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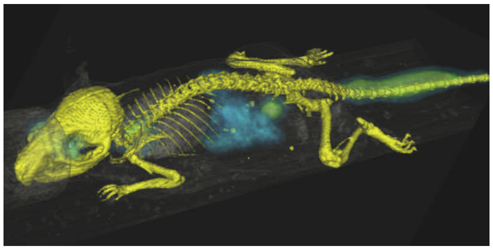
TOP Trends IN Life Science RESEARCH



INCREASED ACCURACY AND THROUGHPUT FOR *IN VIVO* IMAGING

Carestream Molecular Imaging

One great challenge is achieving greater accuracy and throughput for *in vivo* imaging of small animals. Researchers want to study the same mice repeatedly over time to understand how cellular processes change. By conducting longitudinal studies researchers gain better statistical power, use fewer animals, and arrive at a conclusion quicker than with cross-sectional studies.

Researchers and probe developers also need *in vivo* imaging systems that combine advanced multispectral fluorescence, luminescence, digital x-ray, and radioisotopic imaging in a single system. This provides the flexibility to answer complex biological questions using as many different approaches as possible since each modality posesses its own set of strengths and weakness.

Carestream Molecular Imaging is addressing the need for *in vivo* imaging systems that combine advanced multispectral fluorescence, luminescence, digital x-ray, and radioisotopic imaging in a single system. Multispectral tuning of excitation light provides enhanced sensitivity that helps users identify and separate multiple fluorochromes, along with removing the autofluorescence background.

CELLULAR IMAGING

Applied Scientific Imaging

Keeping the cells you are studying alive so you can see what they are up to is a real big trend. This involves a whole range of technical feats from tempature and environmental control, to high resolution microscopy to ultra precise motion control for maintaining focus. The ability to automate protocols to generate large volumes of repeatable data is also important. The latter requires a range of automation from the simple automation of an existing microscope in a university lab, to fully automated robotic systems that can perform tasks like genetic sequencing and drug discovery with minimal human intervention.

Applied Scientific Instrumentation (ASI) has been designing and building microscope automation product for more than twenty years, and over this period of time it has worked with leading researchers to develop and perfect products to aid them in their research. The company addresses issues such as precise motion control positioning to allow multipoint time-lapse imaging. Controlling illumination to prevent photo bleaching and prolong cell life, and maintaining precise focus over time. All of its products have evolved out of an interactive process between the company and the researcher. The researcher tells us what their requirements are, and ASI works to develop products to meet their needs.

ELIMINATING INEFFICIENCY

BioCision, LLC

Although the advance of automation in the research laboratory is undeniable, the lion's share of discovery science continues to be a hands-on endeavor. This being the case, many methodologies and techniques become institutionalized without re-examination or upgrade as they are passed along. As a result, an incredible amount of inefficiency exists in today's laboratories.

As discovery progresses to the clinic, **BioCision** is seeing an increasing number of life sciences companies that are seeking ways to eliminate these institutionally ingrained inefficiencies. Particularly as the size and complexity of laboratory experiments increases, these companies are looking for new tools to improve workflow, and ultimately the quality of their experiments.

BioCision has developed and expanded a line of laboratory tools that reexamines the way temperature-sensitive samples are handled and meets the need for more efficient laboratory practices.

BIOFUELS FROM ALGAE

Glen Mills Inc.

The area of algae to biodiesel research has generated interest since the carbon source would not be competing with food based agricultural products (such as "corn-to-fuel" programs). A key step is the disruption of the algal cell wall to release lipids and fatty acids for eventual conversion to diesel fuel. Breakage of algae and yeast cells is difficult, but the DYNO-MILL (bead mill) from **Glen Mills** has proven successful.

The alternate technologies have shortcomings. For example, high pressure systems are prone to problems when confronted with debris, require multiple passes, and they operate very hot. Heat can especially be a problem when inflammable solvents are used. Another group of cell breakage methods, the use of chemicals or lysates, puts an added burden on the effluent treatment steps.

Advantages of the DYNO-MILL include 95+% breakage in one pass, cool operation, and the ability to accommodate renegade solids debris that might be introduced with the cells. When using solvents for extraction, the DYNO-MILL is available in explosion proof versions. Scale up to industrial quantities has been demonstrated.

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FRET IMAGING

EXFO

FRET (Förster Resonance Energy Transfer) microscopy imaging is a widely used technique to determine protein interactions inside living cells. It can answer several questions about the extent of protein colocalization, dimerization, folding, molecular motors, and transduction pathways. FRET is a quantum mechanical process involving the radiation-less transfer of energy between fluorophores over a small distance (1-10 nm). If the molecules are close enough, the donor fluorophore transfers its energy to the acceptor fluorophore. Monitoring the ratio of the fluorophore emissions provides valuable information to researchers about the spatial localization of the proteins being studied.

EXFO's customers have found that using the X-Cite exacte system reduces the need to normalize the ratio of the fluorescence signals. The X-Cite exacte provides illumination that is more stable than the traditional fluorescence arc-lamp and offers greater control over variables that cause undesirable artifacts in a FRET set up. Researchers can modulate the light output to optimize imaging conditions and minimize photobleaching, while having a stable light source for imaging over long periods of time (10-24 hours time-lapse FRET experiments).

CREATING BIOBANKS THAT SUPPORT COLLABORATIVE RESEARCH PROJECTS

Hamilton Storage Technologies

In the past 10 years, biobanks have been established to support general research in pharmacogenomics and medicine, as well as more focused studies of specific diseases. These biobanks can cost tens of millions of dollars to construct and are located at one main site, isolating samples from other research institutions and separating scientists from their invaluable "assets." Lately, there is a trend toward collaborative research between different institutions, creating a need for smaller, localized and linked biorepositories. The challenge is how to share the sample data between the sites.

Hamilton Storage Technologies has developed web-based application programming interface (API) software to link multiple biobanks, creating a sample data network that scientists can access. Each laboratory has a local, automated biobank linked with a secure web interface to a common laboratory information management system (LIMS).

With the creation of integrated biobanks, scientists can share data with other laboratories without losing ownership of their invaluable samples. Allowing scientists to maintain their own samples locally facilitates a common approach to biobanking while increasing the quality of biological research programs.

SMALL ANIMAL *IN VIVO* IMAGING

LI-COR Biosciences

Small animal *in vivo* imaging continues to be a trend in pre-clinical research. Researchers require instrumentation and fluorescent labels that can bridge to translational applications. Although a number of modalities are available, *in vivo* imaging at 800nm offers distinct advantages, especially for deep tissue penetration.

"Near-infrared fluorescence provides researchers with greater clarity when imaging tumors in mice," says Mike Olive, vice president, translational research, **LI-COR Biosciences**. "Background from tissue autofluorescence is virtually eliminated at 800 nm, which enables earlier target detection than other methods."

"Imaging at this wavelength provides a pre-clinical solution that is compatible with systems intended for human imaging that are currently available or in clinical trials," adds Olive.

For *in vivo* imaging applications, LI-COR offers a family of optical agents based on its IRDye infrared dyes and the Pearl Impulse small animal imaging system. The Pearl incorporates a two-laser system that can simultaneously detect two near-infrared probes and perform real-time imaging. The Pearl is a user-friendly and sensitive platform for small animal imaging, receptor and transporter targeting, structural vascular/lymphatic imaging, and biodistribution studies.

INCREASED THROUGHPUT OF COMPLEX ASSAYS

GE Healthcare

Bringing new drugs successfully to market has been, and will continue to be, a tremendous challenge for the pharmaceutical and biotech industries. There is also demand for shortened timelines for development, and scientists are exploring more new and novel drug targets than ever before. On top of this, there is an ever increasing pressure from patients and regulatory agencies to collect and present more and more detailed data for proof of drug safety and efficacy.

It is therefore necessary for instrumentation to support greater throughput of complex assays, in order to more fully investigate drug-target interactions and their biological consequences. Over the past year, **GE Healthcare** has made substantial advances in label-free compound screening and characterization and high-content cellular analysis, with the introductions of its Biacore 4000 and IN Cell Analyzer 2000 systems.

Biacore 4000 is a solution for large-scale, label-free molecular interaction analysis. The system delivers binding, kinetic, affinity, concentration, and specificity data in both screening assays and detailed characterization studies. It is designed for large-scale parallel interaction analyses, with the capability to analyze up to 4800 interactions in 24hrs.

The IN Cell Analyzer 2000 is a flexible cell imaging system for High Content Analysis with excellent image quality, speed and ease-of-use for screening and research. The flexibility of the system enables scientists to perform a wide variety of previously challenging experiments with a single instrument: from investigative microscopy through to automated screening, and imaging of organelles, cells, tissues and whole organisms.

TOP Trends IN Life Science RESEARCH

STANDARDIZING THE UNIT OF MEASUREMENT FOR IMAGING DATA

Photometrics

"People in my lab produce different answers from the same fluorescence experiments, over and over again," says Alex Rodriguez, assistant professor of cell biology at **Rutgers University**.

Identifying why results differ is problematic for Rodriguez and other researchers because current microscope cameras report data in arbitrary units. These units—known variably as fluorescence units, grey scale units, analog-to-digital units, etc.—are merely electronic representations of incident photons. Individual cameras, even of the same make and model, produce these representations differently. User-changeable settings, such as gain, and sensor aging also variably affect the representations.

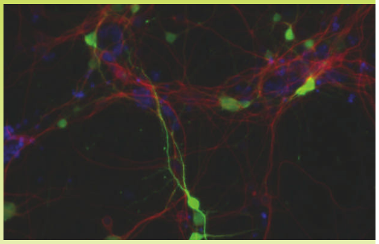
Standard units of measurement that directly correlate with incident light are needed so that data can be directly compared within and between labs.

Photometrics has engineered the Evolve EMCCD Camera, which reports live data in standardized units: photoelectrons. Produced directly by incident photons, photoelectrons are independent of user-changeable settings, camera make or model, and sensor aging.

"Photometrics' Evolve camera finally gets rid of arbitrary gray levels in favor of photoelectron counts, a meaningful standard that scientists can use for comparing their imaging systems and their image-based data," explained Sidney L. Shaw, assistant professor in the Department of Physics at **Indiana University**.

NEURON TRANSFECTION

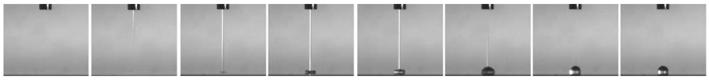
Lonza Cologne AG



Neurobiology research often involves transfection of primary neural cells, which can be a challenge. Lipid-mediated methods usually do not achieve high efficiencies, while viral transduction can be efficient but requires experience and effort in generating the viruses and holds safety concerns.

Since 2003 **Lonza's** non-viral Amaxa nucleofector technology has aided neurobiology research by allowing highly efficient transfection of primary neurons, glial cells, and neural stem cells. However, as an electroporation-based method, it has thus far required cells to be transfected in suspension and as a consequence could only transfect neurons straight after isolation. Neurons at later developmental stages could not be transfected as they cannot be brought back into suspension once they adhered.

After extensive R&D Lonza has now introduced the first of a series of Nucleofector AD Kits that enable Nucleofection of cells in adherence. With the Basic Neuron Nucleofector AD Kit primary neural cells can be cultured prior and post Nucleofection for up to 14 days in special Nucleocuvette AD Plates and transfected at any time, i.e. also at later developmental stages. The plates are suited for analysis of cells by transmission light or fluorescence microscopy as well as absorption, luminescence or fluorescence assays.



PRODUCTIVITY - MORE SAMPLES IN LESS TIME

IDEX Corp.

The trend for improved productivity has been developing for some time. Initially with the use of autosamplers and computerized data analysis, but more recently, incorporating robotics, liquid handling devices, and optimized sample and reagent movement and delivery. The trend to increased productivity is accelerating with the technology and computing power available to deliver results. Current examples of this are robotic liquid handling for genomic, proteomic, and PCR analysis and Ultra High Performance Liquid Chromatography (UHPLC) for chromatographic and mass spec analysis.

In the area of robotic liquid handling sample dispensing has quickly evolved from the use of 96 well plates five years ago to 384/1536 well plates today with the need for even greater assay densities with or without well plates in the near future. This trend is not without its own pain points.

In the area of UHPLC, the chromatographic system pressure and temperature have been modulated to increase sample throughput. Pressures of 15,000 psi are common today with the trend to 25,000 to 30,000 psi in the near future. The challenge of providing system components at these pressures is affected by both system and component design and the materials chosen for the job.

SHIFTING FROM QUALITATIVE TO QUANTITATIVE ANALYSIS

LI-COR Biosciences

The shift from qualitative to quantitative analysis is a significant trend in protein detection methods such as Western blotting. Researchers have recognized that quantitative measurements provide a more accurate view of cellular events.

"Target identification and measuring efficacy against a target are significant for drug discovery research," says Mike Olive, vice president, translational research, **LI-COR Biosciences**. "To accurately monitor protein expression and cell signaling, you need quantitative data."

Two-color, near-infrared (NIR) fluorescent detection of Western blots eliminates many of the variables of chemiluminescent detection and enhances accuracy.

"With NIR fluorescence, a researcher can use multiplex detection to simultaneously measure the total amount of target present and the level of phosphorylation of that same target," adds Olive. Accurate, quantitative measurements facilitate many types of research, including cell signaling studies, systems biology, and stoichiometric analysis of protein interactions.

LI-COR developed the Odyssey Infrared Imaging system and family of IRDye infrared dyes and reagents to facilitate simultaneous analysis of multiple protein targets from a single sample. Multiplex detection increases efficiency and accuracy and is ideal for rare or limited samples. The systems are used for a variety of applications, including cell-based assays, array-based approaches, and *in vivo* molecular imaging.

THE RISE OF GENOMICS AND PROTEOMICS

Thermo Fisher Scientific

A key factor in genomics and proteomics has been the use of multi-stepped workflows to generate meaningful data. Proper quality control (QC) measures are critical in any lab working with nucleic acid and protein analysis. One important QC steps is to determine the quantity and purity of the DNA/protein at various steps throughout the workflow.

Conventional spectrophotometers used to be a common way to perform this quantitation/purity check. These require the use of cuvettes, dilution of the sample, and significant lab space. The advent of novel microvolume technology that eliminates the need for cuvettes and dilutions has eased this step. NanoDrop spectrophotometers, such as the NanoDrop 2000c, are an example of this. Many life science labs have reported performing more QC steps within their workflow since using the NanoDrop 2000c. This QC strategy ultimately results in greater confidence in the downstream results.

REQUIREMENTS ON OPTICS

Edmund Optics

Genomics, proteomics, and bioinformatics are transforming biotech research, affecting everything from healthcare to environmental and agricultural biotechnology. **Edmund Optics** supports these evolutionary technological changes in the biotech field not only with an extensive inventory of new optical products such as custom engineered high performance filters, imaging lenses, and other optical components, but also with application engineering and design support to scientists and engineers globally. With increasing complexities and downward pressure on costs of medical and biomedical instrumentations, Edmund Optics with its "design for manufacturability" expertise in optics and imaging, is pulled into early stages of components and instrument specifications development. Traditionally focused on the visible optics realm, Edmund Optics has aggressively expanded its design and manufacturing capabilities and off-the-shelf and customized optical components to UV and IR spectral regions to accommodate the latest optical requirements and technology trends in life sciences.

LARGE SCALE CELL CULTURING

Glen Mills Inc.

The ability to culture large amounts of adherent cells in a natural 3-D matrix is now possible with the Z RP BIOREACTOR System. This rotating-bed Bioreactor and supporting Incubator and Control Systems is able to culture a large mass of cells (to 10^{10}) in a compact apparatus just the size of a desk top. The gentle motion and efficient exchange of nutrients/products/ waste allows for continuous growth for up to one year. Intermittent extraction of biochemicals or cells has been demonstrated.

Proven applications include perfusion chemicals production, stem cell culturing (both with and without differentiation per passage), and fully developed Extra Cellular Matrix (ECM) for cell study.