

Phenotype MicroArrays

for Microbial Cells.

Phenotype MicroArray™ Technology enables researchers to characterize cells in up to 1,920 assays and evaluate cell changes under thousands of culture conditions and physiological states in a simple, rapid, efficient and cost-effective manner. By measuring a cell's response to a genetic or environmental alteration, this integrated system of cellular assays, instrumentation, and bioinformatics software reveals invaluable information to speed insight and discovery and expedite scientific publication. Phenotype MicroArrays (PMs) have broad applicability for genotype-phenotype characterization as well as for determining optimal conditions for cellular growth, sporulation and germination, production of secondary metabolites, or enzymatic activities in cell lines.

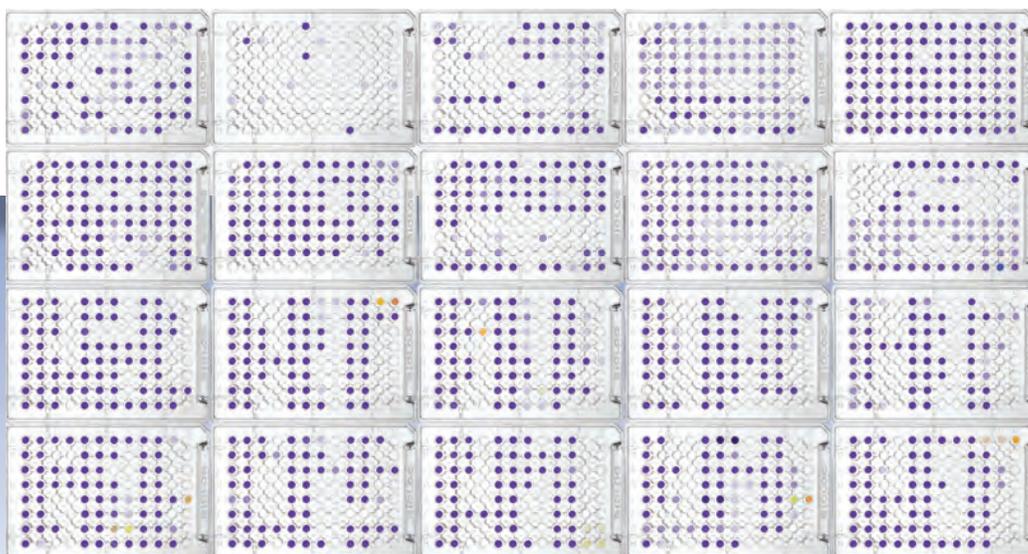
Phenotype MicroArrays are a proven method of cellular screening that is extremely beneficial in a wide range of research applications:

- discovering effects of loss or gain of gene function
- measuring/documenting changes in cell metabolism over time or under different environmental conditions
- improvement and QC of phenotypic stability of cell lines
- improved efficacy in the production of compounds in biological fermentation processes
- evaluation of new drug/antibiotic candidates in toxicological profiling and mode of action studies



The Biolog OmniLog® incubates and monitors 50 microplates, or 1,920 phenotypic assays simultaneously to measure physiological responses in diverse microbial cells.

**BiOLOG**

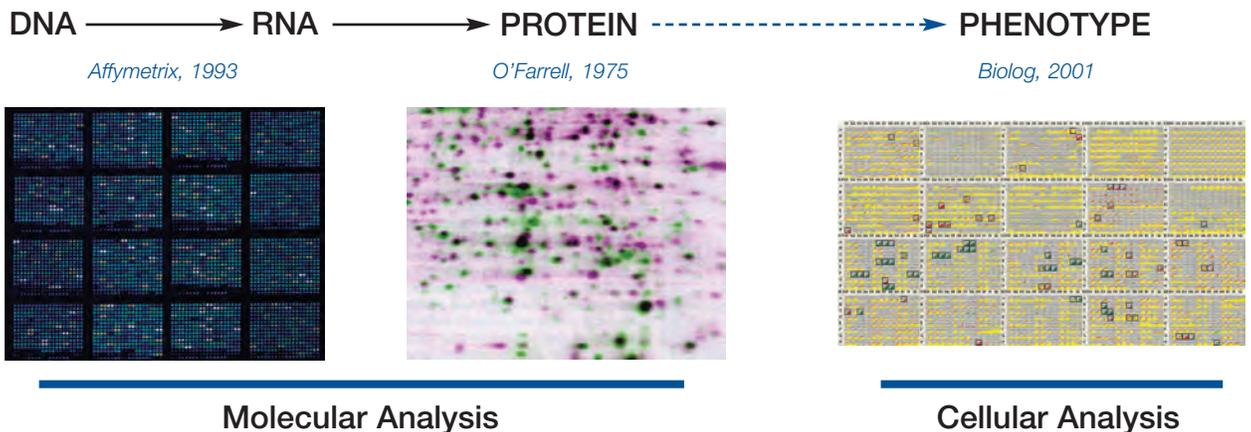


A BREAKTHROUGH TECHNOLOGY

Phenotype MicroArrays represent the third major technology, "Phenomics", alongside DNA Microarrays and Proteomic Technologies, that is needed in the genomic era. Just as DNA Microarrays and Proteomic Technologies have made it possible to assay the level of thousands of genes or proteins all at once, Phenotype MicroArrays make it possible to quantitatively measure thousands of cellular phenotypes all at once.

DNA Microarrays and Proteomic Technologies allow scientists to detect genes or proteins that are coregulated and whose patterns of change correlate with something important such as a disease state. However there is no assurance that these changes are really significant to the cell. Phenotype MicroArrays are a complementary technology providing the needed information at the cellular level ... and much more.

Phenotype MicroArrays provide comprehensive cellular profiles that can be used to identify gene function, validate drug targets, and streamline lead validation, optimization, and toxicology studies. After a genetic change or exposure to a drug lead, the researcher can directly evaluate the cellular response to that change.



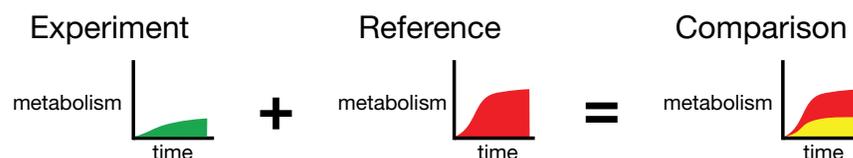
HOW PM TECHNOLOGY WORKS

Phenotype MicroArrays are preconfigured sets of phenotypic tests deployed on microplate panels. Each well of the array is designed to test a different phenotype after inoculation with a standardized cell suspension, allowing simultaneous testing of thousands of phenotypes in a single experiment.

PMs use Biolog's patented redox technology, with cell respiration (NADH production) as a universal reporter. If the phenotype is strongly "positive" in a well, the cells respire actively, reducing a tetrazolium dye and forming a strong color. If it is weakly positive or negative, respiration is slowed or stopped, and less color or no color is formed. The redox assay provides for both amplification and precise quantitation of phenotypes.

Incubation and recording of phenotypic data is performed automatically by the OmniLog[®] instrument, which captures a digital image of the MicroArray several times each hour and stores the quantitative color change values into computer files. The computer files are then displayed in the form of kinetic graphs. Thousands of phenotypes are monitored simultaneously, and more than 470,000 data points can be generated in one 24 hour run.

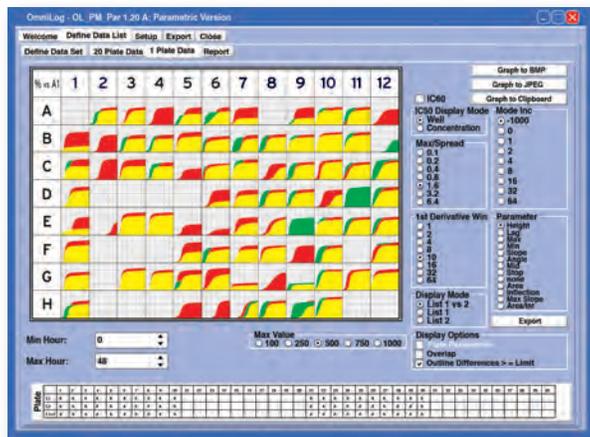
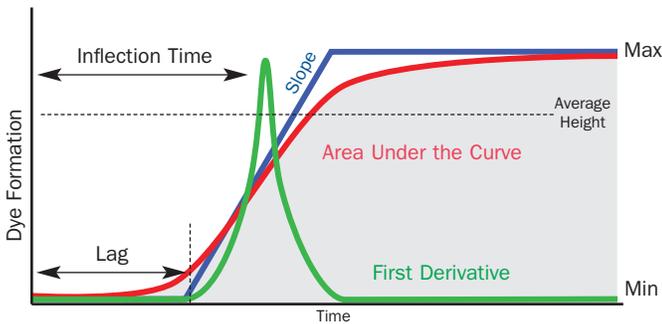
To compare the phenotypes of two cell lines, one is recorded as a red tracing and one as a green tracing. These graphs can then be overlaid by the bioinformatic software to detect differences. Areas of overlap (i.e. no change) are colored yellow, whereas differences are highlighted as patches of red or green.



KINETIC DATA CAPTURE AND ANALYSIS

OmniLog PM software contains a suite of algorithms that work in conjunction with the OmniLog PM system and Phenotype MicroArray panels to automate incubation of up to fifty microplates at a fixed user-controlled temperature with complete collection of colorimetric assay data over time. These programs allow for display of kinetic data from PM panels recorded by the OmniLog PM system, manage and analyze the data, export it in a variety of raw and processed forms, and generate reports.

Many Parameters are calculated from Kinetic Plots by PM Software



Phenotype MicroArray Single Panel Comparison Display showing Cellular Responses for 96 Kinetic Assays

Software Functions

- Drives the operation of the OmniLog PM system
- Guides loading and reading of plates or PM panels
- Creates a kinetic data file for each plate or PM panel for use in the other program modules

File Management/Kinetic Analysis

- Assembles plate or PM panel data files into data lists
- Displays kinetic plots of the data
- Allows export of kinetic plots as bmp or jpeg files

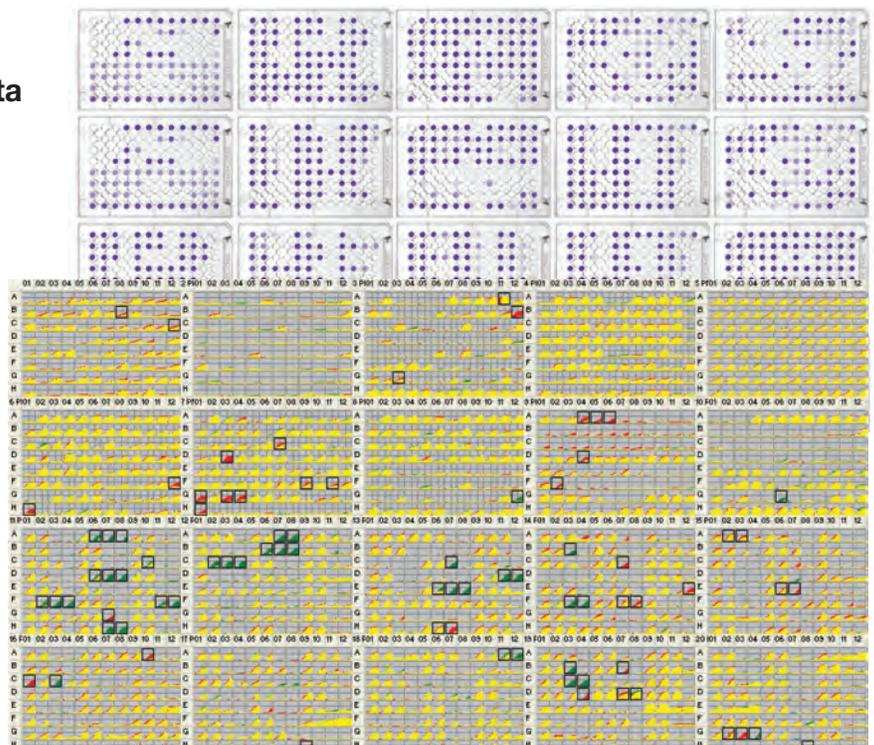
Parametric Analysis

- Extracts data lists from the File Management /Kinetic Analysis module
- Calculates parameters from kinetic data
- Allows comparison of two data lists
- Highlights wells and generates a report on PM phenotypes that differ significantly in any selected kinetic analysis parameter
- Allows identification of substrates in all PM panels
- Links metabolic substrates in PM panels to KEGG database
- Export the original OmniLog kinetic data
- Export data parameters for statistical & bioinformatic analysis

Capture and compare kinetic assay data from 50 microplates at a time

Preconfigured PM panels yield nearly 2,000 response phenotypes which are informative for studies of:

- Cell surface structure and transport functions
- Catabolism of carbon, nitrogen, phosphorus, and sulfur
- Biosynthesis of small molecules
- Synthesis and function of macromolecules & cellular machinery
- Cellular respiration functions
- Stress and repair functions
- Other cellular properties



Phenotype MicroArray Applications

More than 200 scientific publications and presentations have documented the effectiveness and productivity of PM technology. For a complete listing, see our web site www.biolog.com.

Phenotype MicroArray Technology is now available for applications with nearly all important species of bacteria and fungi. Simple protocols are available for testing nearly 2000 cellular phenotypes simultaneously.

Uses with microbial cells

- Determine gene functions.
- Compare gene knock-out mutants to wild types.
- Compare naturally-isolated strains with different genetic backgrounds.

Identify novel antimicrobial targets by finding genes unique to pathogenic microorganisms

- Find phenotypes present in pathogenic but not in non-pathogenic strains.
- Find phenotypes present in pathogenic microbes but not in host cells (animal or plant).

Test antimicrobial targets and drug leads by comparative phenotyping.

- Determine MOA of drug leads.
- Compare phenotypic changes caused by target gene knockout versus drug addition.

Bioprocess improvement

- Compare and analyze different generations of production strains.
- QC fingerprint production strains.
- Scan 2000 culture conditions simultaneously to optimize the growth medium for product yield.

General cell characterization

- Determine metabolic properties of any microbe.
- Determine drug/chemical sensitivities.

Panels for mammalian cell studies are also available with over 1,000 responder assays for metabolic phenotypes and chemical sensitivity.

OmniLog PM Systems



The OmniLog PM system includes software for analysis of Biolog Phenotype MicroArray panels. The OmniLog II Combo System has additional software and a database for identification of aerobic bacteria using Biolog's Gen III microplates. The OmniLog II Combo Plus System adds the capability for identifying anaerobes, yeast and filamentous fungi. Each system includes the OmniLog instrument, software as indicated, multimedia computer, LCD flat panel monitor, 8-channel electronic pipettor, turbidimeter, user guide, training and 1-year warranty. The OmniLog II Combo system also include the MicroStation microplate reader and a printer. Organism databases (for microbial identification), consumables and other accessories are purchased separately.

Specifications

Size: 21 in x 32 in x 23 in (53 cm x 81 cm x 58 cm)

Power: 100 to 240 volts, 50 to 60 Hz

Operating Temp Range: 18° to 28°C

Operating Humidity Range: 20% to 80% non-condensing

Incubation Temperature Range: 22° to 45°C

Temp Consistency: ±2°C in the tray chamber

Incubation Humidity Range: Ambient

Test Capacity: 50 microplates

Data Capture: CCD images of each microplate every 15 minutes

Temperature Control: Input of set temperature by external computer

Temperature Indication: Output to external computer and 7 segment display

Monitor: LCD flat panel, 17 in viewable image size