

S+ArrayAnalyzer®

S+ARRAYANALYZER®— SCALABLE DATA ANALYSIS SOLUTION FOR MICROARRAY EXPERIMENTS

In the highly competitive environment of drug discovery and development, improvements in the accuracy of decisions, including identifying and validating new targets, and profiling or evaluating therapeutic candidates for continued development, can return huge dividends in cost savings and time to market. S+ArrayAnalyzer from Insightful provides new leading-edge statistical and graphical methods for controlling the false positive and false negative rates and improving the design and analysis of microarray experiments. Based on recent methods developed by researchers at Harvard, Berkeley, Johns Hopkins, University of Virginia, Bioconductor Project and Insightful R&D, S+ArrayAnalyzer offers the latest statistical workflows for analyzing microarray data in an easy to use and extensible environment.

USE THE LATEST STATISTICAL METHODS FOR MICROARRAY ANALYSIS

- Advanced probe-level analysis for Affymetrix® chips including RMA, GCRMA, MAS5, MBEI and combination methods.
- Powerful tests - distribution and permutation-based tests; linear models (ANOVA) for time course and multi-factor designs.
- Increased accuracy for low replicate experiments.
- Rich clustering - hierarchical, partitioning, and model-based.
- Annotation and gene list management.
- NEW: Probe-level analysis and linear model methods are optimized and are now faster and more scalable in combination with S-PLUS® 7.

S+ArrayAnalyzer provides a comprehensive suite of statistically-rigorous microarray data analysis methods for accurate and powerful analysis of gene expression. Applications include: optimal target identification and validation; safety and efficacy profiling; clinical biomarker development; mRNA decay rate estimation and mRNA comparative experimentation. The software provides a structured and comprehensive analysis of Affymetrix and two-channel microarray data using Insightful's data analysis platform, S-PLUS and Web deployment environment S-PLUS Server.

PERFORM ADVANCED MICROARRAY ANALYSIS QUICKLY AND EASILY

- Rigorous statistical analysis
- Interfaces for desktop and Web deployment
- Graphical and tabular reports
- S-PLUS scripting environment—extensible applications

S+ArrayAnalyzer makes it easy for statisticians and biologists in functional genomics, computational biology, toxicogenomics, bioinformatics and biostatistics departments to access, explore, model and communicate findings across their organizations. Import and analysis of two-channel (e.g. cDNA) and oligonucleotide (e.g. Affymetrix) data including GeneChip® MAS5 and CEL/CDF files is straightforward. S+ArrayAnalyzer can also import image extraction formats including all versions of GenePix®, as well as Spot, ScanAlyze™ and others.



DRAMATICALLY BOOST THE RETURN ON YOUR MICROARRAY TECHNOLOGY INVESTMENTS

- Precisely identify targets and candidates accelerating the drug discovery process
- Identify expression biomarkers in combination with clinical data
- Reduce expense of developing unpromising compounds
- Leverage in-house resources more effectively by not wasting time pursuing false positives
- Increase accuracy of results even with limited replications
- Use sophisticated analytics to identify gene activity that may have gone unnoticed



"After an exhaustive review of several microarray data analysis software vendors, we selected Insightful's S+ArrayAnalyzer to deliver analysis and reporting tools to our researchers. Unlike competitive products, S+ArrayAnalyzer provided the flexibility and extensibility we needed to customize our solution to meet our organization's needs. Further, the software has an excellent feature set, combining the best of the academic Bioconductor community with a commercial-grade software implementation. The probe-level methods, linear models for multifactor experiments, statistical cluster analysis and gene list management and annotation tools provide comprehensive workflows for extracting key information from microarray experiments. These workflows improve the accuracy of our analysis results and enable our organization to analyze microarray data more quickly and effectively, improving our productivity."

Richard Park
Computational Data Analyzer
Joslin Diabetes Center

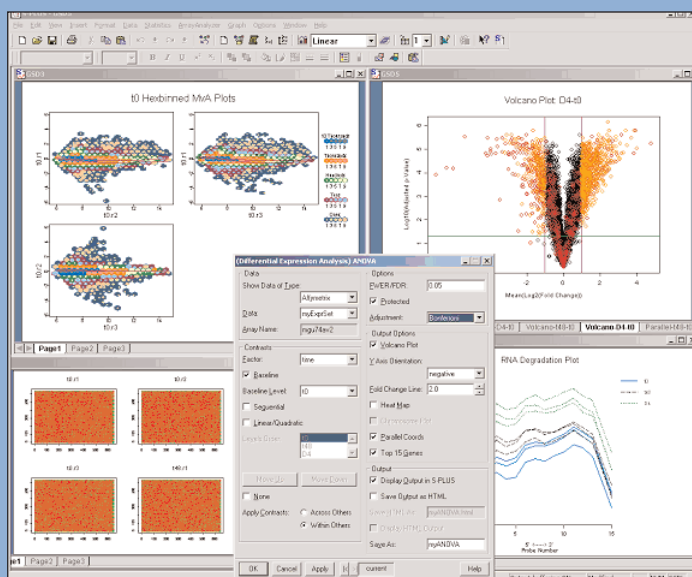


FIGURE 1:
S+ArrayAnalyzer desktop showing volcano plot, hexbin MvA plot, array image plot, RNA degradation plot and interface for multifactor linear model (ANOVA) analysis.



INTUITIVE USER INTERFACE

An intuitive graphical user interface guides users through data import, exploratory data analysis, normalization, differential expression testing and supervised and unsupervised learning models. Results from analyses are presented as interactive tabular and graphical reports using S-PLUS Graphlets® in S-PLUS 7. In addition to providing interactive graphs in a Web browser, Graphlets enable connections to annotation databases such as those at NCBI GenBank and to drill-down S-PLUS graphical and tabular summaries.

By working in collaboration with the leading researchers in the field, and incorporating methods from the open-source Bioconductor project and from our own research collaborations with leading universities, we've been able to provide a comprehensive suite of methods for microarray analysis to provide improved accuracy for low-replication and larger designed experiments and a dramatically reduced false discovery rate.

IMPROVED ACCURACY FOR LOW-REPLICATION EXPERIMENTS

In many experiments, the variance of differential expression intensity values may be a function of the size of the intensity values. For experiments with few replicates, the degrees of freedom for estimating standard errors is small. The LPE (Local Pooled Error) testing method estimates the standard error based on pooling variances for genes with similar average intensities. Combined with a resampling approach for specifying the false discovery rate, this model borrows strength across genes and improves the power of identifying truly differentially expressed genes while holding the false discovery rate to an acceptable level.

RICH CLASS OF EXPERIMENTAL DESIGNS AND ANALYSES

S+ArrayAnalyzer includes a rich set of experimental designs and linear models for analyses of multi-factor experiments. Reference, loop and 2-sample designs with options for dye-swap are available for 2-channel arrays. One-way and two-way ANOVA and nested models are available for analysis and several options for contrasts between factor levels are included e.g. baseline, sequential and polynomial.

DRAMATICALLY REDUCED FALSE DISCOVERY RATE

Numerous methods have been proposed for controlling the family-wise error rate (FWER) and false discovery rate (FDR) when many tests are performed. The FWER is controlled by using adjusted p-values for each gene so the overall Type I error rate is maintained at a desired level. The FDR sets the proportion of false discoveries in the gene list.

SHARE ANNOTATED RESULTS WITH INTERACTIVE, INFORMATION-RICH TABLES AND GRAPHS

S+ArrayAnalyzer produces interactive tabular and graphical summaries of differentially expressed genes resulting from a variety of available differential expression analyses. These results are linked to public and proprietary databases for rapid identification and annotation of differentially expressed genes. S+ArrayAnalyzer's interactive reports can easily be shared across the Web with other colleagues, even if they don't have S+ArrayAnalyzer.

AN OPEN AND EXTENSIBLE ENVIRONMENT, TO STAY ABREAST OF THE LATEST ADVANCEMENTS IN BIOINFORMATICS

Because S+ArrayAnalyzer is integrated with the S-PLUS data analysis environment, it can adapt to the rapidly-changing world of microarray analysis. Instead of being locked in to black-box algorithms, S+ArrayAnalyzer's algorithms are highly extensible. And by using the award-winning S programming language—including a suite of object-oriented tools provided specifically for microarray analysis—S+ArrayAnalyzer is an ideal environment for developing your own microarray analysis applications, or for integrating third-party methods.

ABOUT INSIGHTFUL CORPORATION

Insightful Corporation (NASDAQ:IFUL) provides enterprises with scalable data analysis solutions that drive better decisions faster by revealing patterns, trends and relationships. The company is a leading supplier of software and services for statistical data analysis, data mining and knowledge access enabling clients to gain intelligence from numeric and text data.

Insightful consulting services provide specialized expertise and proven processes for the design, development and deployment of customized solutions.

SYSTEM REQUIREMENTS

- S-PLUS 7 for Windows or later
- Pentium processor with a minimum 1 GB of memory
- Microsoft® Windows® XP Pro, 2000, 2003

A COMPLETE SOFTWARE ENVIRONMENT

- Rigorous statistical analysis e.g. probe-level summary, normalization, differential expression, class discovery and prediction
- Intuitive desktop workbench user interface
- Full integration with the flexible, extensible S-PLUS language for customized analyses
- Interactive graphical and tabular reports linked to annotation databases
- NEW: Probe-level analysis and linear model methods are optimized and are now faster and more scalable in combination with S-PLUS 7.

ACCESS MICROARRAY DATA

- Affymetrix GeneChip MAS5 summary data (CHP and flat files)
- Affymetrix probe-level (CEL, CDF) data
- Affymetrix binary file formats (CEL, CHP)
- Two-channel data including Agilent, GenePix, Spot, ScanAlyze formats

ADVANCED DATA PREPARATION METHODS

Normalization Methods:

- CEL methods: quantiles with robust option, invariant set, constant, contrasts, loess, vsn
- MAS update methods: median, inter-quartile, vsn, quantiles, scale
- 2-channel, within-chip: median, loess, 2-D loess, print-tip loess, MAD, global MAD, print-tip MAD
- 2-channel, between-chip: vsn, quantiles on R/G, quantiles on A

Probe-Level Summary Methods:

- RMA (Irizarry et al., Bolstad et al.)
- GC-RMA (Wu et al.)
- MBEI (Li and Wong)
- Mix and match methods

QC Diagnostics and Filtering

- Principal components
- RNA degradation
- Box plots
- MvA plots
- Rich gene and chip filtering

RIGOROUS ANALYTICS

Differential Expression Tests:

- Two sample and paired t-test
- Linear models including one-way and two-way ANOVA using fast, scalable linear model methods
- Wilcoxon test
- Local pooled error tests (borrowing strength across genes)
- Distribution and permutation-based tests

FWER and FDR control:

- Bonferroni
- Hochberg (1988)
- Holm (1979)
- Westfall & Young (1993)
- Benjamini and Hochberg (1995)
- Benjamini and Yekutieli (2001)
- Resampling (LPE): Reiner et al. (2003)

Clustering:

- Hierarchical
- Partitioning (kmeans, pam)
- Model-based

ANNOTATION & GENE LIST MANAGEMENT

- Interactive tabular and graphical reports hyper-linked to gene annotation metadata and summary information e.g. volcano plots, parallel coordinate plots, whole genome plots, heat maps, silhouette plots, principal component biplots, Venn diagrams.
- Interactive gene list management and functional enrichment analysis with Onto-Express and David/EASE.
- Annotation through interaction with Stanford Source, Unigene, LocusLink, PubMed, AmiGO, Affymetrix NetAffx and other online or internal databases

OPEN AND EXTENSIBLE FRAMEWORK

- Includes Bioconductor 1.4 as foundation layer and base analyses
- Rigorous analytics layer for microarray analysis—no "black box" algorithms
- Open GUI layer through S-PLUS and C++ on desktop and ASP and JSP on server
- Fully integrated with the interactive S and S-PLUS data analysis environment, with access to its full range of statistical and graphical methods

For more information visit <http://www.insightful.com> or send e-mail to info@insightful.com



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