators will interfere with the signal from sequencing extension products in the 0 to 150 base range and cause problems for base-calling algorithms. Common methods such as gel filtration and ethanol precipitation are problematic to automate. MagneSil offers a distinct advantage of a truly "hands-off" protocol. The Wizard MagneSil Sequencing Reaction Clean-Up System is designed to purify BigDye terminator cycle sequencing reactions, and Promega qualifies the system to achieve 98% accuracy to 600 bases of sequence; however, sequence purified by this method routinely achieves 98% accuracy to 700 bases.



Beckman Coulter is partnered with Promega to distribute the MagneSil systems for plasmid purification, PCR clean-up, and dye-terminator sequencing clean-up. The flexibility and open integration design of Biomek<sup>®</sup> workstations are suited to offer complete automated solutions for these three MagneSil applications on either the Biomek 2000 or FX platform. Please stay tuned for the complete validated solutions from Beckman Coulter for Biomek 2000 and FX by the end of 2001 and beginning of 2002, respectively. 

## Cell-Based High-Content Screening—The Next Frontier

**LYNN AGAJANIAN**  
**BECKMAN COULTER, INC.**

### INTRODUCTION

In the 21st century, drug discovery has entered the next frontier. It's moved beyond high-throughput screening (HTS) into high-content screening (HCS), providing researchers deeper biological information from a single cell. This

information, early in the drug discovery process, allows you to determine more quickly whether to proceed with further testing and shortens the time to begin phase 1 clinical trials.

In previous issues of *T<sup>3</sup>*, we've referred to Beckman Coulter's relationship with Cellomics' and our automated solutions for cell-based screening. This article focuses on a Cellomics HCS assay and the benefits

it brings to the drug discovery process.

Stay tuned for future issues of *T<sup>3</sup>* where we will continue to share informative updates on cell-based HCS.

To obtain a reprint of this poster presentation, please go to the Cellomics web site at [www.cellomics.com](http://www.cellomics.com) and click on Technical Presentations.

## Determination of Cytotoxic Effects Using a Multiparametric Cell-Based Cytotoxicity Assay

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**AND RICHIK GHOSH**  
**CELLOMICS, INC.**

*In-vitro* screening of active compounds for toxic effects earlier in the drug discovery process will help identify problems and reduce the high failure rate of current clinical candidates. Cell-based toxicity assays are crucial in this effort but are limited by the result generated—usually cell death. Thus, we have developed a more sensitive multiparameter cell-based cytotoxicity assay that quantifies early changes to



key aspects of cellular physiology that can lead to cellular toxicity. This assay uses our ArrayScan<sup>®</sup> System High Content Screening (HCS) platform that simultaneously measures changes in nuclear morphology, cell permeability, and lysosomal physiology for individual cells, and also changes in cell density in microplate wells. Dose response and time course data demonstrating the assay's multi-parametric nature

will be presented for sample compounds that affect the cellular targets in various cultured cell lines and also rat primary hepatocytes. Our data show the assay's ability to capture cellular reactions to compounds

and correlate multiple toxicological indicators at a single cell level. This assay represents a distinct advantage for HCS as a screening tool early in the drug discovery process.

### HIGHLIGHTS OF THE ASSAY

- Ability to use negative control wells as calibration wells to automatically set thresholds for normal physiological range of nuclear morphology/size, cell membrane permeability, lysosomal physiology and cell density per field.
- Multiparametric assay that measures changes in nuclear morphology/size, cell membrane permeability, lysosomal physiology and cell density.
- Provides data as a well-based average and also at the single cell level allowing cross correlation of compound effects at a single cell level.
- More sensitive than cell viability as an assay for cell health.
- Applicable to multiple cell types.



## POSTER PRESENTATIONS

## Optimization and Miniaturization of Caspase 3 Assay in 1536-Well Microplate Format on a SAGIAN™ CORE System with an Integrated Acquest\* Reader

**RAJ KURAPATI, KEVIN BANG,  
GRAHAM THREADGILL  
BECKMAN COULTER, INC.**

**A**poptosis is characterized by proteolysis of specific cellular proteins by a family of cysteine proteases known as caspases. In particular, the activation of caspase 3 has been shown to be important for the initiation of apoptosis. Since apoptosis is an important cellular process that is related to many diseases, indication of apoptosis has become an important target for screening of potential therapeutic agents.

EnzChek® Caspase 3 Assay Kit from Molecular Probes has been used for the detection of apoptosis activation by assaying for increased caspase 3 activity. In the present study, we have used this assay to screen approximately 48,000 compounds from a library supplied by Coelacanth Corporation in barcoded 96-well plates. Prior to screening, the compounds were reformatted into 384-well plates.

The screen was carried out in 1536-well plates in order to reduce time and storage requirements. In order to accomplish this task, the EnzChek Caspase 3 assay was first optimized for running at low volume using EnzChek Caspase 3 Assay Kit.

The screening system included an Acquest® reader from Molecular Devices and a Biomek® FX liquid handler integrated onto a SAGIAN™ CORE system. Data management and real-time data analysis during the screen were accomplished using Firepower® software (Exegetix, Inc.) in conjunction with Spotfire® software (Spotfire, Inc.)

The data presented here demonstrate the automation of the screening process in 1536-well format from assay development through primary screening and data management to trace the primary screen hits back to the compound library.

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## Automated Methods to Simplify Sample Processing for DNA Sequencing Using the Biomek® 2000 Laboratory Automation Workstation from Beckman Coulter

**RAJ KURAPATI AND  
GRAHAM THREADGILL  
BECKMAN COULTER, INC.**

**U**sing robotics to automate front-end sample preparation significantly simplifies the DNA analysis process. We have developed a suite of methods for the Biomek® 2000 liquid handler from Beckman Coulter that completely automates the sample preparation for DNA analysis. This “Molecular Biology Suite” consists of automated methods for plasmid DNA purification, quantitation, normalization, sequencing reaction

set up, and post sequencing reaction clean up.

All the methods in the suite were designed to handle up to six 96-well plates simultaneously. The plasmid DNA was purified using Promega's Wizard® SV 96 plasmid DNA purification system available from Beckman Coulter. Real-time quantitation of samples was accomplished with the use of an integrated microplate reader. For normalization of samples, we developed a software wizard that automatically calculates concentrations and generates Biomek 2000 workstation methods to create

normalized plates. Following normalization, a simple pipetting method was used to set up sequencing reactions. The post-sequencing reaction clean up method was developed using an ethanol precipitation protocol with programmed pauses for manual centrifugation.

In this poster, we present the improved throughput and quality of data generated using this “Molecular Biology Suite” of methods to sequence samples from control plasmids and genomic libraries.

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## Automated, High-Throughput Plasmid Purification Methods on the Biomek® 2000 Laboratory Automation Workstation Using the Promega Wizard MagneSil\* System

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**BECKMAN COULTER, INC.**

**DOUGLAS WHITE, DONALD SMITH, JOSEPHINE GROSCH, PH.D., STEVE KRUEGER**  
**PROMEGA CORPORATION**

### POSTER ABSTRACT

**M**ethods for automated, high-throughput purification of sequencing-grade plasmid have been developed using Wizard MagneSil\* reagents on Beckman Coulter's Biomek® 2000 Laboratory Automation Workstation with an integrated orbital shaker.

The Promega MagneSil system uses silica-coated magnetic particles to clear bacterial lysates and bind plasmid. Fully automated 1x96-well

and 6x96-well plate protocols have been developed on the Biomek 2000. No manual interventions are required for either protocol after initial setup. Plasmid yields gave final DNA concentrations sufficient to be used directly in a sequencing reaction. DNA templates prepared by this method were sequenced by capillary electrophoresis. Details of the Biomek 2000 methods, and data generated from these methods, are discussed in this poster.

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## Automated, High-Throughput PCR\* Reaction Cleanup on the Biomek® 2000 Laboratory Automation Workstation Using the Wizard MagneSil\* PCR Clean-Up System

**CHAD PITTMAN, LAURA PAJAK, PH.D., GRAHAM THREADGILL, PH.D.**  
**BECKMAN COULTER, INC.**  
**PAULA BRISCO, STEVE KRUEGER, STEVE EKENBERG, ELAINE SCHENBORN, PH.D., PAUL OTTO**  
**PROMEGA CORPORATION**  
**MADISON, WI**

**T**he Wizard MagneSil® PCR Clean-up System provides a new, high-throughput means to purify PCR products. Two methods have been developed using a Biomek® 2000 Laboratory Automation Workstation with an integrated orbital shaker to purify

either a single plate or multiple plates of PCR samples; multiple-plate processing was achieved by the incorporation of a high capacity stacker carousel to deliver consumables.

PCR products are typically purified to remove excess nucleotides, salts, primers and small, non-targeted amplification products like primer-dimers that can interfere with downstream applications. The Wizard MagneSil PCR Clean-up System removes such impurities while maintaining high recovery of PCR products. The system utilizes MagneSil paramagnetic silica particles developed at Promega and provides ease of use, flexibility and

efficient DNA purification that is not obtained with alternative methods such as centrifugation and vacuum-based formats. PCR products greater than 150 bp in size are selectively isolated from primers and primer-dimers with high yields and purity in a 96-well plate format. The purified PCR products are eluted directly in water and provide excellent substrates for downstream fluorescent DNA sequencing and microarray analyses.

Details of the Biomek 2000 methods and data generated from these methods are discussed in this poster.

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## Expanding the Core Continuum

The Core Continuum was developed to rapidly provide new technologies to our Core Systems customers. Since its inception, over twenty new instruments have been added to the Continuum, dramatically expanding the list of solutions a Core System can provide.

While the Core Continuum continues to expand, this month's article comes from a long-time Core Partner, MJ Research, Inc. In this article, they highlight new developments that make thermal cycler automation more robust and reliable.

Also, stay tuned for more exciting announcements on high-throughput molecular biology automation in the next issue of T<sup>3</sup>.

— Jan Pursley  
Beckman Coulter, Inc.

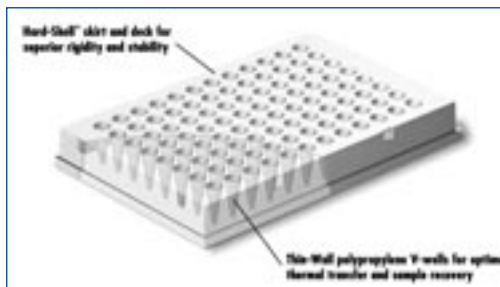
## MJ Research Provides Solutions for Problems in Thermal Cycler Automation

**DIANE ERICKSON AND  
DAVID TITUS, PH.D.  
MJ RESEARCH, INC.**

Polypropylene has long been the plastic of choice for DNA sequencing and amplification reaction vessels. Polypropylene (PP) exhibits very low DNA binding, is resistant to high temperature, and can be readily molded into thin-wall tubes and microplates. Unfortunately, thin-wall PP microplates are less rigid and therefore less than ideal for robotic handling. Furthermore, PP is prone to heat-induced shrinkage and distortion when exposed to the high temperatures employed during thermal cycling or heat sealing operations.

Plate warping and shrinking depends on the exact temperatures employed in the protocol but, in severe cases, users may experience a range of annoyances, including:

- difficulty removing the plate from the thermal cycler block
- poor fit in plate readers used downstream
- plates not sitting flat on the deck
- automated liquid handlers not delivering or retrieving the correct amount of liquid
- broken/bent needles in liquid handlers
- unreliable handling in plate stack loaders
- robotic arms having difficulty picking up plates



Researchers have tried a number of techniques to combat this troublesome issue, including special plate adapters, vacuum fixtures, and modified thermal cycling protocols.

A suite of new products recently introduced by MJ Research, Inc., Beckman Coulter's automation partner for thermal cycling, now promises to solve these problems. These products include new designs for thin-wall microplates, non-stick cycler blocks, and spring-loaded plate lifters for the cycler blocks.

The novel Hard-Shell<sup>®</sup> thin-wall microplate (patent pending) employs two-component molding technology

to achieve its impressive performance (see figure). The skirt and deck are molded from a rigid, thermostable polymer that completely resists the warping and shrinkage experienced with traditional, one-component polypropylene microplates. In a separate step, the thin-wall wells are molded into the hard shells, using virgin polypropylene selected for low DNA-binding.

This unique two-component design offers many advantages for the high-throughput laboratory as well as additional benefits for other applications. The footprint and well spacing fit proposed industry standards and these dimensions remain stable even after the thermal stresses of thermal cycling or heat sealing (see table). The extremely rigid sidewalls exhibit very little deflection under pressure and thus are ideal for plate gripper arms and plate stackers. Raised rims around each well allow tight sealing with a variety of systems, including pressure-based pads, adhesive films, and heat-sealing methods. Recommended thermal cycling volumes are 5 to 125  $\mu$ L for the 96-well plates. Bar-coded plates and a 384-well version of the Hard-Shell microplate are due to be released soon.

Unique two-component design — Superior dimensional stability and flatness for precise positioning in lab automation

Hard-Shell <sup>®</sup> 96	Before Cycling	Difference After Cycling	Proposed Industry Standards
X-axis footprint	127.82±0.13mm	<0.04mm	127.76±0.25mm
Y-axis footprint	85.61±0.12mm	<0.04mm	85.48±0.25mm
Well-to-well spacing	9.00mm	<0.01mm	9.00mm
Flatness—max. deviation from flat plane of well bottoms	0.1mm	No change	0.38mm
Sidewall rigidity—flexure under 1kg load	0.6mm		3.0mm

Additional performance data and instrument compatibility charts are available at [www.mj.com](http://www.mj.com).

The plates are produced in stringent clean-room conditions and are certified by an independent laboratory to be free of contaminating DNase, RNase, and human DNA.

Two other recent advances meet the need for 100% reliable plate retrieval from cycler blocks. MJ Research 96-well and 384-well blocks are now supplied with a non-stick coating that greatly diminishes problems due to plate sticking after

thermal cycling. The thermal properties of non-stick blocks are virtually identical to previous blocks, so protocols developed for older blocks are transferable to newer blocks. To further help retrieval of plates from cycler blocks, MJ Research, Inc., has created spring-loaded plate lifters that elevate the plates 5 mm above the block surface after cycling when the lid is opened. These simple devices can be retrofitted to any MJ Research 96-well or 384-well

block, but are most effective when used in combination with the newer non-stick blocks. This small vertical change can dramatically improve plate access by robotic arms, and is also a convenience for those who manually remove plates from cycler blocks.

For more information or to request microplate samples from MJ Research, Inc., visit [www.mjr.com](http://www.mjr.com) or call (888) 735-8437.



## Promega's SV 9600 Kits Provide Cost-Effective Plasmid Prep with Beckman Coulter's High-Throughput Automation

**JASON FAWCETT**  
**BECKMAN COULTER, INC.**

It is no secret that Beckman Coulter and Promega are working together to provide customers with rock-solid chemistry and breakthrough automation. Now another kit has been released to cater to the high-throughput plasmid prep customer. Beckman Coulter is now providing the Wizard<sup>®</sup> SV 9600 purification kit, which is the bulk version of the SV 96 kit. All reagents are provided in larger quantities in larger bottles for easier use and storage. Designed to reduce unwanted plastics and leftover reagents, the kit contents can be ordered individually (see Table 1) allowing only the reagent needed to be reordered instead of an entire kit.

There are many benefits to using silica filtration methods: no spinning, no manual handling, no making of solutions, and no extra costs. The kits are extremely flexible and can accommodate a wide range of culture variations. Everything comes ready-to-use with no surprises. The SV 9600 provides everything essential for your plasmid prep at a great value.

Beckman Coulter has also produced a high-throughput method

using the Biomek<sup>®</sup> FX. The method, "Promega Twelve Plate Plasmid DNA Miniprep," is designed to use Promega's bulk plasmid purification kit. However the single- and five-plate kits can also be used. The twelve-plate plasmid purification method can purify 1200 samples in less than 3.5 hours. The SV 9600 is well suited to supply the reagents for this high-throughput plasmid purification solution.

Beckman Coulter is committed to creating robust, flexible, and easy-to-use automated solutions. Methods developed by Beckman Coulter have been validated and proven to

work reliably over and over again. The software allows easy modifications to any method to suit specific needs.

The combination of Beckman Coulter's automation and Promega's leading chemistry provides you with a complete out-of-the-box solution that you can rely on.



The Biomek FX automated system for the twelve-plate plasmid purification using the SV 9600 kit.

**Table 1. SV 9600 Kit and Kit Contents**

Product	Size	Part Number
SV 9600 Kit	100 x 96 preps	725200
SV 96 Wash Solution	370 mL	725211
SV Neutralization Solution	900 mL	725212
SV 96 Lysate Clearing Plate	100 plates	725213
SV 96 Binding Plate	100 plates	725214
SV 96 Cell Resuspension Solution	800 mL	725215
SV Cell Lysis Solution	800 mL	725216
Water, Nuclease Free	150 mL	725230

## Improving Accuracy by Use of Technique Calibration

LISA KNAPP AND CURTIS FARLEY  
BECKMAN COULTER, INC.

For any given assay, many laboratory and environmental conditions can contribute to the accuracy of dispensing with an automated liquid handler. Among the obvious are liquid type, technique, solution retention in the tips, laboratory humidity, and laboratory temperature.

When determining the accuracy of a liquid handler, it may not be suitable to check accuracy gravimetrically. For volumes less than 10 µL, difficulties with gravimetric measurements are encountered due to volume loss through evaporation.

As a result, it is desirable to use an indirect, spectrophotometric method to determine the accuracy of low-volume dispenses. This method can be performed for any volume and in any lab with access to a spectrophotometer.

Assuming that the precision of a particular technique has been optimized to meet the requirements of an assay, then the accuracy of the dispense will be a matter of calibration. The Biomek® FX software offers a feature to manipulate the Scaling Factor and Offset of the volume displaced inside the mandrels for any particular technique, thus giving the user a method for adjusting the accuracy of the dispensed volume.

This Technical Information Bulletin will show the steps involved in improving the accuracy of the dispensed volume by using the calibration feature of the Biomek FX software. To accomplish this, an introduction to Techniques and the Technique Browser will be presented, followed by a more in-depth look at the Calibration tab within the

Technique Editor. A detailed description of the process used to calibrate a pipetting technique will then be shown by example.

Briefly, the process of calibration involves:

1. The creation of a standard curve with a calibrated hand pipettor.
2. The Biomek FX is used to pipette the desired volume using the selected technique with the default Scaling Factor and Offset values of 1 and 0, respectively.
3. The actual volume dispensed is calculated by comparison of the A510/650 from the plate dispensed with the Biomek FX to the standard curve.
4. A graph of the desired dispense volume vs. the actual volume dispensed is created and the slope and Y-intercept are determined.
5. These calculated values replace the default values for the Scaling Factor and Offset, respectively, in the technique.
6. Another dispense is performed with the Biomek FX using the same technique with the new Scaling Factor and Offset, and determines if the accuracy requirement of the assay has been met.



[from a Technical Information Bulletin, number T-1915A, available online at [www.beckmancoulter.com](http://www.beckmancoulter.com)]

**Technique Editor - Low-Volume**

Pipetting Template:

It may be necessary to adjust the displacement volume to account for varying properties of liquids such as viscosity to accurately deliver a desired volume. Using the equation:

$$\text{Displaced Volume} = (\text{Desired Volume}) * (\text{Scaling Factor}) + (\text{Offset Volume})$$

adjust the offset (a fixed volume) and the scaling factor (multiply, amplify, etc. the desired volume) to deliver the desired volume.

Scaling Factor:  Offset:

---

Using these parameters, the instrument will displace  µL to deliver the desired volume of  µL.

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Minimum pipetting height:  mm above the well bottom.

The Calibration tab within the Technique Editor of Biomek FX v2.1 software.

## 2002 Training Classes

CLASS	DATE	LOCATION
SAGIAN™ Core System User Training	January 8-11	Indianapolis, IN
	February 26-March 1	Indianapolis, IN
	March 19-22	Indianapolis, IN
	April 23-26	Indianapolis, IN
SAGIAN Core System Advanced User Training	June 19-20	Indianapolis, IN
Biomek® FX User Training	January 9-11	Munich, Germany
	February 13-15	Munich, Germany
	February 27-March 1	Munich, Germany
	March 6-8	Munich, Germany
	March 13-15	Munich, Germany
	April 17-19	Munich, Germany
	May 22-24	Munich, Germany
	TBD	Indianapolis, IN
Biomek FX Advanced User Training	Scheduled as needed	
Integrator's Training—ORCA® Transportation Module	Scheduled as needed	
SILAS™ Developer's Kit	Scheduled as needed	

## Trade Shows 2002

SHOW	DATE	LOCATION
Lab Automation	January 27-29	Palm Springs, CA
PittCon	March 17-22	New Orleans, LA
Forum Labo	March 26-29	Paris, France
Drug Discovery Technology	April 15-18	Stuttgart, Germany
Analytica	April 23-26	Munich, Germany
MipTec-ICAR	May 27-30	Basel, Switzerland

## Current Software Version Information

PRODUCT	SOFTWARE	VERSION
Biomek 2000	BioWorks™	3.2
Multimek™ 96	Multimek Pro	1.4.4a
SAMI®	SAMI	3.5
AAO	SAGIAN Automated Assay Optimization	1.5
Biomek FX	Biomek FX System Software	2.1a

## Current SAGIAN Core System Menu

### TRANSPORTATION ROBOT

- ORCA 1-Meter Rail
- ORCA 2-Meter Rail
- ORCA 3-Meter Rail

### LIQUID HANDLING WORKSTATIONS

- Biomek FX
- Biomek 2000
- Multimek 96

### SAGIAN STATIONS

- Bar Code Reader
- Plate Shaker
- Hotel and Carousel
- Plate Sealer
- CS Incubator (4 and 8 position)
- Filtration Station
- Lid Removal/Storage Station
- Tip Lift (Biomek & Multimek)
- CO<sub>2</sub> Incubator with Hotel Carousel
- Lid Disposal Station
- Print & Apply

### CORE COMPLIANT INSTRUMENTS

- Acquest\* (Molecular Devices)
- ALPS 300\* Sealer (ABgene)
- Analyst\* HT (Molecular Devices)
- cytomat\* 2 and cytomat 6000 Series Incubators (Kendro Laboratory Products)
- ELx405 Magna (Bio-Tek)
- FLIPR<sup>384</sup>\* (Molecular Devices)
- Multidrop Deepwell (Titertek)
- PlateCrane\* (Hudson)
- SPECTRAMax\* GEMINI XS (Molecular Devices)
- SPECTRAMax PLUS<sup>384</sup> (Molecular Devices)
- SPECTRAMax 340PC (Molecular Devices)
- Victor<sup>2\*</sup> V Reader (PerkinElmer Life Sciences)
- ViewLux\* Microplate Imager (PerkinElmer Life Sciences)

### CORE PARTNER STATIONS

- 1420 Victor<sup>2</sup> Reader (PerkinElmer Life Sciences)
- ArrayScan\* HCS System (Cellomics)
- ELx405UV w/Waste Collection (Bio-Tek)
- FLUOstar Galaxy (BMG Lab Technologies)
- KineticScan\* HCS System (Cellomics)
- LUMIstar (BMG Lab Technologies)
- MicroBeta\* TriLux Detector (PerkinElmer Life Sciences)
- Multidrop 384 Dispenser (Titertek)
- POLARstar Galaxy (BMG Lab Technologies)
- PTC-225 DNA Engine Tetrad Thermal Cycler (MJ Research)
- SPECTRAMax 190 (Molecular Devices)
- Uninterrupted Power Supply (Best Inc.)

### DISCONTINUED CORE PARTNER INSTRUMENTS

- ALPS 100 Sealer (ABgene)
- EL404R Microplate Washer (Bio-Tek\*)
- FLUOstar 97 (BMG Lab Technologies)
- POLARstar (BMG Lab Technologies)
- SPECTRAMax 250 (Molecular Devices)
- THERMOmax\* (Molecular Devices)

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