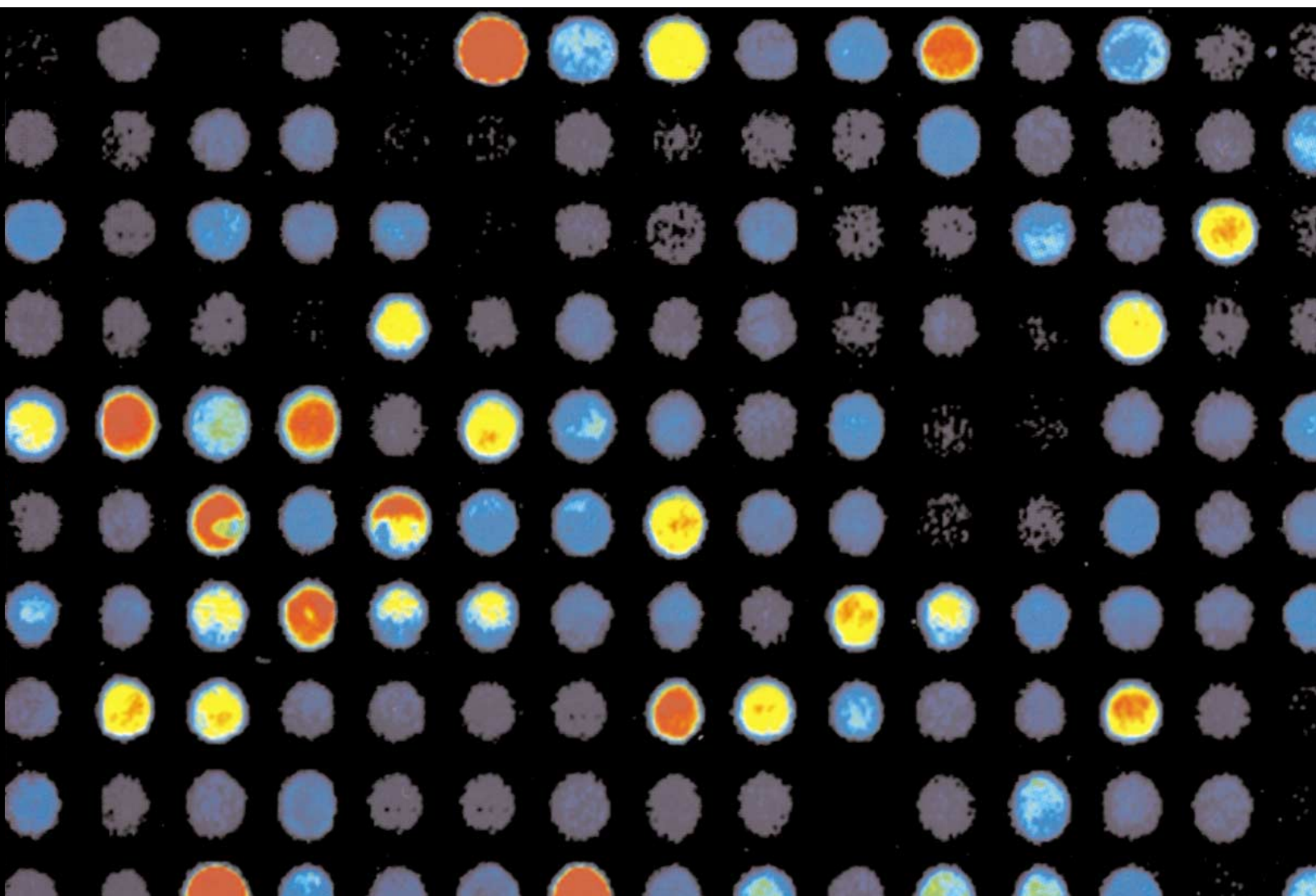
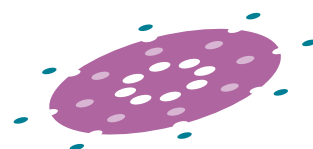


ARRAY-PRO[®] ANALYZER



**THE TOTAL SOLUTION FOR MICROARRAY AND HIGH-DENSITY
ARRAY IMAGE ANALYSIS**



MediaCybernetics[®]

From Images to Answers[®]

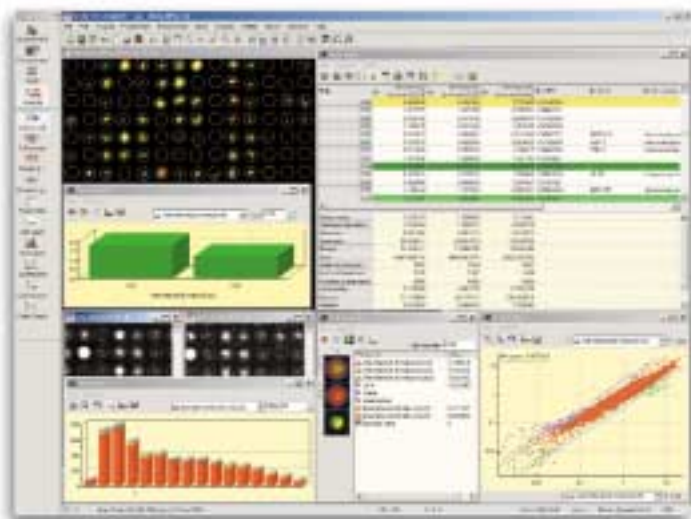
Array-Pro[®] ANALYZER

The Automated Solution™

Array-Pro[®] Analyzer v. 4.5 Software

Automated analysis from the leader in imaging software solutions

At last, microarray analysis software for the molecular biologist that gives fast, accurate, and repeatable results has arrived. Array-Pro Analyzer is based on the tools found within Image-Pro Plus, the world's premier image analysis software. These tools have been applied to the specific image analysis challenges of high-density array analysis. Unlike first generation microarray analysis software, which requires tedious manual grid alignment and offers few choices to be able to discern



Array-Pro Analyzer Results

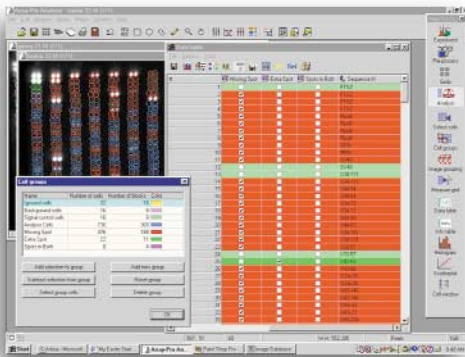
signal from background contribution, Array-Pro Analyzer provides every conceivable image analysis tool to characterize the measurement system in order to achieve maximum signal/noise, repeatability, and quantitative accuracy.

Array-Pro Analyzer is an indispensable tool for the nascent microarray and high-throughput screening research that is fueling the genomics, proteomics, drug discovery, and bioinformatics revolution.

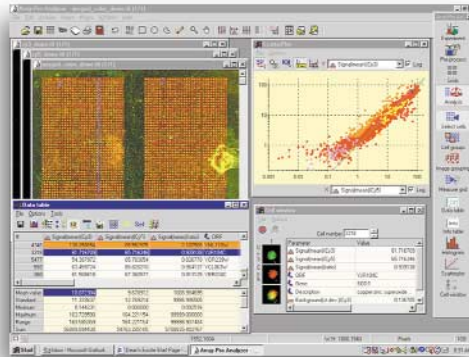
- Perfect for microarray **gene expression, typing, HTS, and sequencing** analyses
- **Automatic grid, subgrid, and spot finding** overcomes tedious spot template assignment
- **Reproducible!** Get the same numbers from user to user
- Detect **low-level expression** using extensive background and signal options to optimize results
- **Characterize data** more precisely through grouping by cells, grids, and images
- Receive **statistical feedback** to determine experiment quality
- Perform **cluster analysis, PCA, and self-organizing map** analysis across huge datasets of multiple experiments with **GeneMaths™**

New in Array-Pro Analyzer 4.5!

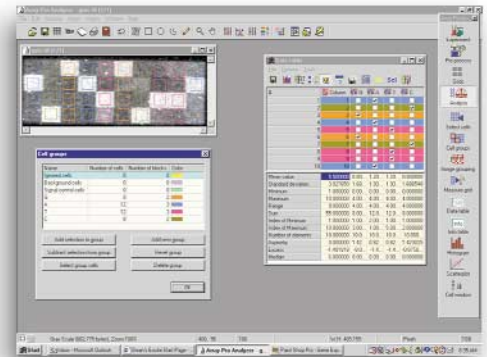
- Pixel-by-pixel cross-correlation method to segment signal, background, and artifact pixel populations.
- Normalization using Loess best-fit, signal control cells, or all cells, by image or sub-grid.
- Statistical control of pixel segmentation and signal calculation.
- Re-organization of the toolbar and menus to be more streamlined, easier to use, and more descriptive of the functions.
- Complete control via menus in addition to the toolbar.
- Improved candidate spot finding (for line determination) via morphological validation of spot shape.
- Scores of morphological measurements. This is attractive for quantitative evaluation in production of microarrays.
- New auto-alignment techniques for grids that make it easy and faster to make a template and execute grid finding.
- User can display multiple scatterplots and histogram displays to look at many variables at once.
- New data graph to show individual measurements across many image sets. Useful for viewing time series experiments or other variables across experiments.
- Option for variable cell boundary definition for each spot.
- Automatic population of cell groups according to user-defined criteria.
- Equation editor to build practically any kind of custom measurement.
- Option to store layout and measurements within an experiment.
- Option to automatically assign image names to labels and groups.
- Option to automatically tint images.
- Time-based experiments are supported via rate measurements and input of time via the file or user.
- Ability to display individual cell histograms (with statistics indicators) and adjust the threshold graphically.
- Option to use irregular AOI to select cells on the scatterplot.
- User-assigned axis values for the scatterplot, histogram, and data graphs.
- Option to rename measurements in the table and hide or rearrange columns.
- Dynamically linked to GeneMaths 2.0 such that updates in Array-Pro can be shown interactively in GeneMaths.



Typing



Gene Expression



Sequencing

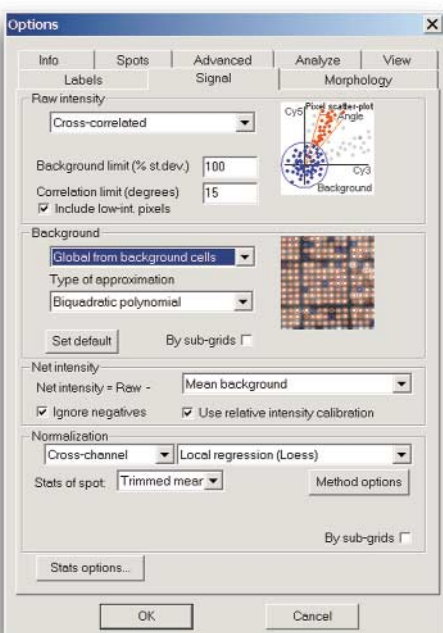
Sample Experiments

Array-Pro Analyzer can be applied to any kind of microarray analysis.

Reproducibility

Media Cybernetics has had long experience in extracting image features through pattern recognition. Array-Pro Analyzer sets a new standard for automation of spot identification by taking advantage of the inherent periodicity of spot spacing into grids and subgrids on the substrate. The benefit is the ability to reproduce exactly the same results of analysis from user to user. Through computer algorithm automation, results are absolutely repeatable. This is the key to scientific advancement. One scientist must be able to duplicate the experiments of others within acceptable error.

Practically any grid and subgrid pattern may be found automatically. Orange packing, irregular subgrid spacing, and variable subgrid size are supported. Algorithms for donut-shaped spots, uniform distribution spots, and completely irregular spots ensure that the cell boundaries will be defined accurately and reproducibly.



Background and normalization determination

Speed

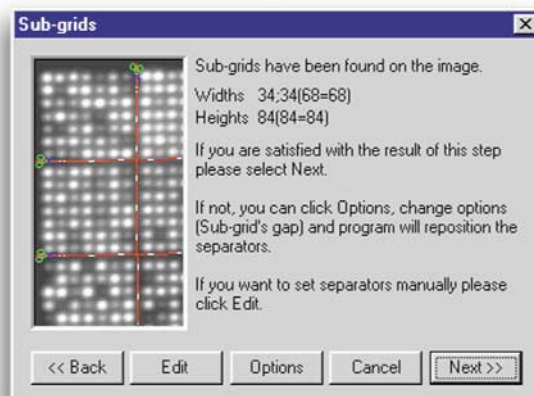
An extremely beneficial side effect is the speed of analysis. Typically a scientist could take days to manually define grid, subgrid, and spot locations for the hundreds of thousands of spots. And the results were never the same since a position change of a single pixel for spot definition can make dramatic differences in quantitation. With Array-Pro Analyzer, the execution now takes place in seconds.

Extraction of Information Despite Low Signal-to-Noise

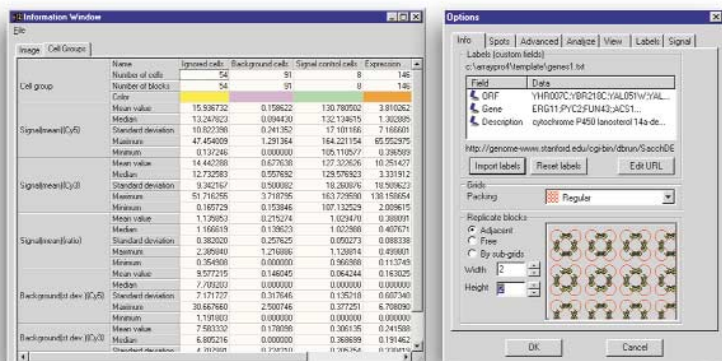
One of the biggest problems in microarray analysis as applied to gene expression has been the extraction of small signal changes in the presence of the vast sources of background noise (cross-hybridization, optical effects, dust, etc.) Scientists have found that clusters of genes that indicate phenotypes or disease states tend to be expressed at these low levels. Again, with Media Cybernetics' experience in characterization of signal and noise, users are able to optimize signal/noise by the adjustment of several control parameters and numerous choices in background methods.

Simple Method Development

An analysis wizard takes the user through grid, subgrid, and spot finding parameters in order to establish the methodology for each type of array image. Once these parameters are stored as an experiment type, subsequent analyses can be performed without user intervention. This is the key to reproducibility and efficiency.



Method setup wizard



Identification of spots and groups

Statistical Feedback

Array-Pro Analyzer also offers extensive statistical user feedback to establish the quality of the data and the experiment. The old adage of computing, "garbage in is garbage out," is certainly appropriate in dealing with the large amounts of data involved with microarrays. The user may accurately calibrate the signal and background based on standards, controls, and replicates.

Group Identification

You may set up, name, and assign colors to groups of information that are meaningful to you and your colleagues. Or you can arrange to have the software create groups according to your criteria automatically. You can import as many spot labels as desired into separate fields. Cells can be arranged into replicate blocks in three ways: adjacent blocks, the same position in each subgrid as being the same name, or free form assignment. Images can be grouped together with their own custom group name and color. Even collections of image groups may be combined and named. Measurement and statistical information is available for any of these group modes.

Groups can be made automatically via user criteria. For example, all cells with a high standard deviation could be put into the group of ignored cells and the data table would show them but not include the data in calculations.

Numeric and Graphic Feedback

Array-Pro Analyzer dynamically links all data and graphic display windows. Highlighting selected cells in one view also highlights the corresponding cell information in all other views. User-selected color coding aids the user in cell group identification. For example, if you want to see all ratios over a certain value, just outline those cells on the histogram, scatterplot, or data table.

Connectivity

One of the advantages of microarrays is to aid discovery. If the user finds a gene of interest that is expressed in some unique way, the user may automatically launch a search via an internet connection to a user-selected database to gain more information about that gene.



Various data display windows

Programmability

The Image-Pro Plus image analysis platform is a long-established standard that provides a powerful development environment for OEMs, systems integrators, and end users. Array-Pro Analyzer shares this sort of platform development to enable the creation of tailored versions for analytical high-density array imaging. Unlike most programming tool kits, the Media Cybernetics SDK offers a proven host environment that can be easily and quickly customized to solve specific imaging applications without starting from scratch, thereby reducing development risk and cost. Array-Pro Analyzer may be extended and customized using the built-in Auto-Pro programming language, Visual Basic™, or Visual C++. Macros may be created for simple repetitive operations or for more sophisticated needs such as a custom user interface, data analysis, and reporting. This programmability may be useful in such applications like SNP scoring where the methodologies are not well-established.

"We here at the NIA DNA microarray facility have examined a wide variety of automatic spot-calling software for integration into our data analysis process. None of the programs we tested had the full combination of features that we considered to be important. These features included, first and foremost, a robust automatic spot-finding and spot-defining algorithm which required a minimum of external assistance. Secondly, we needed a circular spot geometry which could be flexibly adjusted and, then, once optimized, the selected parameters could be held constant for consistent and reproducible spot quantitation over many samples. Finally we needed a rapid method to translate the calculated intensity data into spreadsheet form for downstream analysis. Our search was over after we tested the Array-Pro software. It is simply the best product out there for automatic spot-calling. We absolutely need Array-Pro in order to handle the steadily increasing volume of microarray image data processed daily by our facility. We recommend Array-Pro to all our colleagues and collaborators. And, by the way, the support service offered by Media Cybernetics has also been outstanding.....timely and invariably helpful."

—Chris Cheadle Ph.D., DNA Array Facility,
National Institute on Aging

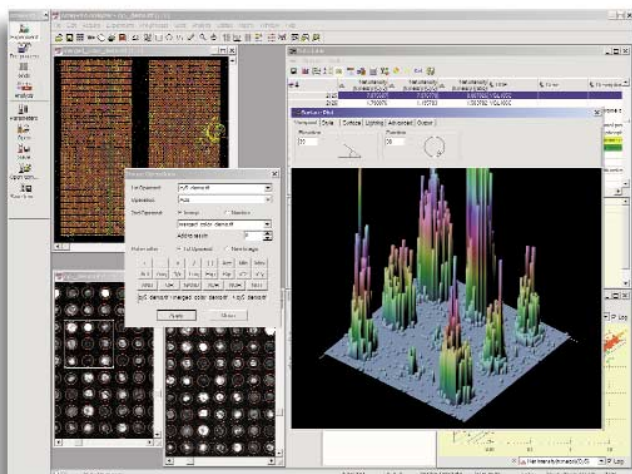


Image Processing

Wide Range of Image Processing Tools

An extensive collection of filters, editing, channel manipulation, arithmetic operations, calibration (ordinate and spatial), graphic display control, etc. are provided.

Vast Image Capture and Data File Format Support

You can use your existing microscope or imager to capture images. Array-Pro Analyzer supports the full complement of Media Cybernetics camera and frame grabber capture drivers. Add the Scope-Pro® plug-in module to automate stage and microscope accessories. If the field of view limits your ability to image the entire array, a composite image can be made through tiling.

- Read, write, and convert files in TIFF, HPP, BMP, CUT, EPS, JPG, Photo CD, PCT, PCX, TGA, and FLAT (Binary)
- Reads files from all major microarray readers: PerkinElmer (Packard/GSI Lumonics), Axon Instruments, Bio-Rad (Virtek Vision), Amersham Biosciences (Molecular Dynamics), Genomic Solutions, etc.
- Supports 8, 12, 16, 24, and 32 bit floating point images
- JPEG, LZW, and RLE compression supported
- Output data files to ASCII, WK1, or XLS as input for spreadsheets
- Transfer images, data graphs, and data files via DDE or Clipboard

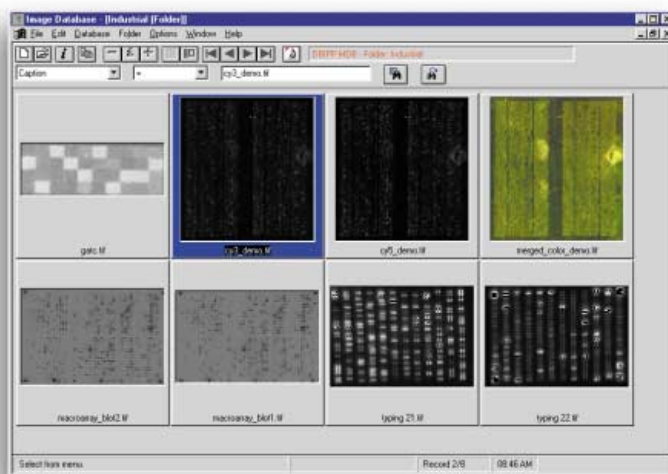
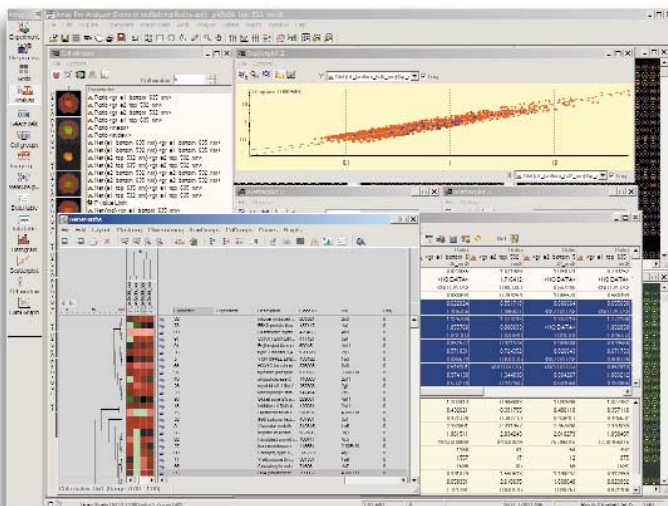


Image Database

Database

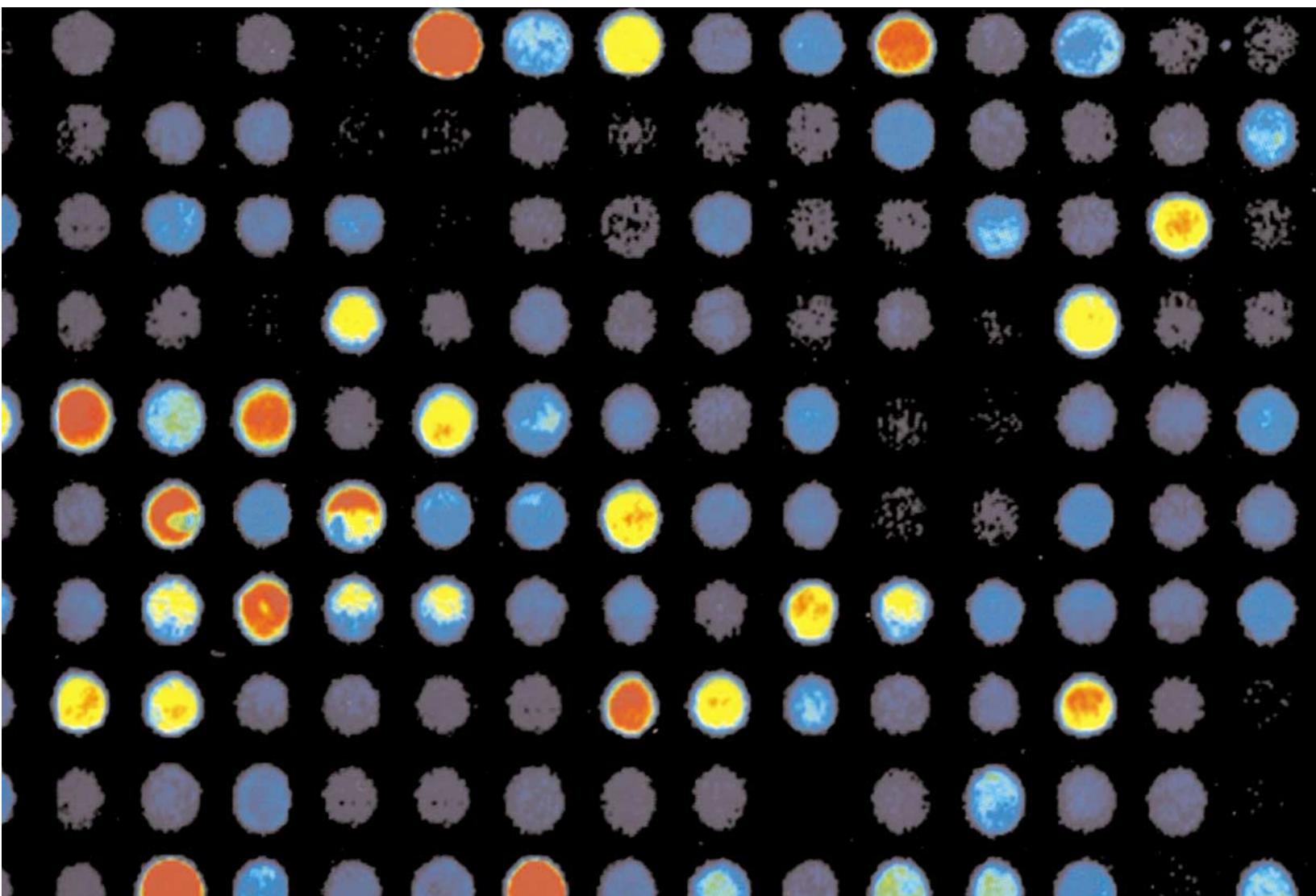
Images and experimental parameters may be stored, searched, and recalled. The database function allows the user to see thumbnail image displays along with experiment field information.



GeneMaths 2.0 advanced experiment statistics

Advanced Statistics for an Experiment Series

Array-Pro Analyzer interfaces seamlessly with GeneMaths™ 2.0 from Applied Maths, a Media Cybernetics distribution partner. Information from a series of gene expression experiments in Array-Pro is immediately available in GeneMaths for statistical treatment via cluster analysis, self-organizing maps, and principal component analysis. GeneMaths information is dynamically linked. Thus selecting a cell group in Array-Pro Analyzer also selects and highlights the same genes in GeneMaths.



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HEADQUARTERS

Media Cybernetics, Inc.
8484 Georgia Avenue, Suite 200
Silver Spring, MD 20910 USA
Phone: +1.301.495.3305
Fax: +1.301.495.5964
Email: info@mediacy.com
Web: www.mediacy.com

INTERNATIONAL OFFICES

South America:
Phone: +55.11.4427.7803
Fax: +55.11.4427.9527

Europe:
Phone: +31.715.730.639
Fax: +31.715.730.640

Asia Pacific:
Phone: +65.6245.4965
Fax: +65.6245.4967

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