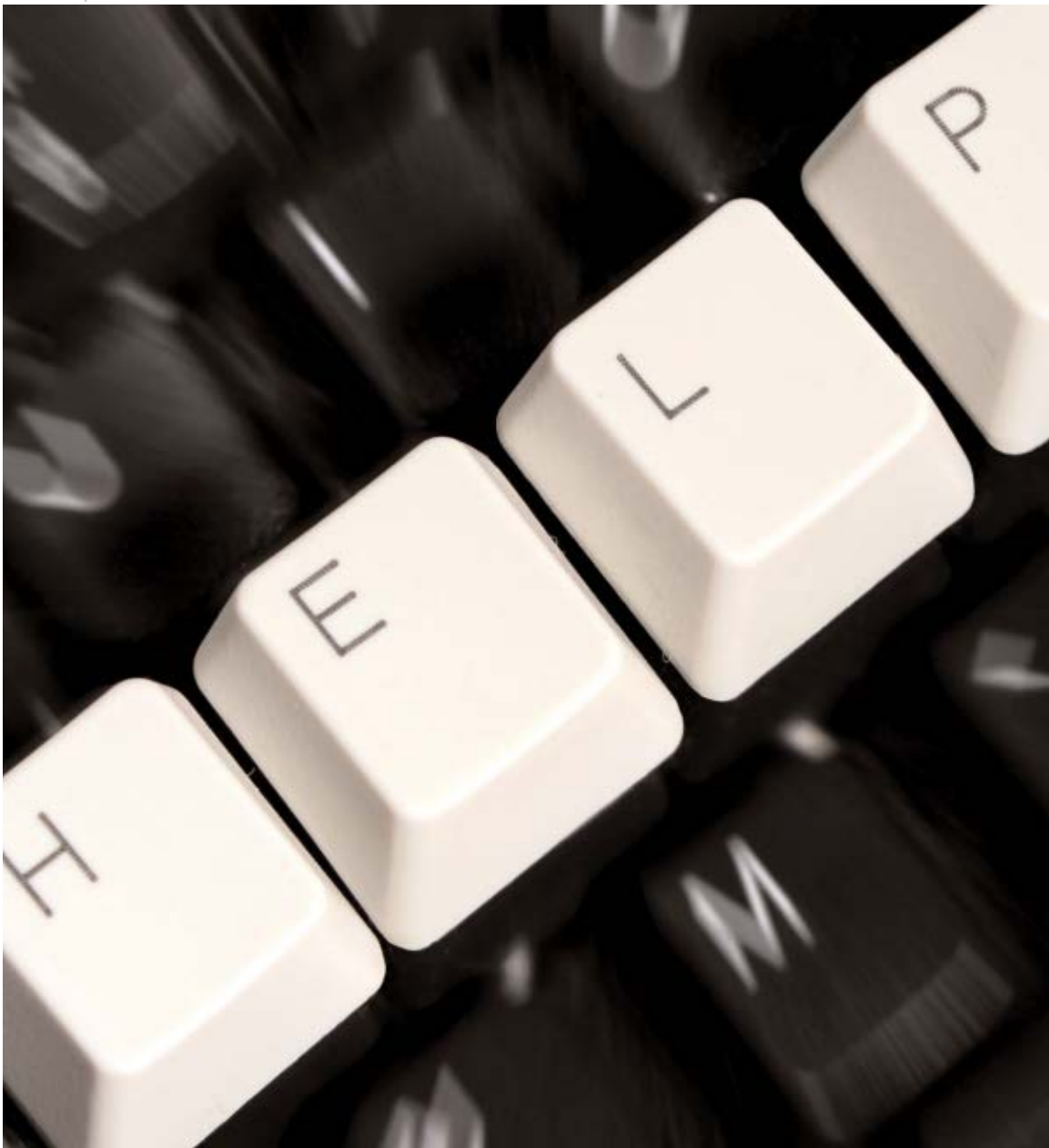


Lab Manager[®] MAGAZINE

Where Science and Management Meet™

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Big Labs, Small Labs — Similar Problems, Different Solutions
Logjam, Bottleneck, Pinch-point: Creating Efficiency in the Lab
Integrated Service Models for Smaller Labs
Setting Up and Running a Protein Microarray Facility

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The article review process should begin with a query by email or phone followed by a brief abstract or outline. Please state your topic and objective, and indicate your perspective as well as your professional relationship to the topic. Content must be unbiased and cannot promote a particular product or company. Article length may range from 1500-2500 words. All manuscripts must be submitted electronically by email or disk.

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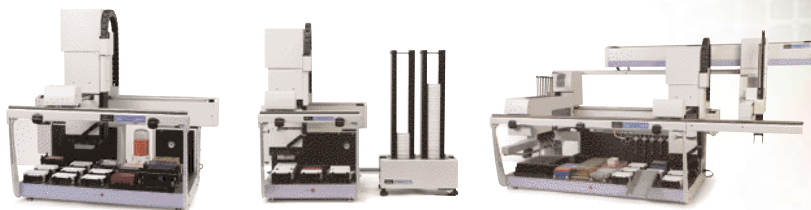
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How to Succeed in Management Without (looking like you're) Really Trying

I love the names of high dives, gymnastic flips, and figure skating jumps. Anyone who has watched the Olympics knows that they are in for the thrill of victory or the agony of defeat when the announcer says that the diver is stepping up to the edge of the springboard to do his back two-and-a-half somersault with two-and-a-half twists in the pike position. Or when the small but all-muscle gymnast puts a carefully pointed toe onto the mat in preparation for her triple front double flipping salto. And then there's the figure skater. Will he land on his blade or backside after attempting the triple lutz double salchow with a flying camel?

Though the feats they perform are complicated and take years of training, in those split seconds when they are flying through the air, it looks effortless. In fact, being a great athlete means making it look easy. So easy that viewers think they can leap out of the bleachers or off the couch and perform the perfect double hecht kip summy, or swoosh the three-pointer from half court, or hit the homerun with bases loaded. Pick your sports analogy — most of us have had the feeling we could just get up and do it too, only to realize that it's much harder than it looks.

Good management can also look deceptively easy. There are managers who seem like they can do it in their sleep. They are comfortable in their role. They behave with fairness and are consistently respectful in their interactions. They remain calm in the face of problems and crises. People gravitate to them for their opinions and ideas.

Are there management naturals? Can a great manager be made or is it in the DNA?

Toning the management muscle is probably like anything else — practice, practice, practice. But where to begin? Maybe by watching a pro in action.

Observing people whose management skills you admire can help identify skills worth cultivating. Just saying you want to be more like them is not enough. What specifically do they do that makes them successful in that role? Do they multi-task and never lose patience? Encourage with sincerity, correct with tact? How would you define their management style? Maybe, if they are not an ideal manager, is there is a particular skill that you would like to learn? You also don't have to do this from afar. Talk to people about their management philosophy. Maybe even pose a few "how would you handle this" type scenarios from your own work experience.

When you find people with a knack for management, copying their style won't do the trick for you. Adapt what they do to make it your own. Put the new skills and ideas into practice and maybe one day you'll be able to do the management equivalent of the triple lutz twisting pike half gainer ... and stick the landing.

Patrice Galvin

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Big Labs, Small Labs —

Similar Problems, Different Solutions

BOTH BIG AND SMALL LABS HAVE MANY PROBLEMS IN COMMON BUT OFTEN USE DIFFERENT METHODS TO SOLVE THEM.

Some formerly disparate big and small lab practices are merging due to changing economic trends, new technology, and new outsourcing options. Nowhere is this truer than in hiring.

HIRING

Both big and small labs want to staff their labs with the best available scientists who have the appropriate backgrounds for the available positions. But they have different problems in doing so. Large labs are deluged with applications, many of which come through their websites. Many scientists apply for jobs for which they are not qualified in the hopes that another job for which they are qualified will become available. Even with keyword searching of electronic resumes, sorting through candidates is tedious and time-consuming for human resources staff and hiring managers. Small labs often have the opposite problem — not enough candidates because few people have heard of the firm.

Large companies have historically held the advantage in finding qualified candidates. Their size permits larger recruiting budgets for advertising, maintaining a careers section on their corporate website, and offering on-campus visits. Virtually continuous recruiting by large labs provides economies of scale. In contrast, recruitment is much less continuous for small labs. The need for a new hire occurs and advertising for that job opening is placed. Once the hire is made, proactive sourcing for candidates halts. Intermittent recruitment is more expensive on a per candidate basis. Small company staffing efforts are often geographically limited, notes Dr. Rita Boggs, President of American Research & Testing, Inc.

However, small labs today have the opportunity to gain the same advantages that, until recently, were only economically feasible for large labs. For example, the shift from expensive newspaper and trade magazine recruitment advertising to online job boards represented a major shift in reach for candidate sourcing. For small labs, job board advertising rates were often too steep while the geographic reach was broader than they needed. However, they now have inexpensive advertising available from online sites, such as craigslist.org. Google Base, a massive classifieds database, combines listings aggregated from other sites along with postings which are currently free.

With so many job-hunting scientists in this country on student visas, hiring a new employee often means completing and filing the lengthy paperwork required by the federal government to get the prospective employee a “green card.” Large laboratories have amply staffed human resources departments experienced in doing this. Small laboratories once passed on these job candidates because they had no one who had mastered the lengthy, complex, and costly visa application procedures. Now firms that work on a contract basis provide this service for small labs.

ACQUIRING EXPENSIVE EQUIPMENT

Purchasing or leasing expensive instrumentation and equipment is a financial challenge for



Small labs today have the opportunity to gain the same advantages that, until recently, were only economically feasible for large labs.

managers of both large and small labs. To justify purchases, labs have long used instrumentation for solving plant operational problems in addition to solving R&D problems. However, sometimes this is not enough to keep expensive instruments operating frequently enough to justify the expenditure for their purchase. As a result, both large and small firms have long used contract laboratories to provide analytical and other services when they cannot cost effectively maintain their own capabilities in certain areas.

High throughput screening (HTS) combined with combinatorial chemistry, while significantly enhancing product development productivity, is quite expensive whether the laboratory purchases and operates the equipment itself or outsources the work to a services firm. Hence, it remains primarily the bailiwick of large labs. Originally this approach was used large in pharmaceutical and biotechnology research. More recently, chemical companies have been applying HTS to develop new polymers, such as Dow Chemical's Versity and Infuse elastomers. Often the development and evaluation of new catalysts using HTS is critical to the development of these new products. For example, Symyx Technologies, a major HTS outsourcing firm, worked with Dow to develop catalysts to produce new elastomers, with Celanese to develop a new catalyst for manufacturing vinyl acetate and with ExxonMobil to develop a new refining catalyst. These research collaborations are not cheap. Dow has a \$120 million, 5-year contract with Symyx while ExxonMobil's 5-year alliance is costing the oil company \$200 million.

The broad scope of these collaborations is one reason for their high cost. Still, these sums suggest that outsourcing combinatorial chemistry/HTS, even for smaller projects, is beyond the financial capacity of most small laboratories.

Purchasing the equipment needed to run these experiments in one's own lab is costly. In addition, analyzing the huge amount of data generated in high throughput screening studies requires a lot of expensive computing capability. According to Mike Fasolka, Director of the Combinatorial Methods Center at the National Institute of Standards and Technology, his organization is trying to develop less expensive high throughput techniques. Should these efforts succeed, they may make the technique more affordable for smaller laboratories.

Large labs frequently use simulation software to solve problems in design of drugs and other products, manufacturing process development, modeling the use of their products and services, and modeling the exploitation of natural resources. Modeling problems are as varied as observing drug-molecule interactions with cell enzyme

production sites and determining the most efficient production methods for an oil field.

Large laboratories using this software extensively can afford access to the large amount of data processing capacity required to operate such software. Researchers who set up problems and operate the software are specialized and highly trained. Small labs often lack the financial resources for these and may have only intermittent needs for such capabilities. However, some firms that have developed this software, such as Accelrys and Tripos, provide the service of using their software to solve research problems for laboratories lacking the resources to do so on their own. Both the Internet and tradeshow offer an excellent means of identifying firms that provide "software as a service."

As some larger firms have sold divisions and reduced R&D staffs, keeping their analytical staff members and expensive instrumentation productively occupied has increasingly become a challenge. Firms with large, but under-utilized, analytical staffs and expensive instrumentation have offered their services to other firms — even competitors. Firms taking this approach include DuPont, Shell Chemical, DSM, and ConocoPhillips. Other large firms such as BP are selling under-utilized analytical lab assets to contract laboratories such as IntertekCalebBrett. These contract labs operate the laboratories on the former owner's premises using staff scientists and technicians who used to work for the original owner. They take in work from other firms to keep both staff and instruments more fully utilized than possible for the former owner.

Meanwhile small firms simply can't afford some expensive instrumentation and equipment. Some others do not operate this equipment often enough to justify the expense. Their options are to use contract laboratories or nearby university laboratories. Internet search engines have made it easier for small labs to find providers of these services.

SAFETY AND REGULATORY MATTERS

The scope of workplace safety and environmental regulations (their complexity and reporting requirements) continues to increase. Economy of scale permits large labs to maintain adequate numbers of well-trained full-time staff members to comply with these regulations. Formerly, the primary option for small companies was to have people handling these matters who also had other job responsibilities. Now a wide variety of outsourcing options are available to small labs to deal with this problem. Some firms, such as Northwest Hazmat, Inc., provide spill response services. Others such as 3E Company offer online regulatory compliance tools. Organizations such as Lab Safety Institute and Advanced Chemical Safety provide laboratory staff safety training.

However, the resources of large labs continue to enable them to deal with issues that small labs often cannot afford to address. For example, large laboratories such as Shell's Westhollow Technology Center have people trained in ergonomics to assist employees with individual laboratory and workstation design. At many small laboratories this is done, if at all, on an informal basis.

INTELLECTUAL PROPERTY CONCERNS

While most (but not all) large firms operate their own legal departments to deal with patent and other intellectual property matters, small companies find it more cost effective to hire law firms to handle these matters. Again, the issue is staff utilization. The many researchers at a large lab can generate a constant stream of invention disclosures to be turned into patent applications that are prosecuted to obtain domestic and international patents. Matters, such as monitoring and paying patent maintenance fees and pursuing licensing options, must be dealt with. In contrast, smaller labs generate only an intermittent flow of invention disclosures. Smaller labs, usually affiliated with smaller firms less international in scope, may pursue fewer foreign patent filings. All this means that many small firms often cannot keep a patent attorney sufficiently busy to justify having one on their own staff. As a result, this work has long been outsourced.

Intellectual property concerns are becoming of ever greater interest as both large and small firms try to find profitable uses for their technology besides commercializing their own new products and process. New firms are springing up to match technology holders with firms interested in licensing such technology for various uses. These include yet2.com and NineSigma.

REDUCING OPERATING EXPENSES

Both large and small laboratories are reducing operating costs by outsourcing support operations such as janitorial services. Due to their larger scale, it often makes more sense for large laboratories to outsource operations such as mailroom services than it does for small labs for which the scale of support needed is too small to interest an outsourcing firm.

Some large labs are outsourcing more sophisticated services such as mechanical and electrical support of their pilot plants and laboratories. Some large labs also outsource library and information science support services and graphic services to firms such as Kellogg, Brown, & Root and Pitney Bowes who operate facilities on the large laboratory site. Small labs also frequently outsource these services but often the providers do not routinely operate on the lab site.

OPERATING UNDER-UTILIZED LABS

Besides strategies dealing with under-utilized analytical laboratories mentioned above, some large laboratories have considerably more space than they need. This has become a problem for many large labs as their corporate parents reduce R&D operations. The still-operating portions of the laboratory must cover the overhead expenses for the vacant lab space.

Some large labs have dealt with this problem by filling vacant lab space with tenants. For example, since the early 1990s, Shell Chemical has sold about half their chemical businesses substantially reducing the need for lab space at their Westhollow Technology Center in Houston. Much of this lab space is now rented by the new owners of these businesses such as Dow Chemical, Hexion, and Kraton. Some government laboratories such as the Marine Biological Laboratory (Woods Hole, MA) also rent lab space. This practice is becoming global. Solvay operates as a laboratory incubator for start-ups at its Brussels' laboratory. Some universities, such as the University of Albany and West Virginia University, have built incubator facilities near their campuses for small start-up firms. These firms are often based on the research of university faculty members.

Whenever two or more firms operate research labs in the same building, they must set up programs and procedures to protect the security of their intellectual property.

WRAP-UP

The difference in the scale of their operations and (usually) in their financial resources means that large and small labs often must solve similar problems in different ways. Business trends and online technology have provided both new solutions and increased access to them by both large and small labs. No doubt the skills of managers of both large and small labs in dealing with the challenges outlined above will continue to evolve.

Dr. Borchardt is a consultant and technical writer. The author of the book "Career Management for Scientists and Engineers," he writes often on career-related subjects. He can be reached at jkborchardt@hotmail.com.



Logjam, Bottleneck, Pinch-point:

The Efficiency Drain for the Modern Laboratory

IN RECENT YEARS, THE GROWING TREND TO RESOLVING WORKLOAD JAMS AND BOTTLENECKS WITHIN LABORATORIES HAS BEEN TO RELY ON AUTOMATION. BUT IS MACHINERY AND AUTOMATION REALLY THE ANSWER, OR IS THE PROBLEM MORE DEEPLY SEATED? COULD THE ISSUES INSTEAD BE RESOLVED BY LOOKING AT THE PROCESSES AND METHODS OF WORKING?

As the pressure on modern laboratories to improve efficiency and throughput grows, there has been a reluctance for scientists to borrow models from the manufacturing and engineering markets in order to overcome common bottlenecks and pinch-points in the laboratory process. Commercial payback comes from being able to get more robust processes to market quicker. Where does payback come from laboratory operations that are not measured, per se, using payback equations that relate to cost of goods or loss from inefficiency?

Laboratory managers are often faced with complex and fragile processes that last hours or days. However, their responsibility is to conduct the experiments and assays, and often not to address the efficiency of the laboratory. So, at what point does the manager decide it is necessary to change a laboratory workflow or process? The answer may lie in finding new or at least tailored metrics to make an assessment of routine laboratory operations as quantitative as the related production operations from which many of the guiding concepts of continuous improvement come.

CHANGING HABITS

Recognizing that a laboratory needs to change its practices is not easy, and finding solutions can be even more difficult. Short-term options are often taken to ease the immediate burden but long-term decisions, which take into account the organization's future plans, can be time consuming. The ownership of the problem can pass from one person to the next without the underlying issues ever being resolved. While universities and training teach scientists to work in a laboratory, staff are not often taught to look at management issues, such as workflow, efficiency, and productivity.

More often than not, change is instigated from the bottom-up, with pressure placed on a director inadvertently from the manager and staff. Some may resist the changes for fear of staff reductions or fear of stepping out of the established comfort zone. However, a change in processes does not necessarily lead to job cuts. It can improve the working environment for many while increasing throughput and the quality of results. Gone will be the mundane and tedious tasks and introduced will be the ability for highly trained staff to apply their skills in other areas. Where inefficiencies can be identified, one often sees areas of high staff turnover, where much of the staff will be in training at any one time, and natural wastage can occur.

In addition, laboratory processes often have high levels of variation, making the development of a robust and reliable process inherently difficult. Couple this with the high intrinsic value of the end product and a laboratory increasingly has to acknowledge and accommodate a degree of risk during its sample management, R&D, and processes. Mitigating this risk is becoming a common goal for more and more laboratories.

COMMON WORKFLOW BOTTLENECKS

No matter how well the space and laboratory apparatus were originally set-up (and this has usually

Although the advantages to automation are widely documented (greater accuracy of results and faster delivery times to name but a few), not every process is suitable for automation.



been on an ad-hoc basis, driven by utilities and network issues rather than laboratory efficiency), as the workload and sample/specimen load increase, and common laboratory practices change and expand, it is necessary for the process to be critically reviewed in terms of workflow bottlenecks or logjams that affect the overall operation and productivity.

The first step usually taken is to look for instrumentation and software platforms that can automate a common process. But this is not always the best move. Although the advantages to

automation are widely documented (greater accuracy of results and faster delivery times to name but a few), not every process is suitable for automation. For example, instruments rarely can multitask, which renders some actions more viable for humans to perform.

Automation may solve some of the efficiency issues in a modern laboratory; however, this will not overcome common logjams and bottlenecks in a process. Therefore, it is necessary to start modeling the process and assessing workflow needs in order

to identify where the bottlenecks are, what processes are suitable for automation, and which workflows need to be rearranged or amended. This may include some physical alterations to the laboratory work space.

A general laboratory manager often does not have enough expertise and experience to start modelling the process. This is where process engineering companies can put the long-standing practices of productivity improvement and process automation to work for the laboratory industry. They can exploit available process models from the manufacturing environment (e.g., lean manufacturing or Kanban practices) in order to improve laboratory workflow.

DEVELOPING A ROADMAP

It may be possible for an organization to reassess its processes in-house. One way is to invite a manager from within a different department to spend time analyzing processes. He/she can bring an unbiased viewpoint. The downside is that to model the process, create a roadmap for the future, and implement it demands time that many in-house managers lack.

Outsourcing a process automation project is often seen as the first step in overcoming workflow issues. The first phases of the project — the development of specifications and user requirements — are paramount. Without the right leaders to drive the process, laboratories waste valuable time and money before this has even started. Laboratory managers can therefore leverage the specialist experience and knowledge of process engineers as an approach to solving the problem. Learning from other people's experiences provides faster, more efficient, and more cost-effective pathways to improving processes.

The following approach sets out a typical workflow evaluation project:

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4. Assess and map the approaches that merit consideration. Factors to consider include use of capital, workflow optimization, space requirements, and planned future expansion options.
5. Determine a control strategy to ensure that the CSAs are optimized and that future additions to laboratory instrumentation can fit seamlessly and efficiently into the new process.

COMMON PINCH-POINTS

A typical high-throughput pharmaceutical laboratory will put all of its plate readers in one room and will program all of the readers to analyze the well plates overnight. This is a common bottleneck in a high-throughput laboratory, making it difficult for a team of scientists to obtain results all at the same time. Historically, it will have been set up in this way by IT and engineering for utilities, cabling, and network optimization. By examining issues such as the location of equipment, and organizing a staggered timetable for research, blockages, and pinch-points can be removed. The result can be better staff utilization, wait times for analyzers

reduced or eliminated, and more assay results per unit time. All of this can be accomplished without significant investment in new equipment; it instead involves rationalizing the layout, workflow, and positioning of key assets in the laboratory.

CONCLUSION

Laboratories need to be aware that changing the processes may lead to cost savings. Staff may not need to be deployed to another area. Instead, consider that payback will come in the form of a decrease in turn-around time, decrease in waiting times for results, staff retention, and greater accuracy of results derived from greater efficiencies.

Everyone who experiences problems and workflow logjams should look at the current processes — are these troublesome now and would suggestions made now relieve problems in the future? Do not be afraid to speak up where you can see a way to help and improve the working environment. Achieving the ultimate efficiency is the responsibility of everyone in a laboratory.

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Integrated Service Models:

a cost-effective way to maintain equipment for smaller labs

JUST AS THERE ARE A VARIETY OF OPTIONS TO CHOOSE FROM WHEN SELECTING AN INSTRUMENT, THERE ARE A VARIETY OF WAYS TO MAINTAIN THEM. ONE SUCH OPTION IS THE INTEGRATED SERVICE MODEL, WHICH SEEMS TO WORK BEST FOR A LAB OF OUR SIZE, WHOSE OUTPUT IS APPROXIMATELY ONE THOUSAND SAMPLES A DAY.

In the realm of life sciences, equipment isn't cheap. The purchase of two hybrid triple quadrupole/linear ion trap systems — "Q Traps" — earlier this year cost our laboratory nearly one million dollars alone, a pricey but necessary move to fulfill increased client demand and improve quality and turnaround time. Assuming the normal growth rate of any lab is eight to ten percent in net revenue, most will make just one major instrument purchase a year. Therefore, emphasis is placed not on obtaining new instruments but properly caring for those already hard at work in production.

THE EPITOME OF FLEXIBILITY

When it comes to product maintenance, an integrated service model is the epitome of flexibility. Rather than selecting one method by which to care for all production equipment, subscribing to an integrated approach allows lab managers to determine an instrument's level of protection based on a machine's unique characteristics. Newly marketed instruments and those on the brink of extinction have different roles in production and thus different maintenance requirements, something a blanket "one-size-fits-all" attitude can't sufficiently address. Also, exploring different options can often mean big savings on the overall bill, especially in the case of third-party service vendors, who usually offer price breaks to labs that sign a contract for multiple instruments.

Integrated service models are not to be confused with instrument service delivery (ISD) models; that is, when a third party places someone on-site to perform necessary maintenance. In that situation, the ISD provider serves as the sole point of contact for any type of service taking place in the lab; with an integrated service model, the lab manager calls the shots.

HOW IT WORKS

AIT has followed an integrated service model for years, relying on a combination of original equipment manufacturers (OEMs), third-party vendors, and in-house maintenance. For each piece of equipment, a service model was chosen based on a variety of factors relating to the capabilities of the instrument, the manufacturer, and our staff.

For instance, in the case of our two Q Traps, we maintain an OEM contract. The rationale? Q Trap technology was introduced into production this past spring and is now our workhorse for all opioid and benzodiazepine urine confirmations. The instrument's sensitivity allows us to measure analytes more simply, thereby cutting our extraction time in half and saving the company \$25,000 a month in overall costs. We can't afford to have them out of the production loop for longer than a couple of hours, so it's worth the extra money to enlist the help of the original manufacturer to get it repaired quickly. The manufacturer will have



For each piece of equipment, a service model was chosen based on a variety of factors relating to the capabilities of the instrument, the manufacturer, and our staff.

Shelby Davis III, Andrea Terrell, and Breain Ma'Ayteh Dunscombe



immediate access to replacement parts, research and development staff, customer service information, and other matters that could take one of our lab managers an entire day to work through, a costly expense in and of itself. In addition, Q Traps haven't been on the market longer than a few years; most third-party vendors and in-house production managers simply don't have the knowledge required to provide adequate service.

Other reasons for signing on with the manufacturer include instrument software safety codes to which only they have access and qualifying an instrument for special analysis.

(One piece of advice: Before you sign on the dotted line, check to see if the piece is still under warranty. If it is, you won't need to purchase any kind of contract until the warranty expires.)

For our GC-MS equipment, AIT calls upon a third-party vendor, mainly because the technology has been around for decades and there's a wider pool of vendors capable of servicing them. There are some pieces on which we don't carry any type of service contract at all, like our spectrophotometer, refractometer, and some HPLC systems, because our staff can service them internally. You may also forgo a service contract on instruments where the technology is being phased out of production. In that case, the money designated for a service contract might be better spent on a brand-new instrument.

This integrated approach to instrument maintenance has worked well for AIT. Each instrument has the level of care appropriate for its role in production, and our lab administrators are spared the time and effort it takes to service equipment outside their expertise. However, it can

be difficult to determine which instruments would benefit from specialized care, which pieces could be properly maintained under a single third-party contract, and which ones aren't worth the bother. Then there's the task of managing each contract. The time commitment alone may outweigh the benefits.

Then again, if done correctly, an integrated service model can save the company a considerable amount of money in operating costs, not to mention a lot of aggravation.

SERVICES COVERED

When it comes to a third-party vendor, service contracts are typically designed to cover any high-level preventive maintenance that would normally take internal technicians an extended period of time to perform, as well as any repairs your employees aren't qualified to handle. You'll also want to include parts that aren't considered consumable — i.e., any permanent parts that typically don't require any sort of repair.

Services not covered include daily maintenance and normal wear-and-tear. It's similar in theory to auto insurance — you pay a thousand dollars a year in comprehensive coverage because you want to protect your investment against significant damage in an accident or natural disaster, not score free oil changes and tire rotations.

THE INTEGRATED MODEL IN ACTION

Several years ago, AIT purchased a service contract with a third-party vendor for an HPLC at a price tag of \$3,000 per year. After one year of ownership, the instrument's pump head suddenly stopped working, a part that normal-



ly would have taken \$3,000 to repair. However, since it was covered under the terms of the service agreement, the part was replaced at no charge. Factor in consultation and labor charges that would've accrued had the matter been handled internally, plus the extra time it would've taken for an employee to perform such high-level maintenance, and the service contract has paid for itself and then some.

If the analysis is rigorous and decisions are made well, most service contracts will yield similar results. In the event this is the first time you're considering an integrated model and are hesitant to make a year-long commitment to a third-party vendor, or if it appears that one of your instruments will no longer require high-risk repair, be sure to work with a vendor willing to negotiate a shorter period of time (usually six months). The contracts themselves are a little more expensive, but the peace of mind they'll give you is priceless.

WHO WILL BENEFIT?

Companies that offer a broad spectrum of testing and therefore require a variety of instrumentation — usually smaller companies — stand to reap the largest benefits from an integrated service model, as well as any company willing to increase risk as a means to cut costs. AIT uses instruments like the GC-MS, LC-MS, HPLC, LC-MS/MS, and a host of others because of the breadth of testing we do. It makes sense that a lab such as ours would be attracted to a more flexible model. On the flip side, a laboratory with a narrow focus and little to no variation in instrumentation will most likely fare better with traditional service contracts maintained by the original manufacturers.

For those labs interested in exploring their options, though, a word of caution: In order to implement this model successfully, a great deal of time must be dedicated to researching the needs of each instrument and the different service plans offered by OEMs and third-party vendors, so you can accurately compare the pros and cons of each in relation to every piece of equipment you have. Then, you'll need to spend the same amount of time investigating potential vendors to make sure you're getting the best deal.

SELECTING A THIRD-PARTY VENDOR

As with any service provider, all third-party vendors are not created equal. Each must be evaluated against a series of criteria, including but not limited to cost, contract options, technical knowledge, quality of service, response to call time, parts inventory, and local reputation. A vendor with impressive technical knowledge is no good to you if the company's closest technical service representative is six hours away; likewise, a vendor

with easy access to parts means nothing if the staff lacks the skill to install them.

Also pay special attention to a particular provider's accreditation. You want a vendor to be accredited by the original manufacturer of the equipment you want serviced.

CONCLUSION

All laboratories are different, and a business practice that proves successful for one may be disastrous for another. Only you know what's going to improve production in your particular facility. However, if you're the type of lab that likes to save money, the integrated service model may be worth your while.

Shelby Davis III, Andrea Terrell, Ph.D., DABCC, and Breain Ma'Ayteh Dunscombe, MA are employed with the American Institute of Toxicology, Inc. (AIT Laboratories); www.aaitlabs.com.

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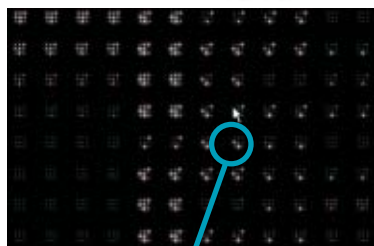
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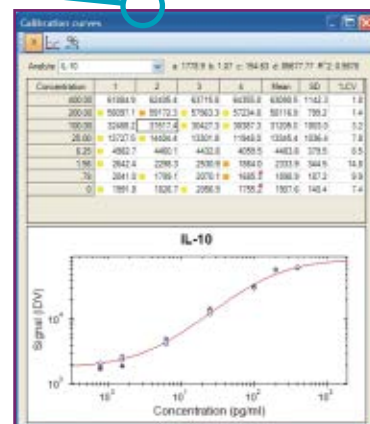


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Setting Up and Running a Protein Microarray Core Facility

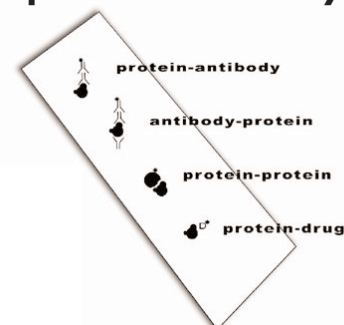
MICROARRAY MANUFACTURING IS AN AREA THAT IS PLAGUED WITH NUMEROUS TECHNICAL CHALLENGES DUE, IN PART, TO THE COMPLEXITY OF THE SYSTEMS INVOLVED AND TO THE VARIETY OF PROTEINS AND POTENTIAL ASSAYS USED.

The development of manufactured protein arrays is currently a hot topic because of the existence of an immense field of applications, including biosensors, diagnostics applications such as serum-based diagnostics, and pharmaceutical target design. The latter typically involves the study of protein targets through protein-protein interactions, enzyme-substrate reactions, receptor-ligand interactions, and drug-target binding. Protein microarrays can also be used to miniaturize and multiplex immunoassays and have performed better than enzyme-linked immunosorbent assays in both sensitivity and quantitative range for use in immunoassays. They are particularly well suited for immunoassay screening applications, such as inflammatory cytokines, allergens, and disease markers, and recombinant cDNA library screening for drug development applications. However, the data generated by a protein microarray can only be as good as the microarray itself. The purpose of this article is to introduce the reader to the fundamentals of setting up a protein microarray facility as well as provide some advice based on our past experience.

Protein arrays possess very specific chemical and physical properties. They are very sensitive to temperature, pH, and ionic strength. Furthermore, the considerable heterogeneity of proteins in solution is a major challenge that limits the physiochemical setting for retention of the protein's functionality. As a consequence, current manufacturing procedures suffer from complexity and low throughput. Several key factors should be considered when embarking on the manufacturing of protein microarrays: design of the array, type of dispensing system used and its cleaning routine to avoid carry-over issues, the environment in which dispensing is carried out, appropriate choices of chip type, reagents and buffers, and imaging technology. Optimizing the process parameters to manufacture high quality protein arrays can be time consuming and costly. Thoughtful process design, bearing in mind equipment limitations, is critical to ensuring a smooth transition from research protein microarrays to a scaled up production line.

Thoughtful process design, bearing in mind equipment limitations, is critical to ensuring a smooth transition from research protein microarrays to a scaled up production line.

Applications of protein microarrays



Examples of protein associations on an array slide

DISPENSING PLATFORMS

Commercially available nano- and pico-liter dispenser platforms are available to perform a wide variety of applications at a variety of scales, from laboratory to full scale production. Their design must exhibit some degree of flexibility to adapt to the variety of applications of protein microarrays and should include a number of features critical to demanding processes encountered for diagnostic applications: aspirate and dispense capability, wash and dry stations to avoid carry-over issues, drop monitoring system, humidity and temperature control, flexible and easy array map



software, flexibility of the number of dispensing channels, high throughput and ability to customize deck configurations for different chips.

The dispensing technology is critical to the quality of the final protein microarray. Non-contact dispensing technology is adaptable to a variety of dispensing platforms and is completely scalable from a single channel on a small R&D platform to a multi-channel overhead gantry production system without significant revalidation of the dispensing process. A non-contact, piezo-electric arrayer will deliver high throughput and high quality prints for high density microarrays in a picoliter range thanks to a robust technology based on fluid pressure, piezo-electric impulse, and glass capillary. Contact silicon pin arrayers are recommended for volumes below 100 pL and for applications on robust chips because their contact deposition mode may damage coated surfaces, such as three dimensional membranes that are routinely used to keep the proteins in their native folding structure.

CHIPS

Different chips carry different surface chemistries which make them appropriate or not for different applications. When performing antibodies assay, or when doing interaction studies, a directional binding is important, such as the one present with tagged surfaces Ni(II)-NTA or streptavidin. To keep the native protein structure in its original 3-dimensional fold, surface modifications are necessary, such as hydrogel™ or nitro-cellulose and zeta-grip™ membranes. High protein binding, 3-dimensional chips like zeta-grip™ are available that provide a porous 3-dimensional environment that protects many epitopes. This translates into better sensitivity and assay performance. These are particularly well suited for colorimetric applications but work with fluorescence as well. They have very low background and very high signal to noise ratio but are not compatible with detergents. For covalent protein binding, additional modifications are required, such as aldehydes, amines, and epoxides. Generally glass slides have a 2-dimensional binding surface and are of limited value in protein microarray studies.

Distinct surface chemistries will be responsible for different spot sizes and morphology of the protein microarrays, causing weaker signals on the detector and possible coalescence and splattering occurrence. Identification of the best possible substrate for a specific protein arraying process is critical to success for manufacturers of protein microarrays.

ARRAYING BUFFER CHOICE

Several arraying buffers are commercially available for protein microarrays but the user must keep in mind that the manufacturer usually optimizes the buffer for one type of glass substrate and for one type of protein array. Buffers such as PBS, Tris, MOPS, and Hepes will provide good arrays for soluble proteins but for insoluble proteins special buffers are required,

such as acetic acid buffer for collagen. Optimization of the arraying buffer often turns out to be a tedious task bearing lots of compromises. To a lesser extent, protein array wash buffer and protein array blocking buffer are also critical to the process. The latter is usually developed for one specific detection method, while protein array buffers are typically designed to enhance protein stability and signal intensity. The spot roundness and size for protein microarrays are highly depending on the arraying buffer.

CARRY-OVER ISSUES

When defining a cleaning strategy, it is important to consider the particular characteristics of the proteins arrayed and to choose cleaning reagents appropriately. Certain proteins or protein diluents may be incompatible with water and prefer organic-based cleaning solutions. Cleaning of proteins from dispensing tips can be achieved using a simple aspirate-and-dispense wash strategy. In high throughput, non-contact arraying, dispensing micro-droplets (nL to µL) of concentrated aqueous solutions of protein can cause blockage of ceramic tips with subsequent damage. Non-contact printing generally suffers fewer problems with reagent clotting because liquid is exposed to the evaporative effects of air for much briefer intervals. However, when highly concentrated solutions are used and hardware washing is infrequent, tip blockage with subsequent over-pressurization induces print failures. Accuracy, precision, production costs, and rates can be compromised in both contact and non-contact arraying when concentrated viscous reagents containing protein, nucleic acid, binders, and other polymers are used. In the non-contact approach, production time allotted to pin cleaning can exceed the arraying period.

FLUID DEGASSING

Non-contact dispensing technology exhibits a high level of reliability for small volume dispensing under the proper experimental conditions. The accuracy and the precision of the drop volume are ensured by a continuous column of fluid inside the dispensing channel — meaning in the absence of any air bubbles. De-aeration of all fluid is thus critical to maintain the fluid path of non-contact dispensers free of any air bubble. The presence of any air bubble would lead to inaccurate dispensed volumes.

An innovative method to achieve efficient degassing is offered by a flow-thru vacuum degassing chamber. This chamber contains a single amorphous perfluorinated copolymer (Teflon® AF) degassing membrane. It comprises a continuously vented mini-vacuum pump with a unitary PTFE diaphragm. This efficient degassing method reduces the dissolved oxygen inside fresh water from 8 ppm for a fully aerated solution to 1 ppm after passing through the degassing chamber. Several vacuum degassing modules may be mounted in parallel on one arrayer. This degassing method elimi-

nates any set-up time required for degassing prior to any dispensing experiment.

ENVIRONMENTAL CONTROL

Both during and after arraying, it is crucial to maintain a controlled environment. Cleanrooms are usually the best environment to obtain high quality protein microarrays. The presence of dust during the arraying process may cause splattering of the spots due to particulates on the substrate surface or clogging the dispensing nozzle. Once a protein array has been spotted successfully, the drying process deserves particular attention. If this process is not thoroughly thought through, the protein array may turn out useless, as the formation of doughnuts instead of homogeneous spots will affect the interpretation of any quantization software. In most cases, it is necessary to maintain a relatively high humidity atmosphere (up to 60–70%) within the print enclosure to prevent the spots from drying out from their external side. The drying out of spots is deleterious in two ways: it creates a dry protein ridge called a “doughnut effect” which affects signal intensity measurements, and it may deactivate the proteins and thus produce false negatives. The addition of glycerol inside a protein solution may be useful to avoid the “doughnut effect” but it creates several challenges. Most commercially available arrayers have difficulties spotting solutions with high glycerol content. Moreover, the drying time is considerably increased by the addition of glycerol. Drying slowly the protein array in a controlled manner usually works well to avoid the “doughnut effect.”

DETECTION

There are two primary ways to detect protein microarrays: fluorescent and colorimetric. Fluorescent detection of protein arrays resulted from translation of nucleotide array technologies to protein microarrays. They generally have a large dynamic range but limited sensitivity because they are molar based (not enzyme amplified). Enzyme-amplified or “colorimetric” arrays result from a translation of traditional immunoassays and hence are more directly comparable. The primary advantage of performing the chemistry on the surface of the array is the increased signal density. For example, if an enzyme produces X product over volume Y, in the case of ELISA, Y is a large volume, typically 100 μL . However, for the colorimetric array, Y is a low volume and may be less than 0.01–1 μL . Since the signal intensity equals X/Y, the microarray is effectively 100–1000 times more sensitive than ELISA. Fluorescent protein microarrays are reported as having sensitivities equal to ELISA, probably because there is no amplification of signal.

Fluorescent protein microarrays require a fluorescent detection device. This type of scanner typically represents an expense close to the cost of the microarray printer (in the tens of thousands of dollars range). Colorimetric microarrays use a

high-quality photo scanner (~ \$200). This reduced cost often makes colorimetric chemistry a good choice for setting up a system and testing the printer. Assays that are developed using a colorimetric system are easily transitioned to fluorescent by switching the conjugate used in the last step. This approach allows printers and assay to be tested rapidly and at a reduced start-up cost. Users may choose to then label their assay with a fluorescent label and then contact a fluorescent scanner manufacturer and have them scan it as part of a free demo. The data between the two systems can thereby be evaluated without buying the expensive fluorescent scanner. As stated above, fluorescent detection provides a greater range of detection but enzyme-based detection provides sensitivities estimated to be 100–1000 times more sensitive.

Quantification is achieved by saving the scanned image obtained from a flatbed or fluorescent scanner as a 16 bit Tiff file. This file type is accepted by a number of quantification packages developed for microarrays. Several free “share ware” quantification programs are available including “Image Tool” available free at <http://ddsdx.uthscsa.edu/dig/itdesc.html>.

CONCLUSION

The effectiveness of any protein arraying experiment is dependent on the interaction of a variety of components of the system, including the dispenser, the protein, the substrate, the binding chemistries/buffers, and the environmental and handling conditions. While contact printing methods may deposit dot volumes as low as 1 nL, with diameters in the order of 75 microns, contact dispensers are often limited by the viscosity of the solution and by clogging issues.

In considering arraying systems, the user must keep in mind a variety of factors, as discussed above. Key among those considerations is the scalability of the manufacturing process, which is a reflection of the design and manufacturability of the product. Working with equipment manufacturers from an early stage of the product design is crucial to ensuring that process requirements and equipment capabilities match.

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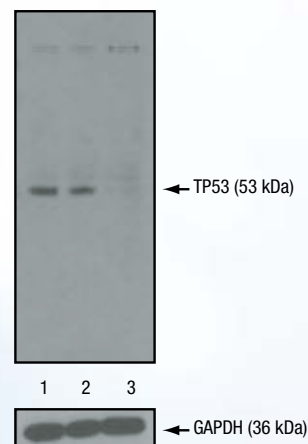
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Western blot data of RNA interference experiment.

A549 cells were transfected with indicated reagents and lysed 72 hours after transfection. Cells were transfected with DharmaFECT® Transfection Reagent alone (Lane 1), 100 nM ON-TARGET^{plus}™ siCONTROL® Non-Targeting Pool (Lane 2) or 100 nM ON-TARGET^{plus}™ TP53 SMARTpool® reagent (Lane 3). Western blot data for GAPDH is included as a control for equal protein loading.



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Shock and Owww!

Web-like, they stretch from wall to wall. Snaking behind equipment and under desks, strung together and strewn over light fixtures and across the top of the fume hoods like orange and black garlands. Poking through holes in walls and ceiling tiles, taped up, stapled down, and snarled into knots that would give sailors nightmares. Often, one grows to several, and then sometimes to even more. Used in the office and lab alike, stretching resources to levels never imagined, often taxing the system well beyond its intended design. What are we talking about? Extension cords, along with cord- and plug-powered equipment, some of the most indispensable tools we use today, but often with little consideration and used in a fashion that could potentially have disastrous results.

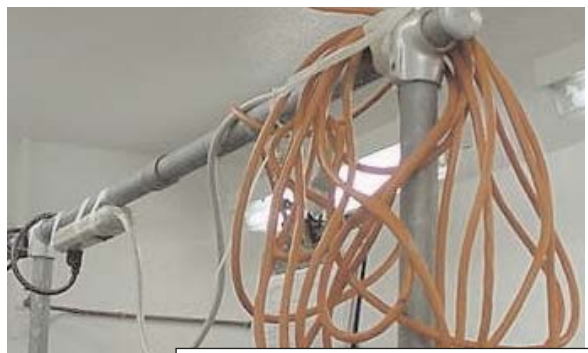
According to the Consumer Product Safety Commission (CPSC), electrical cords and plugs were involved in about 7,100 fires resulting in 120 deaths in 1996. In 1997, more than 12,000 people were treated for electrical shocks and burns. About 2,500 of them were treated for injuries stemming from extension cords.¹ The CPSC goes on to say, “Old extension cords, power strips and surge protectors may have undersized wires, loose connections, faulty components or improper grounding. Old extension cords may fail to meet current safety standards and can be overloaded easily.”²

With a little care, some culling of old equipment and a few precautions, these conveyors of power can be used safely.

One warning, if you have more than a few extension cords powering equipment in your lab, it is probably time to call an electrician to install additional strategically placed outlets, or rearrange equipment. Likewise, if you have any cords running through walls, up through the ceiling, and down to somewhere else, an electrician is definitely required. Extension cords should only be used when necessary and only temporarily. You should always plug equipment directly into a permanent outlet whenever possible. One notable exception is the use of power strips for computer workstations; many jurisdictions permit these as they have internal circuit breakers to provide protection at the point of use. Over the next couple of years we will see a shift to arc-fault protection on these devices as well. Some jurisdictions are already requiring this safety feature.

Wherever it is not possible to plug equipment directly into an outlet, you should begin by selecting the right cord for the job. We generally recommend you purchase cords with polarized, three-prong plugs (ground pin equipped with different size blades) that are approved for both indoor and outdoor use. **Note:** if power is needed in an approved, flammable liquid storage/dispensing room, there will generally be very specific power cord and plug configurations with specific, testing lab approvals for use in these areas; these are not off-the-shelf items. The cord should have a certification label from an independent testing lab, such as UL (Underwriters Laboratories) or ETL (Electrical Testing Laboratories) on the package and attached to the cord. The advantage of the three-





prong (grounded) cord is you would be able to use it on almost any equipment. The two-prong cord sets, while fine for some equipment, cannot be used with equipment needing a path to ground (the third prong).

The cord must be able to handle the intended load. The manufacturer's label on the cord and package should provide the maximum wattage the cord can safely carry. This, in large part, depends on the diameter of the conductors (the copper part of wire). Wires that contain more copper can safely handle more power. The gauge of the wire describes the wire size. You would think that a 16-gauge wire is bigger than a 12-gauge wire, but it's not! As the number gets smaller, the thickness of the conductor gets bigger. A 12-gauge wire can safely carry much more power than a 16-gauge wire.

Always use the shortest extension cord possible to minimize risk of damage to the cord and reduce electrical resistance through the length of the cord. You have picked out your cord, is it safe to use? Extension cords, by the nature of their length and conditions of use, are much more prone to damage than other types of wiring. It is important to check the total length of the cord for damage before putting in use. One should start by looking at the ends of the cords. The male end — the end with the three prongs that fit into an electrical outlet — is the one most prone to damage. The two flat power-conducting

prongs are subject to bending, while the round prong (often called the ground pin), can be broken off. Without the ground pin there is no path to ground through the wires — potentially a very dangerous situation.

Most extension and equipment cords have a tough outer layer that is designed to protect the inner wires. If the outer jacket is damaged, the softer inner insulation around the wires can easily become damaged. Does this mean whip out the tape to repair it? Absolutely not! Damage to an extension cord jacket, or any cord for that matter, should never be fixed by wrapping it with tape. Even electrical tape does not have sufficient strength or abrasion resistance to make a permanent repair as required by OSHA. A taped-up extension or power cord to a piece of equipment is an easy OSHA citation and would make the inspector's day.

So what to do if you have a damaged cord? Cut off the plug and throw it out and replace it with a new cord. Alternatively, the cord can be cut at the point of damage and a new plug installed. If the female end is damaged, do not use one of those 2- or 4-outlet boxes intended for structural use. These are not permitted if the box is designed to be surface mounted. The clue to easy identification is the presence of indentations (knockouts) on the side about the size of a nickel and small holes on the back. There are hard-walled outlet boxes that are approved for use with a flexible cord or on a pendant.

Next, where to plug it in? If you are in a wet or damp location, or next to a water source look for outlets protected by Ground Fault Circuit Interrupters (GFCIs). GFCI are fast-acting devices that detect small current leakage from electrical equipment. In other words, it senses electricity traveling to ground via something other than the wires, such as you. It shuts off the electricity within 1/40 of a second if sufficient current leakage is detected. It provides effective protection against shocks and electrocution. GFCI pigtails, very short cords with a GFCI built in, can be used with plug and cord equipment in areas without protected outlets. Although GFCI outlets are required by building codes in bathrooms, kitchens, rooftops, and garages, they are not always required near laboratory sinks. This requirement varies by locale and code enforcement authority. However, we think it is a good idea and almost always recommend them on outlets within six feet of laboratory sinks.

Before closing, let's take a quick look at what OSHA 1910.305(g) Flexible cords and cables actually says:

- 1910.305(g)(1)(iii) Unless specifically permitted in paragraph (g)(1)(i) of this section, flexible cords and cables may not be used:

- 1910.305(g)(1)(iii)(A) As a substitute for the fixed wiring of a structure;
- 1910.305(g)(1)(iii)(B) Where run through holes in walls, ceilings, or floors;
- 1910.305(g)(1)(iii)(C) Where run through doorways, windows, or similar openings;
- 1910.305(g)(1)(iii)(D) Where attached to building surfaces; or
- 1910.305(g)(1)(iii)(E) Where concealed behind building walls, ceilings, or floors.

Now, you are all set to go. Look for an outlet you can plug directly into. If that is not possible, choose the right cord, make sure it is in good shape, and protected from damage while in use. Remember, use GFCI protected circuits whenever outdoors or in wet locations.

References









1. <http://www.cpsc.gov/cpscpub/prerel/prhtml99/99069.html>
2. <http://www.cpsc.gov/cpscpub/prerel/prhtml03/03119.html>

Glenn Ketcham is a Certified Industrial Hygienist with 22 years experience in the health and safety field. He is currently the Risk Manager for the University of Florida with responsibility for the loss prevention, ergonomics, disaster preparedness, and the occupational medicine surveillance programs. He has managed the laboratory safety programs for both the University of California, San Diego (UCSD) and the University of Florida. In addition, he served as an industrial hygienist with federal OSHA compliance and has a masters degree in environmental engineering sciences with a health physics concentration.

Vince McLeod is a Certified Industrial Hygienist and the senior IH with the University of Florida's Environmental Health and Safety Division. He has 17 years of occupational health and safety experience in academic research with focus in the research laboratory. His specialties are in hazard evaluation and exposure assessments.

The Safety Guys welcome your comments and questions. You can email them at thesafetyguys@labmgr.com.

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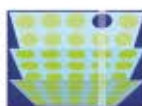
Trends in Drug Discovery
Executive Summit
17-18 January London, England
DrugDiscoveryTrends.com



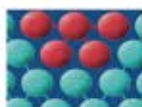
Advances in Protein Crystallography
24-25 January South San Francisco, CA, USA
ProtCrystConf.com



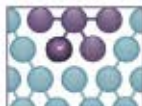
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How IT Works

Flexibility in Liquid Handling

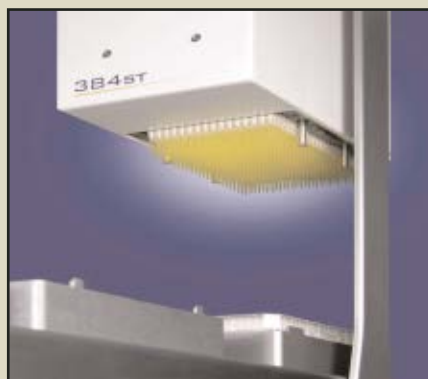
Problem: Compound management and storage incorporates many different types of microplates with varied well densities. Accessing stored samples for screening can be cumbersome because of the difficulty associated with changing between 96 and 384-well heads. Downtimes of over 20 minutes can result from changing pipette heads along with contamination from using tools, and re-teaching new heads all can minimize the advantages of automation.

Solution: A range of plug 'n play multi-channel pipette heads for Velocity11's Bravo liquid handling platform swap in and out for use with 96, 384, and 1536-well plates. With a tool-free docking design, a 96 or 384 channel pipette head easily slides in and is locked down with a simple lever. A sensor detects which head type is installed and no re-teaching is necessary. Utilizing just two heads allows users to span pipetting volumes from 100 μ L to 200 μ L in all types of microplates for a wide range of applications.

The Bravo platform is completely electric which allows for precise control of all axes and minimizes facilities requirements. Precise mechanical control and software flexibility allow for a 96 or 384 channel head to also be used for serial dilutions in rows or columns.



Automated Liquid Handling Platform - BRAVO by Velocity11



384 Channel ST head for precise automated sub-microlitre dispensing with new 10 μ L pipette tips.

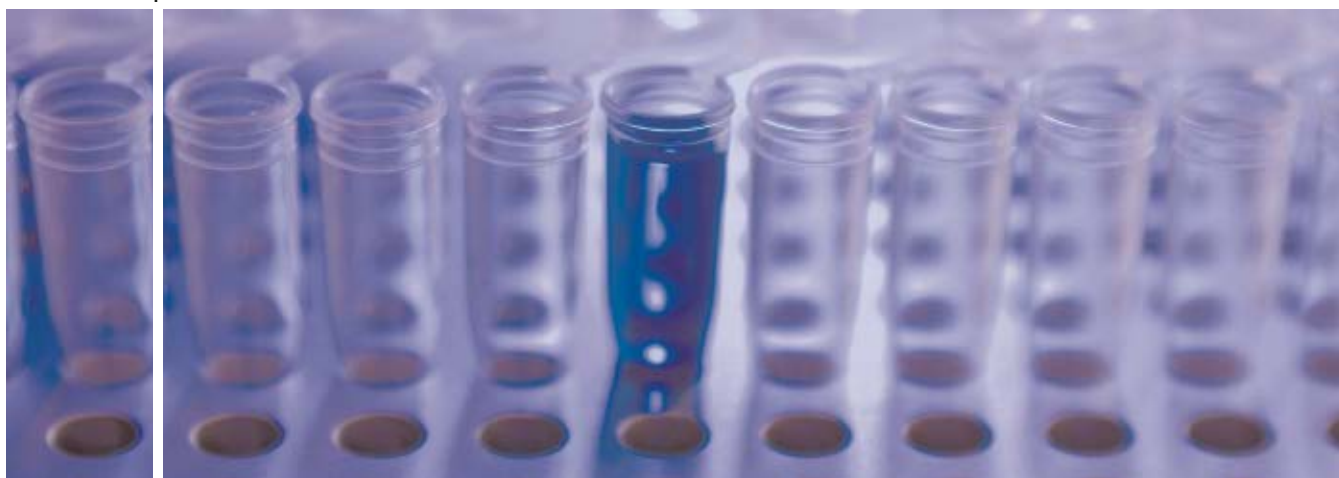
Depending on the channel head, you can pipette single rows of 12 or 24, and columns of 8 or 16. This flexibility allows the Bravo to meet a wide range of applications with a single multi-channel head. The head also senses the attachment of the optional plate-sensing gripper for on-deck plate movement.

More advantages of the Bravo can be found in its open layout platform that is simple to integrate,

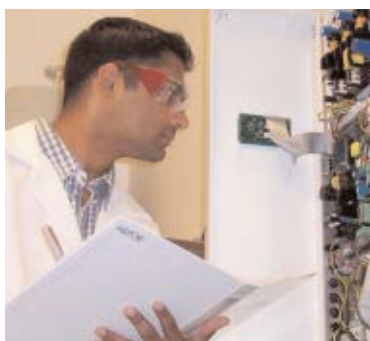
access, and reconfigure. A smooth finish design and no wires or electronics in the deck area allow for easy cleaning and a more sterile environment. Each of the nine deck positions can be configured with heating, cooling, shaking stations, and other accessories as well as for tip boxes, sample microplates and reservoirs.

The Bravo is designed to be used either as a standalone benchtop instrument or as part of a robotic laboratory automation workstation or system. It is also designed to perform inside laminar flow hoods without obstructing the air flow, thereby opening up cell-based plating and assays to an automated liquid handling platform. The accuracy of the Bravo meets or exceeds CVs of 5% and accuracy of $\pm 5\%$ of the desired volume across the practical volume range.

For more information, go to www.velocity11.com or e-mail tanthony@velocity11.com.



product news



VALIDATION SERVICES

Validation and qualification services are now available for the Elix® Clinical water purification systems. Designed to meet Clinical and Laboratory Standards Institutes' guidelines, this validation service allows users to know that their system has been installed and is operating according to pre-determined specifications. Field service engineers can perform the qualifications on-site.

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This data logging/remote control software for the HT-Series II and MEGA high performance evaporator systems enables evaporation data to be stored as part of a GLP protocol and

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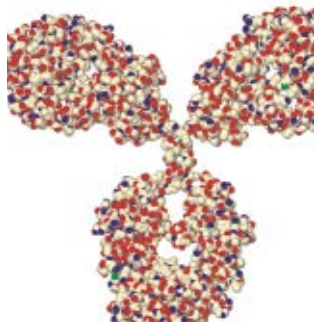
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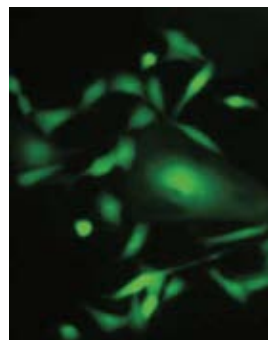


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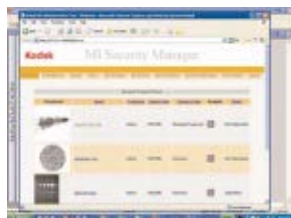
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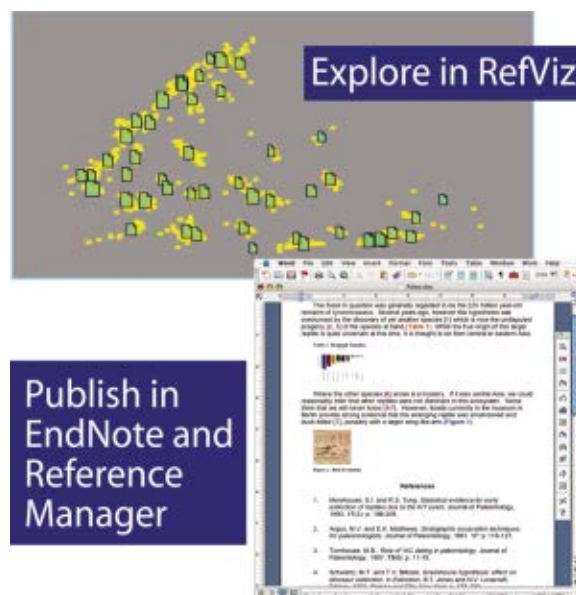
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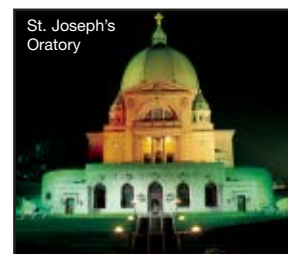
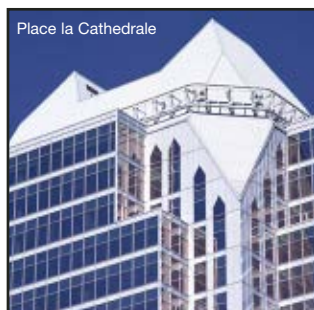
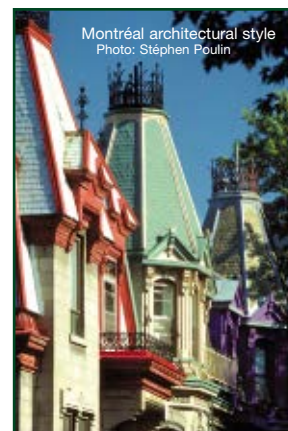
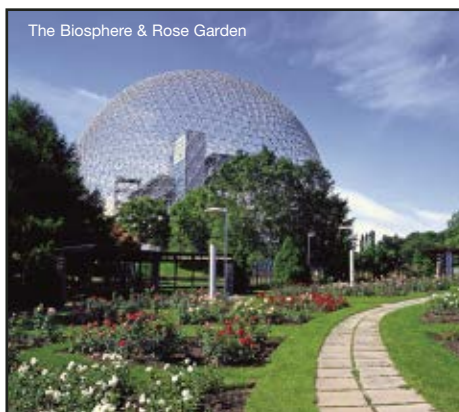
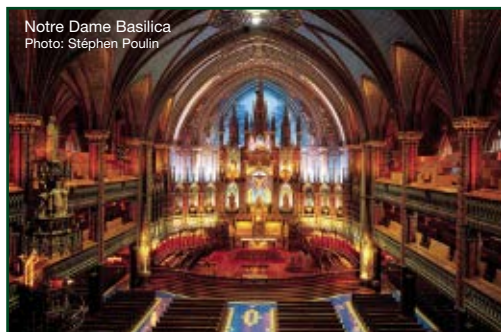
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news notes

ON-DEMAND MOLECULAR MRSA TEST FOR INFECTION SURVEILLANCE PROGRAMS

Cepheid, a broad-based molecular diagnostics company, announced the European release of the Xpert™ MRSA (methicillin-resistant *Staphylococcus aureus*) test for clinical diagnostic use on the GeneXpert® System. The Xpert MRSA test is designed to rapidly detect MRSA in patients for surveillance programs to aid in the reduction of hospital acquired infections (HAIs).

Of critical importance is that each sample is coded for the particular sample preparation protocol, assay type, and patient data so that testing data is highly controlled and monitored. Patients carrying MRSA must be identified and isolated from the general hospital population as quickly as possible. However, the standard culture screening method can take from 48–72 hours and results can be highly variable. During this period, MRSA may be inadvertently spread throughout the hospital. The Xpert MRSA test is intended to detect MRSA directly from a nasal swab specimen and provides results in about seventy-five minutes. The rapid results are expected to allow early identification of potential carriers and to allow the proper precautions to be taken to prevent the spread of disease.

XDX SELECTS FRANEK TECHNOLOGIES TO PROTECT POST-CARDIAC TRANSPLANT RESEARCH

Franek Technologies, Inc has been selected to protect XDx's \$900,000 investment in Applied Biosystems 7900 Sequence Detection Systems used in the company's post-cardiac transplant rejection monitoring research. Based on past experience with brownouts at its research facilities, XDx proactively sought to protect not only its substantial investment in instrumentation, but most importantly, the irreplaceable patient samples for acute cellular rejection in post-cardiac transplant patients.

SEMROCK AWARDED U.S. PATENTS FOR MAXLINE LASER-LINE FILTERS AND STOPLINE NOTCH FILTERS

Semrock, Inc. announced the award of two more U.S. Patents for its thin-film based optical filters. The first patent offers formal protection for the MaxLine series of narrow laser-line filters. The second protects the StopLine series of optical notch filters. These patents will reinforce the company's approach to performance and reliability and join a growing body of the company's patents for its filter products.

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ALFA WASSERMANN PROTEOMIC TECHNOLOGIES ANNOUNCES AGREEMENT WITH PRESSURE BIOSCIENCES

Alfa Wassermann Proteomic Technologies, LLC, (AWPT), a division of Alfa Wassermann Inc, announces an agreement with Pressure BioSciences, Inc. (PBI) to jointly develop sample preparation methodologies that enrich for low abundance proteins and subcellular

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Plasma-based Cleansing Techniques for Biopharmaceutical Research: An Introduction to and Explanation of the Technology

Recently, a device that generates a self-contained, low-temperature, atmospheric plasma for cleaning and sterilizing pipet tips used in automated life science laboratories has been commercialized. This technology uses a dielectric barrier discharge (or gap plasma) that is generated in small, well-like cavities and conforms to a standard SBS footprint. At current the device is passive in that plasma generation is triggered via the insertion of pipet tips, making it easily installed and integrated with most automated liquid handlers. The result is the ionization and molecular breakdown of biological and organic contaminants on both the exterior and interior surfaces of the tips. Unlike traditional solvent-based pipet tip wash methods, plasma as a state of matter (neither a gas nor a liquid) generates no solid or liquid waste and only small amounts of gaseous by-products. Plasma cleaning does not simply dilute contaminants but removes them at a molecular level, allowing laboratories to reuse polypropylene tips and reduce the number of tip boxes needed. This article discusses the mechanism and application behind this cleaning and sterilizing method.

BACKGROUND AND EARLY STUDIES

In 1927, the term plasma was first adopted by Nobel prize winning chemist Irving Langmuir to describe the properties of gases ionized by high voltage to form free electrons and positive ions in a neutral background gas. These ionized gases conduct electricity and are strongly affected by magnetic fields. Although quite common in nature — it is estimated that over 99% of all matter in the known universe is in the form of plasma — lightning and flames are the only two naturally occurring forms on earth (Figure 1). However, through advancements in physics and chemistry as well as the harnessing of alternating currents, the breadth of man-made plasmas continues to widen.

Most of the early studies on man-made plasmas were performed using vessels either under low-pressure or vacuum filled with inert gases providing a ready source of electrons and positive ions. Through the application of a high voltage to metal electrodes within these vessels, electrons are accelerated towards the anode (positive electrode) and conversely, positive ions move toward the cathode (negative electrode). Further, by constantly and simultaneously switching the polarity of each

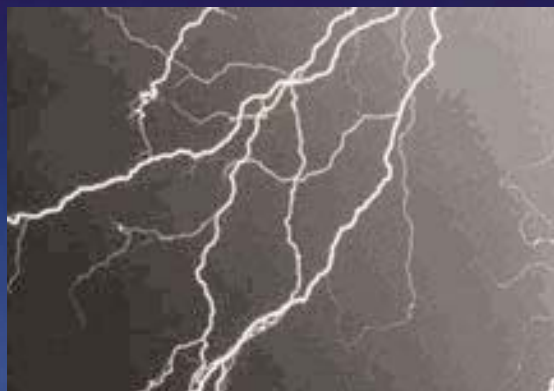


Figure 1. Lightning: a recognizable form of naturally-occurring plasma



Figure 2. Man-made plasma lights up the Las Vegas sky



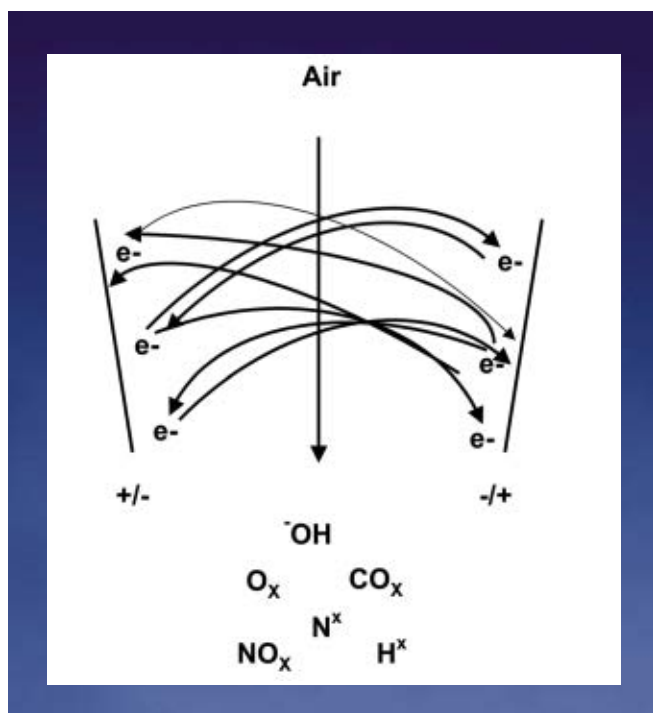


Figure 3. Generation of atmospheric plasma and the subsequent ionization/activation of room air

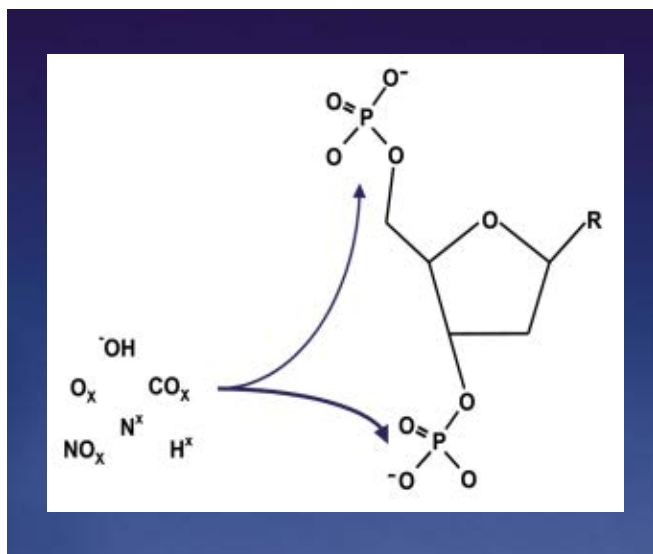


Figure 4. Electron- and ion-driven constituents provide multiple opportunities for oxidation and reduction reactions via electrophilic and nucleophilic attack against deoxyribonucleic acid as an example

electrode, electrons and charged ions continuously move between poles forming what is known as a dielectric barrier discharge. In the presence of a gas, free electrons and activated ions collide with other atoms and molecules present in the gas field resulting in a sustained and steady-state plasma. These experiments ultimately led to the development of neon signs, streetlights, and fluorescent light bulbs (Figure 2).

RECENT DEVELOPMENTS: ATMOSPHERIC-PRESSURE "COLD" PLASMA

Although originally reported by Werner von Siemens in 1857 as a method for generating ozone, the technology remained underdeveloped until modern materials allowed for the production of more effective and efficient dielectric materials. Over the past thirty years advancements in dielectric materials, namely ceramic coated electrodes, provide an insulating layer that allows for stable discharges to occur. The result is the generation of atmospheric-pressure plasmas that form in the absence of inert gases or a vacuum.

The induction of atmospheric plasma begins with the capturing of free electrons to charged dielectric plates. Through changes in polarity, these electrons are forced to mobilize between a set of plates resulting in an electron avalanche. By drawing air in-between these plates and through the electron field, the components of air are bombarded with electrons, causing the fracturing and/or activation of CO_2 , H_2O , O_2 , and N_2 . The result is a "cold" or "non-thermal" plasma field where most of the input energy is channeled to the electron component of the plasma while the resulting ions and neutral components remain at or near room temperature. In addition, highly energetic metastable atomic species are generated. These species have the appropriate number of electrons, but are displaced to higher shells and exhibit high reactivity and some selectivity in their reaction capabilities. The plasma ions and metastable atomic species react rapidly with biologicals and organic solvents to facilitate their breakdown and eventual removal (Figure 3).

In general, there are four prototypical reaction mechanisms that play a role in the removal of material from a contaminated surface. Oxidation (the addition of oxygen to a compound to form an oxide) of the contaminant is the most common mechanism. Reduction of the contaminant (the removal of oxygen) is another possible route. Electron- and ion-induced decomposition processes are two other reaction routes. Common to all processes is the fact that electron-driven dissociation and ionization of the plasma constituents are critical in the formation of reactive radicals and ions. In laymen's terms, the various species and mechanisms of action provide for both electrophilic and nucleophilic attack of organics at the molecular level (Figure 4).

COLD PLASMA IN THE AUTOMATED LABORATORY

At present, most analytical methods used in the biopharmaceutical laboratory require at least one liquid transfer operation, and nearly 100% of those using viable cells or intact organisms call for the use of sterile, disposable pipet tips in order to minimize effects of cross-contamination. Exhaustive solvent-based washing procedures using organic or caustic materials have been the only alternative to the use of disposable pipet tips until the introduction of cold plasma as a safe, reliable, and practical cleaning method.

Since the arc-free dielectric barrier discharge plasma is produced at near room temperature, it draws very little power. The induced plasma field is fully enclosed within a self-cleaning, inert chamber; all by-products of the cleansing process are effectively trapped first by an internal filtration system, and secondly are vented to an external exhaust system.

The unique combination of oxidizing free radicals and metastable atomic species formed within the cold-plasma field promotes the nearly instantaneous conversion, volatilization, and ultimate removal of potential chemical or biological contaminants from pipetting surfaces. These species are readily

pipetted in and out of a pipet when the opening of the pipet is within the plasma field. And because plasma will flow easily into all microscopic surface imperfections and cavities, the process reduces tip-to-tip variations due to random surface properties.

Cold plasma technology offers automated laboratories an opportunity to update and improve their liquid handling processes, eliminating the fear of contamination and carry-over, as well as reduce costs for purchasing, cleaning, handling, and disposing of pipet tips.

(Special thanks to Dr. Kurt H. Becker, Professor and Director, Department of Physics and Engineering Physics, Stevens Institute of Technology)

Cerionx has patented the plasma technology referenced above.

Geoffrey Schwartz (Master of Science and Engineering, Biotechnology) is Product Manager, Drug Discovery at Cerionx, Inc. He can be reached at geoffrey.schwartz@cerionx.com or 856-963-5535.

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Sticky Situations: Six Tips for Managers

Sarah E. Needleman

From CareerJournal.com

When conflicts at work hinge on personal problems, even experienced managers can face a challenge in dealing with them.

No matter how uncomfortable the situation, talking about it with the employee — privately — is usually the first step, experts say. Employees may be unaware of what's wrong, or their behavior may be masking another, undisclosed problem. "If you don't get all sides of the story, you don't get the full picture," says Jay Whitehead, president of Outsourcing Today LLC, a publishing company in Roseland, NJ.

Here are some steps to take when discussing sticky situations — and resolving them:

1. DEFINE THE PROBLEM

Craig Silverman says a midlevel executive at a prior employer began coming to work unshaven, in dirty wrinkled shirts, and smelling. "People didn't want to get into the elevator with him," says Mr. Silverman, who was a vice president at the firm. He approached the problem head-on in a blunt discussion in private. "You need to be clear on exactly what the problem is and what changes need to be made," says Mr. Silverman, now an executive vice president at HireAbility.com LLC, a staffing firm in Salem, NH. The message to the employee: improve his look or he could face possible termination. From the next day on, the executive wore a pressed white shirt and tie, Mr. Silverman says.

2. ASK FOR AN EXPLANATION

Last fall, an employee for software provider CorasWorks Corp., began regularly dialing into conference calls late. Larry Roshfeld, senior vice president at the Reston, VA, software provider, asked him why. He learned that the employee felt overworked and underpaid, Mr. Roshfeld explains. "It became clear that lateness was his way of acting out his frustrations." The employee received help in prioritizing his workload and has since been on time for conference calls, Mr. Roshfeld says.

3. ADD A SPOONFUL OF SUGAR

In 2004, employees at Applied Industrial Technologies, Inc. raised concerns with senior executives about a supervisor's abrasive management style, says Mary Anne Ryan, director, associate relations, career development and staffing at the industrial products company. When she broached the subject with the supervisor, she says, she first talked about his past achievements. Then she described the problem and suggested ways to resolve it. "His tone had veered off the path of being positive and professional," she explains. "He's now back on track. That's the reward we get for going through these difficult conversations."

4. SHOW COMPASSION

A manager's breath was so foul-smelling that executives at the company where she worked were uncomfortable in her presence, says Karen Otazo, then a manager of training and development at the firm. "Things like this are the hardest of all talks to have, because it becomes personal very quickly," says Dr. Otazo, now an independent executive coach who has offices in Houston and London. "You want to be sensitive to their feelings." Dr. Otazo says she urged the manager to gargle with mouthwash twice a day and chew on mints, and her advice was heeded.

5. TAKE QUICK ACTION

Mr. Whitehead says that at his former firm, an employee once accidentally copied an investor on an email that insulted the unintended recipient. Mr. Whitehead immediately summoned the employee to his office to address the problem before the investor had a chance to react. The employee offered to quit, he says. "I said, 'No, instead you're going to do something much harder. You're going to apologize.'" The employee did and "all was forgiven," says Mr. Whitehead.

6. GIVE A CLEAR WARNING

An employee at Panda Software once mouthed off to a manager within earshot of several other employees at an office in Glendale, CA. Brenda Christensen, a director at the Spain-based software provider, says she met with the employee privately and told her that a repeat performance could lead to termination. She also suggested ways to relieve tension, such as taking a break and going for a walk. The problem never resurfaced, she says.

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DEVELOPING STAFF MEMBERS — a Lab Manager's Responsibility

Whether you're a bench chemist supervising one technician or a department manager supervising fifty people, you have a responsibility to develop your staff's abilities. This can increase their contributions to your employer's goals as well as their own job satisfaction and career potential. Developing your staff's potential is an obligation you have to both your staff members and your employer.

Chances are your staff members are capable of more than you are asking of them. How can you help them tap these hidden springs of ability and creativity?

LEARN YOUR STAFF'S CAPABILITIES, LIKES, AND DISLIKES

To begin, you have to understand your staff's capabilities, learn what they like most about their job and what they like least. Learn their ambitions and career plans. This means using a resource that managers have little of — time. Be creative in finding this time. Visiting labs and offices at the beginning of the workday and going to lunch with staff members are two ways to do this. An occasional social event at your home is also helpful.

However, you have to go deeper than casual conversation. In private conversations you can learn more about your staff member's on-the-job likes and dislikes and where they would like to go next in their careers. Find out their professional development plans and provide appropriate advice and encouragement. Ask them how they believe you can help them achieve their professional goals. These conversations should occur more often than just during annual performance reviews. You can often learn what your staff members like most and least about their jobs observing them in meetings and other group situations. Observe how your staff members interact with each other and who takes leadership roles based assignments, job performance, and personal initiative.

What you learn can help you and each staff member prepare a development plan. This should be an integral part of the employee's plan and goals for the next performance review period. This plan should be consistent with the employee's interests and abilities. It should not be a projection of your own personal agenda. For example, as a young

chemist new to working in industry, it took me a while to understand that laboratory technicians were not like graduate students and had different motivations and ambitions. Most were not interested in the motivation and goals I first offered: opportunities to publish papers and attend professional conferences.

TURNING PLANS INTO ACTIONS

The best development plans consist of a series of steps. For example, a laboratory technician on our pulp and paper team was interested in a sales career. Through our team he had the opportunity to first participate in paper mill trials of new chemical products. With increasing experience, he became the person on the site running the trial and making decisions without having to obtain the approval of others. Through my activities in TAPPI (Technical Association of the Pulp & Paper Industry), I was able to provide him with the opportunity to chair a panel discussion that included an active question and answer session. The experience provided him an opportunity to increase his industry exposure and convince himself and others that he could "perform" in front of a large group of people. He soon became a sales representative on this team.

Coaching can include encouraging staff members to take courses and participate in activities that enhance their abilities. For example, many chemical professionals have to present information to others as part of their jobs. I often advise co-workers to participate in Toastmasters International to systematically improve their oral presentation skills. This can enhance the careers of bench chemists, staff engineers, sales personnel, managers and technicians.

MOTIVATION

The best plans won't change anything if the employee isn't motivated to change and improve. You can't really motivate another person. What you can do is create an environment that enables people to motivate themselves. Part of creating this environment is to be sure that the employee's development plan is truly consistent with his/her goals and abilities. People are motivated to fulfill themselves and their basic values.

You may have to create this environment in the context of an organizational environment that

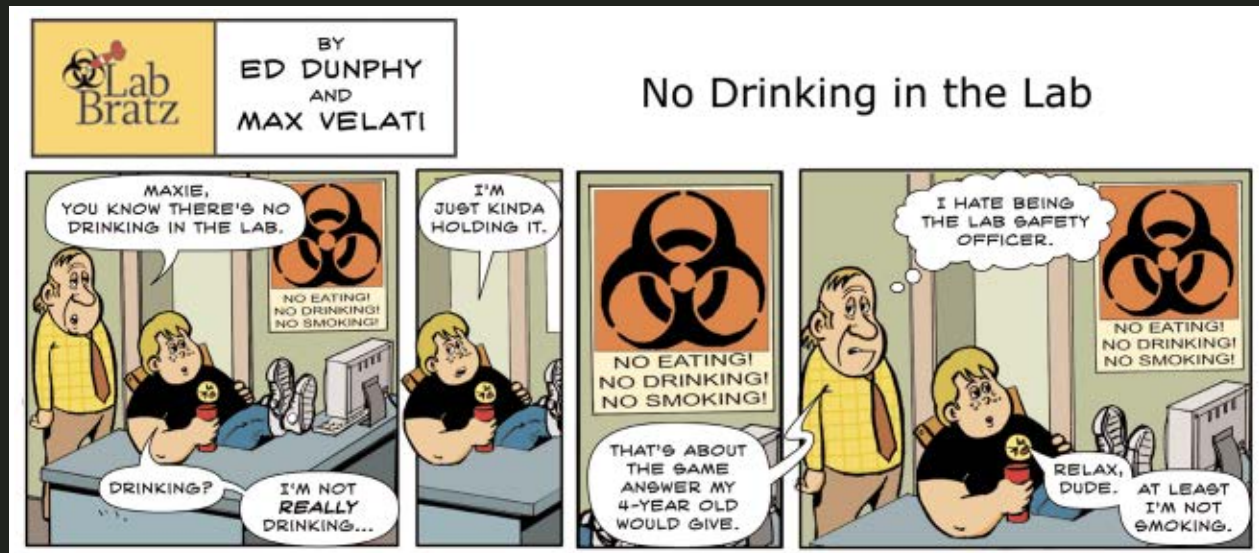


inhibits self-motivation. However, even within this context, there is much you can do to promote self-motivation by establishing working relationships characterized by trust and appreciation.

Today many professionals are frustrated and think to themselves, "I know I was meant for more than this." But they may lack the knowledge they need to equip themselves to be accomplish more. They need help in identify-

ing opportunities to develop and new skills. It is the manager's job to provide this coaching as well as encouragement and opportunities to their staff members.

Dr. Borchardt is a consultant and technical writer. The author of the book "Career Management for Scientists and Engineers," he writes often on career-related subjects. He can be reached at jkborchardt@hotmail.com.



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J.E.J. (Ned) Gravel

Manager, Quality and Training

Canadian Association for Environmental Analytical Laboratories (CAEAL)

First, the good news from Ned Gravel — lab leaders can inspire their dispirited troops to exceed expectations under dire circumstances with room to spare, even eliminating 95% of team grumbling. Now the bad news — few labs get near that lucky. Gravel posits a lab universe that abounds in managers bereft of the right leadership stuff. With the surety of a man possessing a “profound understanding of the selling of ideas and what is needed to motivate others,” he’s on a mission to change leadership orthodoxy, one lab at a time, criss-crossing Canada’s provinces spreading the gospel of “Ned’s Rules of Engagement.”

Forget about the super-sized oeuvre of barnstorming business gurus and talking heads selling leadership formulas; 99% use “leadership” and “management” interchangeably, or promote some astray top-down system. Only a few like Peter Drucker and Warren Buffet (who delegates “almost to the point of abdication”) really get it, says Gravel.

Under Gravel’s tutelage, leaders become superior communicators who can “sell” a collective vision to staff, and develop the capacity to then trust them to implement it. Good leaders create organic organizations with the ebb and flow of a symphony; the analogy of the conductor as leader and staff as members of the orchestra permeates Drucker’s commentaries.

“It fits,” said Gravel, 53. “The conductor ‘motivates’ orchestral members to accept their ‘vision’ of how the piece should sound. This is leadership, not management. When each member of the orchestra has accepted their piece of the overall vision, and what they need to do individually to bring it to fruition, the conductor can be replaced by almost anyone. The piece will be good.”

Management is a science, readily taught. Leadership is an art, and Gravel’s precepts require adherence to uncommon beliefs and skills. Good leadership, insists Gravel, must be bestowed or earned — a far cry from the prevailing leadership ethos of entitlement and power.

Consider Ned’s Rule No. 5: The first goal of a true leader is to become dispensable. Or Rule No. 12: Authority is derived from the organization or person that delegates the responsibility of leadership.

As Manager for Quality and Training of the Canadian Association for Environmental Analytical Laboratories (CAEAL), Gravel is in the standardization business. CAEAL accredits member clients, and works in support of national trade policies.

His ideas on leadership and communication were formed in the Canadian military, or, as his resume states, “twenty-two years commanding soldiers in the delivery of complex solutions under hazardous conditions.”

After leaving the military in 1992, Gravel became operations manager for an electronics testing lab until “the worst day of my career. I gave my boss 20 seconds notice. I could not convince him management by terror was wrong.” Ned’s Rules emerged from his disillusionment with corporate culture and conviction that leadership training works.

Although he quit the soldier’s life nearly 15 years ago to raise a family, military jargon still infuses his conversation. For emphasis, Gravel slows his cadence to enunciate “small unit morale” — the concept that military success only occurs after all individual desire is supplanted by a collective group identity.

Ned’s Rule No. 10: Success is the moment when the last person in an organization adopts their portion of the organizational vision, the main proponent of which is the leader.

“Motivation is really about getting people to believe in themselves again, and what they are doing. That is the idea being sold to them — that they are worth the effort. And that is done one person at a time.”

Leadership is one problem; quality is another. From his perch in CAEAL pushing best quality practices, Gravel’s critical eye wanders over both academia and industry.

“Academia is driven by the same thing that drives its researchers — primarily recognition. Quality is seen as an imposition (with the exception of pharmaceuticals). Industry is focused on surviving, and doesn’t always accept best practice as contributing to the bottom line.”

Where are science and research headed? “We’ll see the most advances where the two drivers — the desire for profit and results — meet, such as biomedical research giving Baby Boomers eternal youth, or when environmentally friendly transportation choices meet profitability regarding our collective desire to reduce greenhouse emissions.”

Francis Key Kidder started out as a journalist before moving on to politics and government relations, where he still keeps his hand in writing. He may be reached at 410-828-6529; info@labmgr.com.



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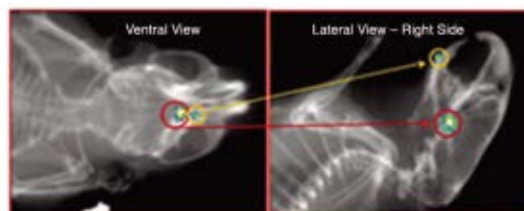
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Ventral position imaging shows two optical signal generating metastatic lesions located in the cranial region

Subsequent lateral position imaging clearly separates the two lesions to specific jaw and skull locations

Images Courtesy Dr. Bohumil Bednar, Merck Co., Inc.

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