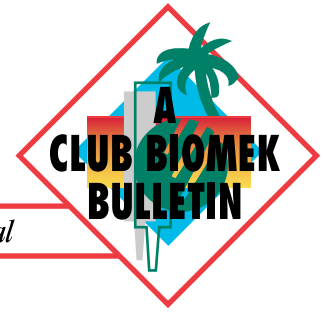


# T<sup>3</sup> UPDATE



Fall 1997

*New tips, tricks and techniques to help keep your Biomek® 2000 performing to its fullest potential*

Volume 1, Issue 5

**W**elcome to the fifth issue of T<sup>3</sup>. This issue finds us in a transition as we continue to integrate *Sage Advice*, SAGIAN's newsletter for core system and custom system biorobotics. In this issue, we introduce options for the core system that will increase "process control" for our Biomek customers.

Also in transition is the marketing editorial staff of T<sup>3</sup>. Congratulations to Charles Powell as he moves to SAGIAN as our Manager of Sales and Support Services. Replacing Charles as Editor and Product Manager for Biorobotics within Beckman's North America Operations — Bioresearch (NAO-B) will be John Gerace, who comes from SAGIAN with more than five years of involvement in the Biomek and custom integration products. Our goal of this newsletter remains the same: to provide timely information to help keep your Biomek 2000 performing to its full potential.

Please read on and feel free to provide feedback via e-mail or fax.

## INTERIM EDITOR

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## NEW PRODUCTS

### *NEW CORE COMPONENTS FOR THE BIOMEK INTEGRATED LABORATORY AUTOMATION SYSTEM*

Beckman Instruments' biorobotics team is continually developing new peripherals for automated microplate operations integrated with the SAGIAN ORCA™ robot and SAMI software. We are increasing our efforts to identify reliable, high-value, third-party devices to include in our product offering. Stemming from this ongoing effort, we are pleased to announce the following devices incorporated into our menu of standard components available within Biomek integrated laboratory automation systems.

- MPS Filtration Station
- MPS Tip Lift & Lid Disposal Unit
- BMG LabTechnologies' LumiStar & FluorStar 97
- Wallac Oy's 1420 VICTOR multi-label counter
- MJ Research's Tetrad thermal cycling instrument
- Best Power's monitored Uninterruptible Power Supply

This list of new components, along with the micro-plate devices already a part of our three system configurations (ELISA, cell-based, binding assays), give any high-throughput screening laboratory a great deal of flexibility while designing a reliable automated solution



## SAGIAN PERIPHERALS

The MPS (microplate systems) Filtration Station is ideal for automated filtering applications involving Millipore or Polyfiltronics 96-well filter microplates. In addition to vacuum filtration, the device also incorporates a liquid dispenser that delivers wash solution to all 96 wells of a microplate simultaneously. The unit is able to perform multiple dispense and filtration cycles. Filtrate can be collected directly into a standard-height or deep-well microplate, or diverted to a waste container.

The MPS Tip Lift offers an efficient solution for bulk storage of tip boxes on an integrated system.

The Tip Lift provides tip boxes for the ORCA™ robot to supply the Biomek® 2000 workstation. The MPS Tip Lift accommodates a maximum of 96 200- $\mu$ l tip boxes or 42 1,000- $\mu$ l tip boxes. The Lid Disposal Unit is an option that works in conjunction with the Tip Lift to remove and discard pipette tip box lids.

## THIRD-PARTY DEVICES

In addition to the SAGIAN MPS Filtration Station and Tip Lift, a number of third-party devices are now available as standard components that can be incorporated into a complete automation system:

- The LumiStar Microplate Luminometer from BMG LabTechnologies is capable of performing flash kinetic readings as fast as 100 ms, and glow kinetics of up to 12 hours.
- The FluorStar 97 Microplate Fluorometer from BMG LabTechnologies is designed for the widest possible range of fluorescence applications. Readings can be taken above or below the plate.
- The 1420 Victor Multilabel Counter from Wallac Oy is a fluorometer, photometer, and luminometer all in one. This instrument also reads 384-well microplates.
- MJ Research, Inc.'s DNA Engine Tetrad is a single instrument containing four individual 96-well thermal cycling banks, each possessing a remote-controlled automatic

heated lid and providing access to plate placement and removal by the ORCA robot.

- The Uninterruptible Power Supply from Best Power is able to provide 15 minutes of backup power for up to three stations on a system.

## SAMI™ SOFTWARE UPDATE

With the addition of these new peripherals to our core menu offering, the system software has been modified to allow for these multiple, same-component additions to the system configuration:

- Two (2) MPS CO<sub>2</sub> Incubators
- Two (2) MPS Carousels
- Two (2) MPS Shakers
- Eight (8) MPS CS Incubators
- Four (4) MJ Research Tetrads

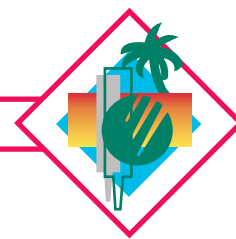
As the Beckman Instruments biorobotics team looks forward to continuing its support of all of our core system customers worldwide, we are excited about the future. Each client stands to benefit

from the unique solutions we can provide as we expand our menu of standard components and continue to increase our software products' utility.

For more information on the menu of peripheral devices for integrated systems, please call your Biomek representative.



Figure 1. The Biomek® core system.



## SOFTWARE INTEGRATION

NEW!

## BIOSCRIPT™ PRO BEING RELEASED

For years users have developed programs to make the Biomek® perform tasks outside the standard software capability. This fall, Beckman Instruments will formally release BioScript Pro. Supported by an owners reference guide, researchers can develop custom Biomek programs to perform functions not possible under standard BioWorks™ software.

BioScript Pro's defined function range is limited only by the Biomek's physical capability. Hence, the flexibility in controlling the Biomek 2000 Laboratory Automation Workstation, Side Loader and accessories is endless.

BioScript™ Pro is a programming language based on Tcl (Tool Command Language). Users with experience in Tcl, BASIC, C/C++, PASCAL, Java or other structure program language will be comfortable programming in this environment; users who prefer Windows\* Icon-Interface-based programming are urged to stick with BioWorks™. Applications that require pipetting into and out of unusual labware or tool movements with custom parameters are examples where BioScript would be appropriate.

For a detailed description of the improvements to be found in BioScript Pro over BioScript, please contact your Biomek representative. Below are the top five highlights in this release.

- BioScript Pro communicates through BioWorks. It provides status information on tips, tools and labware, used in movement commands. Hence, BioScript Pro features obstacle avoidance capabilities.

- DDE (Dynamic Data Exchange) capabilities have been implemented. Applications for work listing and smart pipetting applications are possible. For example, BioScript can direct Microsoft Excel\* to import and manipulate data, and extract the data from Excel when calculations are completed. Imagine a normalization assay after the Gripper Tool loads the 96-well plate on a plate reader: O.D. information is converted to text, a calculation is performed, and the Biomek is directed to pipette liquid, to bring all wells to the same concentration.

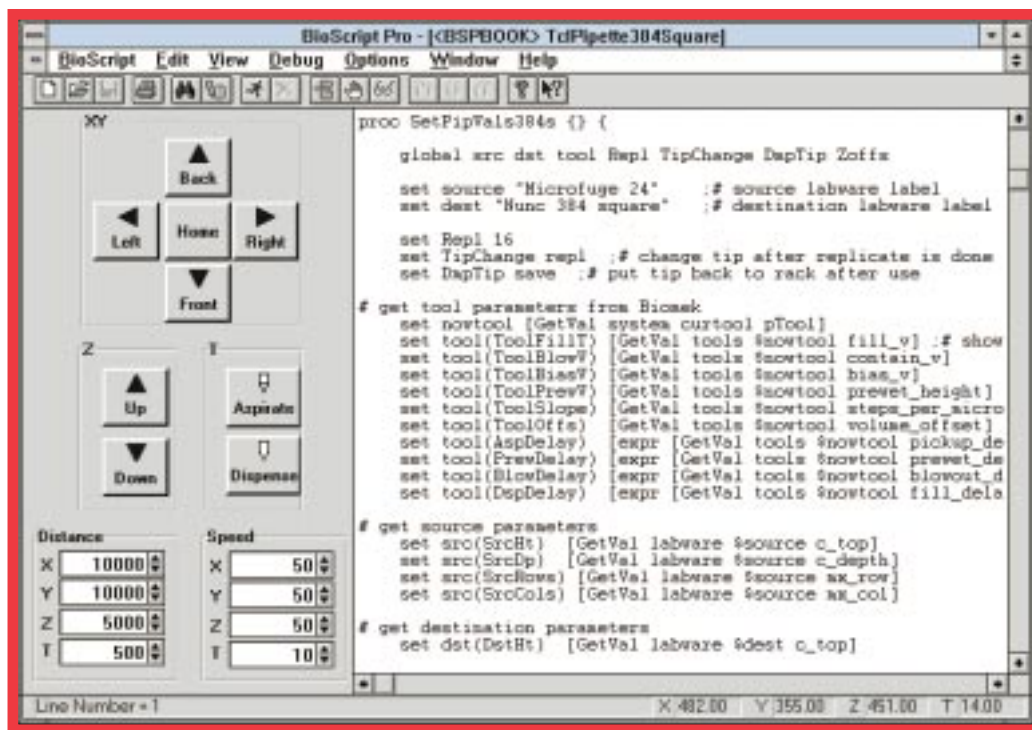


Figure 2. BioScript Pro user interface with a BioScript displayed. Controls for developing instrument movements are on the left.

- Debugging: BioScript Pro facilitates script creation by allowing the Biomek and BioWorks to step through each code, set watch variable and breakpoints. This speeds the development and implementation of scripts.
- Through access to resource variables, custom labware, tools, devices and tips can be defined and utilized.
- BioScripts may be imported and run on systems running solely under BioWorks.



## BioWorks™ VERSION 2.1 ARRIVES

### **What's new**

In response to our plans to release BioScript Pro, we took the opportunity to make a few improvements in BioWorks 2.0. Following is a short list of the features added and the problems fixed in BioWorks 2.1 (This software release is a mandatory upgrade for all Biomek 2000 systems running under Version 2.0.)

- Export of a single method to a floppy disk.
- A more robust method validation check. Methods successfully checked in earlier versions of BioWorks may now produce validation errors.
- Initialization procedure for the Wash Tool has been changed. Users will need to swap the inlet and outlet tubes connected to the peristaltic pump for proper Wash Tool operation.
- Improvements to the installation routine make it more robust.
- Resize button added to Lab Book Manager. This allows the user to shrink a selected lab book to its minimum size, to aid in transfer by floppy disk.
- T-motor stall detection has been added after tip ejection. The system will retry a tip ejection three times if a stall is detected.

There will be an EPROM swap performed by your Beckman service engineer. Other updates will be found in the release notes of the software.

### **Things to Remember**

- This installation updates all Beckman-supplied methods and scripts. If you have modified these methods, SAVE them under a new name before installing version 2.1.
- Any lab books beyond 10 will not automatically convert; these need to be imported after installation.

If you are still running under version 1.4 and are interested in reviewing the benefits of upgrading, call your Biomek® representative.

## TROUBLESHOOTING

### **PLASMID KIT OPTIMIZATION**

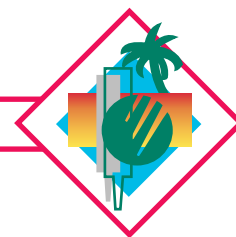
Beckman's Plasmid Purification Kit is a fully automated alkaline lysis 96-well plasmid miniprep kit. It produces 2-10 µg of DNA with purity sufficient for automated fluorescent DNA sequencing. With the use of the Gripper Tool and filtration we avoid ethanol precipitation, as well as centrifugation past the pelleting step. Success is truly a reflection of strict adherence to the protocol and method.

DNA sequencing demands a high level of purity. In this kit, DNA binds to Beckman's Ultrasphere® resin in the presence of a strong chaotrope. Bound to Beckman's modified silica is the template DNA; impurities such as RNA, carbohydrates, proteins, and other small molecules are washed away. A final wash of water and a low salt buffer will elute the DNA with final purity sufficient for two to four sequencing runs. The kit contains all components from lyse and wash buffers to collection plates. The kit will save time and provide guaranteed optimal results. To ensure success, areas of the protocol that users should pay close attention to are cell growth, cell lysis and kit setup steps.

### **Vector and host strain selection**

Plasmid copy number and host strain characteristics are key to affecting yield in a given purification system. Copy number is determined by the amount of DNA that surrounds the origin of replication within the plasmid (a.k.a. replicon). Some DNA sequences, as well as the size of the insert, can have an effect on copy number. As an example, Beckman recommends using pUC, pGEM\*, and pBluescript\* as a preferred vector. Table 1 illustrates discrepancies in results if a high copy vector is not used, especially with a growth volume of 2 ml.

For bacterial strains we recommend the use of *E. coli* DH5 for cell propagation. This mutant is lacking the endA gene coding for endonuclease I, a protein which uses double-stranded DNA as a substrate. In turn, using an endA+ strain in our plasmid amplification step will jeopardize the yield output. Other bacterial strains that have worked well are XL Blue and DH10B. In addition, we have found that JM101, 105, 109, and HB101 have good plasmid yield, but the sequencing data is inconsistent. These strains contain large amounts of carbohydrates that are released during lysis.



**Growth Conditions**

The kit requires stringent growth conditions. Bacterial cultures for plasmid preps should come from a single colony picked from a culture plate. Uneven culture growth will occur if the subculture is from glycerol stocks, or liquid cultures. The kit requires the use of an extra-high-nutrient broth such as TB (Terrific Broth). Magnificent Broth from MacConnell has been reported to work as well.

Growth in the 96-deep-well plate, compared with a 5 ml tube, will produce a lower yield. This is a reflection of the size of the culture tube and volume of media. Allow 20 to 22 hours for proper growth. Whether growth takes place in the Beckman deep-well titer plates or in individual tubes, proper aeration is important. Leave the toothpicks in the tubes and cover with foil.

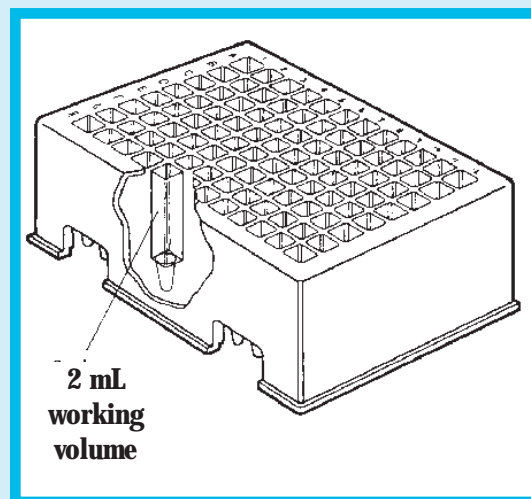
For troubleshooting guidelines, contact Beckman Product Support at 1 (800) 4BIOMEK or 1 (800)854-8067 in the USA; 1 (800) 387-6799 in Canada.

Plasmid	Copy number
pUC	500-700
pGEM	300-700
pBluescript	100-150
ColE1	more than 15
pBR322	more than 25
pSC101	more than 5

*Table 1. Discrepancies in results.*

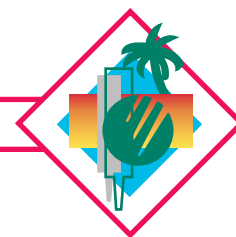
## Square-Well Titer Plates Now Available in Sterile Format

- Provides 2 mL nominal capacity per well in a 96-well format
- Ideal for large-volume applications such as receptor binding assays or growth of host strain in Beckman's Plasmid Purification Kit
- Compatible with Beckman J6 Centrifuges



Part No.	Description	Quantity	Capacity
140504	Square-well plates, polypropylene, nonsterile	24	2 mL/well
609681	Square-well plates, polypropylene, sterile	24	2 mL/well
356980	Adapter for J6, JR3.2 rotor. Holds 4 plates, 1 in each position	set of 4	
356981	Adapter for J6, JR3.2 rotor. Holds 4 plates, 2 in each position	set of 4	

**PLEASE UPDATE YOUR BIOMEK® ACCESSORY CATALOG**



## 1997 TRADE SHOWS AND MEETINGS

Specified Biological Production	October 13-14
Frederick Conference	October 20-22
AAPS	November 3-5
Eastern Analytical Symposium	November 16-21
Human Genetics	October 28–November 1
Bioprocessing	November 3-6
Solution Interaction & Macromolecules	November 15-17
Nucleic Acid Symposium	November 19-21
Cell Biology	December 13-17

## TECHNICAL AND APPLICATION BULLETIN INDEX

The following information is available from Beckman.  
*Technical(T) and Application(A) Information Bulletins*

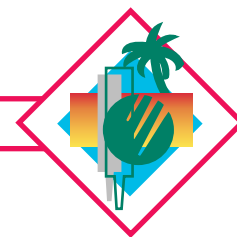
T-1709	The Automation of Three Clinically Important ELISAs with the GenELISA V2.1 System
T-1710A	A Method for Interfacing the High-Density Replication System with the Biomek <sup>®</sup> 1000 Side Loader
T-1711	Preparation of High-Density Colony Filters for Screening Cosmid Libraries
T-1713	Hybridoma Screening Using the High-Density Replicating System on the Biomek 1000 Automated Laboratory Workstation
T-1721	Complete ELISA Automation Using the Biomek 1000 SL and SL Incubator
A-1743	Validation of the Biomek 1000 BioRobotics System for LAL Endotoxin Testing Using the BioWhittaker Kinetic-QCL System
A-1749	Complete Automation of Endotoxin Detection Using the Biomek 1000 BioRobotics System for LAL Endpoint Assays
A-1759A	Use of the Biomek Workstation for Ki Determinations
A-1764A	ELISA Automation: A Biomek 1000 to Biomek 2000 Comparison of Clinical ELISAs
A-1765A	Automation of HIV Proteinase Enzyme Assay Using Scintillation Proximity (SPA) Technology
A-1766A	High-Throughput DNA Sequencing Reactions Using the Biomek 2000 BioRobotics System
A-1767B	Contamination-Free PCR Preparation of Multiple Samples Using the Biomek 2000 Laboratory Automation Workstation
A-1802A	Radioimmunoassay Automation: Development of a Single-Step Assay Using the Biomek 2000 Laboratory Automation Workstation Integrated with the MicroBeta PLUS 96-Well Scintillation/Luminescence Detector

A-1826A	High Throughput Purification of Plasmid DNA Using the 96-Plasmid Purification Kit on the Biomek 2000 Laboratory Automation Workstation
A-1835A	High Throughput Automated Purification of Plasmid DNA Using the 96-Plasmid Purification Kit With the Gripper Tool on the Biomek 2000 Laboratory Automation Workstation
BA96-3145	Biomek 2000 Laboratory Automation Workstation: Modifying Pipetting Tool Specifications in BioWorks Software
BA96-3146	Biomek 2000 Laboratory Automation Workstation: Introducing New Labware Specifications into BioWorks™ Software
T-1809A	Integration of the Biomek 2000 and Wallac MicroBeta Trilux Microtiter Plate Scintillation/Luminescence Detector
T-1832A	The Gripper Tool: Expanding the Functionality of the Biomek 2000 Laboratory Automation Workstation
T-1833A	Colony Selection with an Automated 384-Pin High-Density Replicating Tool (HDRT)
T-1843A	Bioscript™ Pro: Programming Language for the Biomek 2000
T-1845A	Beckman/Sagian “Core” Molecular Biology Systems

## ARTICLE REPRINTS

The following article reprints are available from Beckman.

007-134	A Flexible, Integrated System for Automation of Hybridoma and ELISA Procedures, E.W. Stewart and N.C. Appleby
007-135	Automated Sanger Dideoxy Sequencing Reaction Protocol, J. Zimmerman, H. Voss, C. Schwager, J. Stegemann and W. Ansorge, Federation of European Biochemical Societies, 223: 432-436 (1988)
007-137	Automation of Dideoxynucleotide DNA Sequencing Reactions Using a Robotic Workstation, R. K. Wilson, A.S. Yuen, S.M. Clark, C. Spence, P. Arakelian and L.E. Hood, BioTechniques 6: 776- (1988)
007-138	Automated Methods for Single-Stranded DNA Isolation and Dideoxynucleotide DNA Sequencing Reactions on a Robotic Workstation, E.R. Mardis and B. A. Roe, BioTechniques, 7: 840- (1989)
007-182	Detection and Quantification of Gene Amplification Products by a Nonisotopic Automated System, M. Holodniy, M.A. Winters and T. C. Merigan, BioTechniques 12: 37-39 (1992)
007-320	Pharmaceutical Biotechnology International (1995). Beckman Corporate Profile and High-Throughput Screening Article.



## FREQUENTLY ASKED QUESTIONS

### QUESTIONS

1. When using a quarter horizontal and a half horizontal reservoir with a MP tool, tips may misalign causing the reservoir to flip. How can I correct this?
2. I'm upgrading my BioWorks™ software to version 2.1 and I have 15 lab books. Normal upgrading procedure will not allow me to automatically import more than 10 lab books. How do I import the other 5?
3. If the method crashes, can I start the method where it left off?
4. Can I run more than one plate and use the same tip box?
5. What precision can I expect when using the HDR tool to transfer nl volumes?
6. Can I spot PCR\* products, plasmids or DNA?

### ANSWERS

1. Call Product Support at (800) 854-8067, Ext. 7885 and ask for the file 14a\_res.exe. We have created a lab book file that has been stripped of everything except the definitions for the updated reservoirs. When you receive this file, expand the self-extracting file in a TEMP subdirectory on your hard drive and then copy all of the files to a floppy. Import the reservoir definitions into your current lab book.
2. When your Field Service Engineer installs version 2.1 BioWorks software, inform him/her that you have more than 10 lab books. This procedure requires a modification to the Biomek.ini file.
3. Yes.
  - a. Edit the method by retaining the current Initial Configuration.
  - b. Delete the lines that have been completed.
  - c. Give this method a new name. (If the method crashed in the middle of a plate, the new method will begin at the beginning of the plate.)
4. Yes. Choose the reset tip rack icon off of the function palette and click on the tip rack you wish to reuse. Set the used tip number to "0."
5. On average, 10%. However, the precision one achieves is highly dependent on the type of liquid you are transferring and the surface or solution you are transferring it to. Please reference: Brandt, D.W., "Multiplexed Nanoliter Transfers for High Throughput Drug Screening Using the Biomek 2000 and the High Density Replicating Tool," Journal of Biomolecular Screening, Vol. 2 (2), Summer 1997 (Literature Order No. R-8212A).
6. PCR products, plasmids or DNA can be spotted on filter paper if pins are sufficiently washed using the standard HDR wash solutions in the following order: bleach, water, and ethanol.

# THE 'GOLDEN TIP' SURVEY



**Return via FAX to: Beckman Instruments (714) 773-6611**

**T**his is your big chance to give us your Golden Tips, so Take Time to Talk ... (T<sup>3</sup>!) If you have a great idea or have come up with a novel solution to a bothersome problem, share it with the Club.

**The device(s) I would most like to see integrated into the Biomek<sup>®</sup> 2000 are:** \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**The things I like most about my Biomek<sup>®</sup> 2000 are:** \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**The things I dislike most about my Biomek<sup>®</sup> 2000 are:** \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**I would really like to see, in BioWorks<sup>™</sup>, a way to:** \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**I have got a Golden Tip(s) for you:** \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**Can we talk about...** \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Name: \_\_\_\_\_  
Organization: \_\_\_\_\_  
Address: \_\_\_\_\_  
City: \_\_\_\_\_ State/Province: \_\_\_\_\_ Zip/Postal Code: \_\_\_\_\_  
Phone: \_\_\_\_\_ FAX: \_\_\_\_\_ E-mail: \_\_\_\_\_

FAX TO:  
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