In the EC Literature

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♦ The Electrochemistry of $C_{60}Ph_5Cl$: A Very Special Fullerene Derivative

P.R. Birkett, R. Taylor, N.K. Wachter, M. Carano, F. Paolucci, S. Roffia, and F. Zerbetto, J. Am. Chem. Soc. 122 (2000) 4209-4212.

The chemistry and electrochemistry of fullerenes and their derivatives continue to attract interest. In this study, the redox behavior of $C_{60}Ph_5Cl$ was examined using cyclic voltammetry. Since the voltammograms were not simple, their interpretation required the use of the DigiSim® simulation software. Oxidation of $C_{60}Ph_5Cl$ showed two reversible oxidations. However, three reductions were observed, with two associated oxidations on the reverse oxidation scan. The first reduction was shown to involve two electrons, and was attributed to the homolytic cleavage of the C-Cl bond following the addition of one electron (the second electron was then added to the Cl radical to generate the Cl^- anion). The two subsequent reductions were attributed to the $C_{60}Ph_5^-$ anion. This anion was also oxidized on the reverse scan. The radical generated by this oxidation reacted with the Cl radical generated by the oxidation of the Cl^- anion (the second oxidation on the reverse scan) to form the initial fullerene derivative.

♦ Reagentless Biosensors Based on Self-Deposited Redox Polyelectrolyte-oxidoreductases Architectures

A. Narváez, G. Suárez, I.C. Popescu, I. Katakis, and E. Domínguez, Biosens. Bioelectron. 15 (2000) 43-52.

This study describes a method for building biosensors based on the mediated electron transfer between the surface of an electrode and an enzyme. This method takes advantage of electrostatic interactions between components of the biosensor to produce a self-deposited multilayer structure. The first monolayer consisted of a thiol at one end (which binds strongly to the surface of a gold electrode) with an anionic group at the other end. The next layer consisted of a cationic osmium redox polymer, which interacted electrostatically with the first monolayer. This redox polymer was used to mediate the electron transfer between the electrode surface and the enyzme layer, which was deposited on top of the redox polymer. Each of the different configurations was characterized by cyclic voltammetry using a CV-50W. It was shown that this architecture worked well for the three enzyme systems studied, which were fructose dehydrogenase, horseradish peroxidase, and a bienzyme system consisting of alcohol oxidase and horseradish peroxidase (the alcohol oxidase reacts with methanol to generate hydrogen peroxide, which is detected using the peroxidase layer).

♦ Electrochemical Study of the Redox Dyes Nile Blue and Toluidine Blue Adsorbed on Graphite and Zirconium Modified Graphite

A. Malinauskas, T. Ruzgas, and L. Gorton, J. Electroanal. Chem. 484 (2000) 55-63.

NADH is a cofactor for many dehydrogenase enzymes. Hence, the electrochemical behavior of NADH is of interest as it relates to the use of such dehydrogenase enzymes as part of an enzyme-based biosensor. However, direct oxidation of NADH at an electrode surface requires a large overpotential, and hence mediators are used. Many mediators have been investigated, and it has been shown that the efficiency of the electrocatalytic oxidation of NADH depends on the rate of heterogeneous electron transfer between the electrode and the mediator and on the rate of the electron transfer reaction between the mediator and NADH, which in turn depends upon the redox potential of the mediator. In this study, the electrochemical behavior of two mediators (Nile Blue and Toluidine Blue) was studied by cyclic voltammetry using a BAS 100B/W. The two mediators were adsorbed at a graphite electrode and at a graphite electrode modified with zirconium phosphate (which has been shown to modulate the redox potential of similar mediators). The current response for cyclic voltammetry was complicated by the relatively slow charge transfer between the adsorbed layers. However, the rate of electron transfer between the electrode and the adsorbed species could be extracted by appropriate data manipulation, and was found to be fast.

♦ Detection of Chemically Induced DNA Damage by Derivative Square Wave Voltammetry

J. Mbindyo, L. Zhous, Z. Zhe, J.D. Stuart, and J.F. Rusling, Anal. Chem. 72 (2000) 2059-2065.

It has been well established that the guanine and adenine moeities in polynucleotides and single-stranded DNA are available for oxidation, but are inaccessible in double-stranded DNA. Therefore, the basis of this study was that the formation of single-stranded DNA from double-stranded DNA by denaturation could be followed electrochemically by an increase in the oxidation current. In order to test this hypothesis, double-stranded DNA was immobilized on the surface of a pyrolytic graphite electrode either as a DNA/ionomer film or covalently bound, and these electrodes were incubated with styrene oxide as the model denaturing agent. The oxidation current was monitored by derivative square wave voltammetry using a BAS 100B/W (the use of the derivative enhanced the signal-to-background ratio). The incubation with styrene oxide did indeed lead to an increase in the oxidation current, and it was also found that more reproducible results were obtained for

the ionomer/DNA film than for the covalently bound DNA.

♦ Amperometric Biosensor for Glutathione Based on Osmium-Polyvinylpyridine Gel Polymer and Glutathione Sulfhydryl Oxidase

L. Mao and K. Yamamoto, Electroanalysis 12 (2000) 577-582.

The tri-peptide glutathione is an important physiological species, both in its oxidized (GSSG) and reduced (GSH) form. There is a well established method for the simultaneous electrochemical detection of both these molecules, which uses a dual series electrode. In this study, another well established technology (a "wired" enzyme electrode) was used for their simultaneous detection. Both GSSG and GSH are oxidized by the oxidoreductase enzyme glutathione sulfhydryl oxidase, with the concomittant production of hydrogen peroxide. A bienzyme biosensor can therefore be constructed similar to that reported for other oxidoreductase enzymes, in which the generated hydrogen peroxide can be detected using horseradish peroxidase that is "wired" to the electrode surface via an osmium-based redox polymer (i.e., the electron transfer is mediated). This biosensor was characterized by cyclic voltammetry using a BAS 100B/W, and by amperometry and flow injection analysis using a BAS LC-4C detector. This enzyme showed good sensitivity, a low detection limit, and good reproducibility However, the performance of this biosensor was not compared with that of the established dual series electrode.

♦ Enzyme Inhibition Assays with an Amperometric Glucose Biosensor Based on a Thiolate Self-Assembled Monolayer

P.W. Alexander and G.A. Rechnitz, Electroanalysis 12 (2000) 343-350.

Biosensors based on the catalytic oxidation of glucose by glucose oxidase have been extensively developed for the determination of glucose. However, in this study, a glucose oxidase-based biosensor was developed for determination of species that inhibit the electrocatalytic activity of the biosensor. The crucial component of this biosensor was 2-aminoethanethiol, which had two functions. The thiol group resulted in the formation of a self-assembled monolayer on the surface of a gold electrode, which formed the foundation of the biosensor. This molecule also acted as the mediator for transport electrons from the active site of the glucose oxidase and the electrode surface. The glucose oxidase was added to the self-assembled aminothiol layer, and the structure was completed by a polyvinylpyridine membrane layer. The current response of this biosensor was characterized by cyclic voltammetry and amperometry using a BAS 100B/W, and the biosensor was shown to be stable for about a week, which limits its practical usefulness. The inhibition by mercury(II) ions was shown to be reversible, and it was proposed that this inhibition was due to the reaction of mercury(II) ions with the thiol mediator rather than with the enzyme; that is, the inhibition of the enzyme reaction is indirect.

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In the LC Literature

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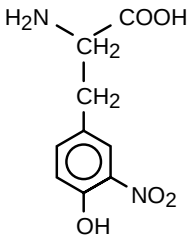
♦ Determination of 3-Nitrotyrosine by High-Presure Liquid Chromatography with a Dual-Mode Electrochemical Detector

R.S. Sodum, S.A. Akerkar and E.S. Fiala, Anal. Biochem. 280 (2000) 278-285.



3-Nitrotyrosine (3-NT) is frequently used as a marker for the presence of reactive nitrogen oxides, and thus of various degenerative diseases. The reactive nitrogen oxides combine with superoxide to produce peroxynitrite, which reacts with tyrosine to form several compounds including 3-NT.

Rats were treated by injection of tetranitromethane to promote the formation of reactive nitrogen species. Plasma samples were hydrolyzed to amino acids and their 3-NT content determined by LCEC. A dual BAS LC-4B amperometric detector was used in the analysis. The 3-NT was reduced upstream at an Au/Hg amalgam electrode set to -0.9 V (vs. Ag/AgCl), then detected at a downstream glassy carbon electrode set to +0.6 V. Detection limits were reported to be in the femtomole range.

♦ Comparison of Detection Methods for Liquid Chromatographic Determination of 3-Nitro-L-Tyrosine

H. Liu, T. Huang, C.B. Kissinger and P.T. Kissinger, J. Chromatogr. B 713 (1998) 289-295.

This paper compares five methods of LC detection for 3-NT: UV detection, oxidation, reduction, redox detection and oxidation of photolysis products.

UV detection at 278 nm proved to be the least sensitive method. The results were linear, but detection limit was only 670 femtomoles.

Oxidative detection at a potential of +1100 mV (vs. Ag/AgCl) on

a glassy carbon electrode was not much better, with a detection limit of 400 femtomoles. With such a high potential, noise and interfering peaks were a problem.

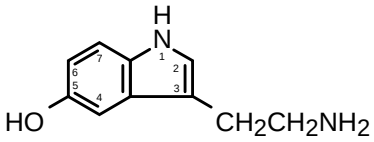
Reductive detection (-750 mV on a glassy carbon electrode) had a detection limit of 42 femtomoles, but the necessity for rigorous deoxygenation of both the sample and the mobile phase makes this a difficult procedure.

Redox detection (-750 mV upstream, +600 mV downstream, on a glassy carbon electrode) resulted in good linearity and a 42 femtomole detection limit.

Finally, photolysis with a TiO_2 catalyzed photoreactor proved to be a highly selective and sensitive detection method. Photolysis by UV converts 3-NT to DOPA, which is easily oxidized at +850 mV, providing a detection limit of 10 femtomoles.

♦ Determination of Plasma Serotonin and 5-Hydroxyindoleacetic Acid in Healthy Subjects and Cancer Patients

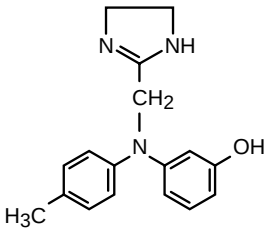
M.S. Lee, F.C. Cheng, H.Z. Yeh, T.Y. Liou and J.H. Liu, Clinical Chemistry 46 (2000) 422-423.



Plasma levels of serotonin (5-HT) and 5-HIAA were determined in normal patients and in patients with liver and intestinal cancers. Plasma samples were prepared by ultrafiltration, then injected onto a microbore liquid chromatograph using a C_{18} reverse-phase microbore column (100 x 1 mm). Analytes were detected with a BAS LC-4C amperometric detector set at +0.75 V (vs. Ag/AgCl). Basal levels of 5-HT and 5-HIAA in healthy patients were 0.6 and 1.9 ug/L, respectively. These values rose to between 4.5 and 7.0 (5-HT) and 7.8 and 10.7 (5-HIAA) for cancer patients. In those patients receiving surgery for intestinal cancer, 5-HT levels dropped significantly, while 5-HIAA levels dropped only slightly.

♦ An Improved Assay by HPLC with Amperometric Detection for the Determination of Phentolamine in Plasma

J. Perez-Urizar, P. Aguirre-Banuelos, G. Castaneda-Hernandez and F.J. Flores-Murrieta, J. Liq. Chrom. & Rel. Technol. 23 (2000) 557-564.

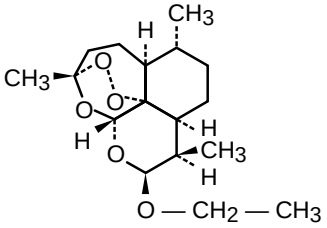


Phentolamine is an alpha-adrenergic antagonist used for the treatment of hypertension and pheochromocytoma. A new use may be the treatment of erectile dysfunction, but current analytical procedures aren't sufficiently sensitive for the low doses involved.

Plasma samples (1 mL) were alkalinized with sodium carbonate, extracted with diethyl ether, then back-extracted into 0.1 N HCl, which was injected. Separation occurred on a C_8 column. The analyte was detected amperometrically using a BAS LC-4C detector with a glassy carbon electrode set to 1 V (vs. Ag/AgCl). Results were linear between 1 and 30 ng/mL, and recovery was 80-90%. The detection limit was 0.2 ng/mL.

♦ Arteether Toxicokinetics and Pharmacokinetics in Rats after 25 mg/kg/day Single and Multiple Doses

Q.G. Li, R.P. Brueckner, J.O. Peggins, K.M. Trotman and T.G. Brewer, European J. Drug Metabab. & Pharmacokinet. 24 (1999) 213-223.



Arteether (ARTE) is one of a series of related antimalarial compounds derived from the medicinal plant qinghauso. Although toxicity in humans is rare, administration in various animal models produces anorexia to the point of death. This paper examines the phenomenon in rats, using measures of food intake and outcomes. Pharmacokinetics was studied by determining ARTE in plasma, using a BAS-200 chromatograph in the reductive mode (-1 V vs. Ag/AgCl). Treated rats showed a decrease of about 50% in food and water consumption. Pharmacokinetic parameters changed with duration of dosing, with area under the curve increasing 5-fold, and clearance doubling, from day 1 to day 7.

In the MD Literature

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♦ The Potent, Selective mGlu2/3 Receptor Agonist LY379268 Increases Extracellular Levels of Dopamine, 3,4-Dihydroxyphenylacetic Acid, Homovanillic Acid, & 5-Hydroxyindole-3-acetic Acid in the Medial Prefrontal Cortex of the Freely Moving Rat

J. Cartmell, K.W. Perry, C.R. Salhoff, J.A. Monn, and D.D. Schoepp. J. of Neuroscience, 75: 1147-1154, 2000.

The Eli Lilly compound LY379268 has previously been shown to reverse PCP-induced schizophrenic-like behavioral changes similar to changes induced by Clozapine, an atypical antipsychotic. From such observations, this Lilly team speculated that perhaps the reduction in certain behaviors by mGlu2/3 agonists might arise via changes in dopaminergic activity. To test this, they compared the effect of LY379268 and clozapine on extracellular dopamine in the medial prefrontal cortex (mPFC).

Using 4 mm BAS microdialysis probes and a BAS electrochemical detector, Cartmell and colleagues sampled DA, DOPAC, HVA and 5-HIAA from the mPFC of rats treated with either clozapine or LY379268. They found that whereas clozapine increased extracellular DA, DOPAC and HVA, LY379268 increased these, and also 5-HIAA. This was a specific effect blocked with the mGlu2/3 antagonist LY341495. The authors summarize their work by noting that mGlu2/3 agonists activate dopaminergic and serotonergic systems in ways similar to those exhibited by clozapine and other atypical antipsychotics.

[In this same J. of Neurochemistry volume, there is a comprehensive review entitled "Regulation of Neurotransmitter Release by Metabotropic Glutamate Receptors" which was written by Cartmell and Schoepp of this group. It includes a thorough discussion of the impact of mGlu receptors upon a variety of neurotransmitter systems, and a two-page table comparing the effect of various mGlu ligands on those systems, as determined by microdialysis and numerous other techniques. J.G.]

♦ Microdialysis Sampling Coupled to HPLC for Transdermal Delivery Study of Ondansetron Hydrochloride in Rats

P. Ding, H. Xu, G. Wei, and J. Zheng. Biomedical Chromatography, 14:141-143, 2000.

Transdermal delivery of therapeutic agents via "patches", such as patches containing nicotine for example, are becoming increasingly popular. Conventionally, the rate of such transdermal delivery is studied in vitro via a section of excised skin, rather than in vivo. As is often the case with in vitro approaches, such in vitro studies may not fully correlate with the situation in vivo. Concerned about this and the rate of drug delivery, Ding and colleagues examined the delivery of ondansetron HCl via transdermal microdialysis probes.

The investigators first bonded a "cell" into which was placed a 0.15% solution of ondansetron, a 5HT-3 receptor antagonist, to the skin of rats. The ondansetron solution also contained varying concentrations (0% control, 2%, and 5%) of oleic acid, a widely used penetration enhancer. They then inserted a microdialysis probe transdermally so the 10 mm membrane was centered under the drug-containing cell. This arrangement allowed them to transdermally sample ondansetron which migrated through the skin of the anesthetized rat for the next eight hours. In vivo recoveries of ondansetron were determined during the dialysis period by the no-net-flux method. No-net-flux determined their in vivo recovery of ondansetron to be 32.5%. The addition of oleic acid did indeed facilitate dermal penetration of the ondansetron, changing the rate of ondansetron penetration from 0.001 to 0.030 and 0.058 mg/hr for control, 2% and 5% concentrations of olenic acid respectively.

The authors describe the advantages of in vivo transdermal microdialysis over in vitro studies as including sampling with minimal tissue trauma; HPLC sample analysis without the need for sample cleanup; target analytes being immediately partitioned from potentially degradative enzymes once through the microdialysis membrane; and the use of significantly fewer animals needed to perform such a study which arises from using the same animal(s) for the continuous study of dermal drug flux in real time, as compared to using multiple different animals at each in vitro time point.

[Transdermal studies such as this are perfect applications for BAS' Linear Microdialysis Probe J.G.]

♦ On-Line Microdialysis-Ion Chromatography Determination of Inorganic Anions in Olive-Oil Mill Wastewater

P.L. Buldini, A. Mevoli, A. Quirini, Journal of Chromatography A, 882: 321-328, 2000.

In the Mediterranean area, waste water from the extraction of olives is a problem. The amount of olive-oil-mill wastewater is about 40% (w/w) of the pressed olives themselves. The waste contaminants may include various ions, sugars, proteins, polyols, fats, gums, glucosides and polyphenols. Unfortunately, the polyphenols act as an antimicrobial which inhibits prompt decomposition of the waste.

For environmental reasons, various components of the waste water must be identified and quantified. However, due to the complexity of the sample matrix, this can be tedious and complicated. Attempting to

simplify the sample clean-up process, Buldini and colleagues utilized microdialysis to separate inorganic anions for analysis. The function of the dialyzer used sounds similar to that of a BAS Rapid Desalting Dialyzer (RDD). The RDD consists of a dialysis membrane inside a tube through which dialyzing water or buffer might flow. It is usually used for dialyzing the unwanted salts out of samples within the membrane, with the waste salts migrating into the countercurrent dialysis flow stream. In this case however, it was the salts that were wanted, so the RDD could be plumbed and the wastewater sample would be the flowing stream, while the salts dialyzed into the membrane and are then analyzed.

Miscellany

♦ Fifth International Conference on Miniaturized Chemical and Biochemical Analysis Systems

Monterey Marriott Hotel and
Monterey Conference Center
Monterey, California
October 21-25, 2001
Abstract Submissions Due:
Friday, April 6, 2001

µTAS 2001 Symposium Chair: J. Michael Ramsey, Oak Ridge National Laboratory, Oak Ridge, TN. *Symposium Website:* For program updates, on-line registration, abstract submission, information on sponsors and to browse abstracts, please visit *www.casss.org/tas2001*. If you have any special needs or request additional information, please contact:
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♦ New Directions in Electroanalysis

University of Salford, UK
April 22-25, 2001

An international symposium on electroanalytical chemistry and its applications, organised by the Royal Society of Chemistry's Electroanalytical Group. See the webpage *www.salford.ac.uk/chemist/NDEA.htm* for details, or contact Dr. Damien Arrigan at:
d.w.m.arrigan@salford.ac.uk, or
fax +44-161-2955111. Deadline for submission of abstracts (one page) is November 1, 2000.

♦ The 9th International Conference on In Vivo Methods: Monitoring Molecules in Neuroscience

University College Dublin, Ireland.
June 16- 20, 2001

First Call

This 9th International Conference on In Vivo Methods will be held on the Belfield Campus, University College Dublin (UCD), Ireland and will focus on the latest advances and review established methods and techniques in monitoring molecules in neuroscience. The meeting is restricted to 400 participants.

Plenary Symposia

- Advances in Monitoring
- Synaptic v's Non-Synaptic Transmission
- Neurotransmission and Behaviour

Parallel Symposia

- Microdialysis
- Voltammetry and Biosensors
- Monoamines, Acetylcholine, 2nd Messengers
- Amino acids, Neuropeptides
- Novel and Combined Approaches
- Drug Action and Development

Local Organising Committee:
Dr. William T. O'Connor, UCD; Dr. John Lowry, NUI, Maynooth; Dr. John J. O'Connor, UCD; Prof. Robert O'Neill, UCD.

Registration fees and deadlines:*
Before March 1: £380 IR
After March 1: £480 IR
Accommodation*:
£128 IR (4 nights)
**Limited student bursaries available*

The deadline for abstract submission is January 15, 2001. Publishers, manufacturers of instruments, equipment, software and literature are also invited to exhibit.

For registration form, student bursary application and vendor information please contact:
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♦ FACULTY POSITION in Analytical Chemistry

The University of Kansas Department of Chemistry invites applications for a tenure-track faculty position at the assistant or associate professor level that will be available beginning August 18, 2001. A Ph.D. in analytical chemistry or a closely-related field is required. Preference will be given to candidates with expertise in mass spectrometry, especially involving applications to bioanalytical problems or in an allied area that complements current research in analytical chemistry at the University of Kansas.

Duties will include the establishment of a vigorous research program and teaching at the graduate and undergraduate levels. Salary will be commensurate with qualifi-

cations and experience. Applicants should provide letter of interest, resume, summary of research plans, description of teaching expertise and interests, and three letters of recommendation submitted to: Dr. Cynthia Larive, Chair, Analytical Chemistry Search Committee, Dept. of Chemistry, University of Kansas, Lawrence, KS 66045 (clarive@ukans.edu), (785)-864-4269. Review of applications will begin October 1, 2000 and will continue until the position is filled. The University of Kansas is an Equal Opportunity/Affirmative Action Employer.

♦ Indiana Instrumentation Institute (III)

Schneider
September 11, 2000

Summary

A new Center of Excellence, the Indiana Instrumentation Institute (III), has been established to promote research and commercialization activities in scientific instrumentation. Participants are Purdue University, Indiana University and various industries in the State of Indiana. The aims include construction of next-generation instruments and increased commercial activity in an area of national academic leadership (the Analytical Chemistry programs at Purdue and IU are both ranked among the top three in the US).

The new Institute should allow resources to be deployed to maximize the competitiveness of this region in an area that underlies much of today's technology. Accelerated transfer of advanced instrumentation technology from the university laboratory to the Indiana economy is expected, in part by assisting graduate students in founding start-up companies based on research work done at Purdue and IU.

These objectives will be facilitated by (i) close industrial partnerships; (ii) a program of research into mass spectrometry, optical imaging and other areas of scientific instrumentation; (III) creation of new specialized facilities and infrastructure needed for development of new types of instruments; and (iv) incentives which draw a larger fraction of our research students into careers in new Indiana high-tech companies.

21st Century Fund

The III has received funding from the Indiana 21st Century Fund which includes Eli Lilly & Co. and other corporate partners SpectraCode, Inc., Environmental Health Laboratories, pHotosomes, Inc., Crane Division, Naval Surface Warfare Center and Endocyte, Inc.

Peter Kissinger, CEO of Bioanalytical Systems (BAS), one of the industrial partners, said, "It is fabulous to see this come to fruition. For 30 years or more, Indiana has been at the forefront of technical developments in this field. While we compete in athletics, we are friends in our laboratories advancing measurement science. Many of the key tools of modern drug development (e.g. liquid chromatography and mass spectrometry) evolved out of basic work at IU and Purdue since 1970. Both schools are still setting the pace. The III brings together those needing data with those innovating how to obtain it—faster, cheaper, better. The ivory towers are now open to the commercial world. Both sides acknowledge they need each other far more than ever."

Rationale

Analytical chemistry and instrumentation is a key to biotechnology, to pharmaceutical manufacturing and to many other components of modern industry. Partnerships among private industry, research universities and government agencies are likely to be especially effective drivers for economic growth. The superior national reputation of both Indiana University and Purdue University in this area makes an IU/Purdue/industry partnership highly desirable. The state of Indiana has recognized this potential, and the 21st Century-funded Indiana Instrumentation Institute (III) provides an opportunity for strong private/public partnerships in this key area. Direct industrial benefits will include rapid introduction of new technology, raising the level of science in a company and allowing rapid exploration of key new areas such as proteomics.

A strong program committed to facilitating company start-ups, novel as well as traditional methods of instruction in the key technologies, and joint industry-industry as well as academic-industry interactions, will create an infrastructure in analytical instrumentation which could focus industrial growth in Indiana. The III provides the infrastructure needed to disseminate problems and link them to solutions, a framework that facilitates these interactions. Money needs to be linked to the interactions. The proposed structure is based on a high level of accountability and competitiveness, especially in interactions with university faculty where projects will need to be continuously justified and will be largely industry-driven.

Projects

Initial III projects include microchemical imaging technology based on fiber-bundle image compression and spectral image classification combined with selective chemical tagging strategies to create a family of new chemical imaging instruments for tumor imaging and diagnostics and surgical applications. The broad aim of this effort is to create new laser-based medical instruments which push tumor detection limits down towards the single-cell level, for early detection and treatment prior to metastatization.

Dor Ben-Amotz, Purdue Chemistry Professor and leader of this project which includes Phil Low and David Thomson, also of Purdue Chemistry, describes it as follows:

"The proposed instrument will combine spectral imaging hardware with tumor selective fluorophore labeling to enhance the optical detection of malignancy and premalignancy in living tissue. Near-infrared (NIR) fluorophores will be used to maximize tissue penetration and discrimination against background optical emission (auto-fluorescence). A key goal of this effort is to enhance the detection of small tumors and related pathological biochemical states which might be missed by conventional biopsy and/or histological analysis. This will be achieved by combining biochemically-specific fluorescent 'beacons', multiwavelength spectral imaging and advanced data processing. A long-range goal of this project is the integration of optical detection with photolytic ablation of tumor tissue using a single surgical instrument."

The field of proteomics—the characterization and understanding of all the proteins in the cell—is the focus of intense effort in labs across the world. A major activity is screening large numbers of proteins and identifying their biological activity in connection with specific disease states. III projects involving Profs. David Clemmer and Milos Novotny at Indiana University in Bloomington, and Scott McLuckey at Purdue University in West Lafayette, bring new tools to bear on this complex system. This group applies novel gas-phase and condensed-phase separation approaches such as ion mobility spectrometry (IMS) and capillary electrochromatography, as well as new gas-phase ion chemistry techniques, including ion/ion proton transfer reactions, in conjunction with mass spectrometry. The increased knowledge of the human proteome which will result from this work will lead to new commercial drug therapies.

A further aim is the construction of novel miniature mass spectrometers for chemical screening in harsh and inaccessible environments (e.g. environmental remediation, chemical and semiconductor process monitoring). Mass spectrometers will also be developed for rapid, high-sensitivity identification, characterization and determination of biopolymers and compounds formed by combinatorial synthesis. Miniature, rapid and parallel-processing instruments are of special interest. Instruments planned will be built based on (i) time of flight (TOF), and (ii) cylindrical ion trap (CIT) technology. Novel ion sources are being developed that will enable atomic, molecular fragmentation and molecular ion mass spectra to be acquired on a time scale compatible with chromatographic separations. It is anticipated that these studies, conducted by another joint IU/PU team (Graham Cooks, Gary Hieftje and Jim Reilly) will enjoy immediate industrial application.

Technology Transfer

The Institute is establishing strong relationships with high-tech industry in Indiana and is committed to assisting graduate students and others in founding start-up companies based on research work done at Purdue and IU.

The technology transfer efforts have taken a fast start, with graduate students in both the advanced medical and materials diagnostics and miniature mass spectrometer areas already moving toward establishing companies and commercializing their laboratory discoveries. These efforts are coordinated by Marie Thursby of the Krannert Graduate School of Management at Purdue and Ron Steuterman, Director of the Technology Transfer Initiative.

Proposed instruments include both immediate upgrades of existing microscopic and endoscopic medical equipment and methodology, and applications involving the creation of completely new molecular scale tools for tumor targeting, imaging and diagnostics.

Future spin-off projects will build on the same chemical imaging technology to create new instruments for industrial quality assurance and manufacturing automation, and to develop new computer algorithms for chemical quantification and mapping.

IU and PU

Recognizing the long-standing strengths in chemical instrumentation and analytical chemistry at both Indiana University and Purdue University, this collaborative institute has been formed to unite the talents of faculty, students and technical staff at both institutions. Through a formal arrangement that involves the Chemistry Departments at both institutions, the Linda and Jack Gill Center for Instrumentation and Measurement Science at IU, and the Purdue Center for Advanced Instrumentation, the participants are collaborating on research projects, education and relationships with industries involved in chemical measurements.

A new program, established at IU in the area of Instrumentation Science, is expected to be of benefit in training students to enter the high-tech workforce, in providing excellent staff for existing Indiana firms and in re-educating those already employed. Further improvement in the instrumentation infrastructure at each university is planned, with effort at Purdue based on a MesoFab facility which emphasizes the (useful) region between nanofabrication (wonderful in principle, difficult in practice) and conventional microscale machining. The MesoFab facility will be used to develop scientific instrumentation on a scale between conventional analytical instrumentation and nano(chip) scale instruments. This relatively little-explored range involves fabrication at the 100's of micron level in a variety of materials. Ideally, components of this facility will exist on both campuses and interactions will be strong with existing precision-machining shops and other fabrication facilities.

Prof. Gary Hieftje of IU said, "The timing for III is perfect. We have great measurement challenges associated with the fusion of biology and chemistry. The State of Indiana has recognized how important this topic is to economic development and in providing opportunities for students. This is a wonderful opportunity for symbiosis: we need industry insights and industry needs new ideas and talented people."

The mission of the III includes the transfer of technology into commercial products and start-up companies in the State of Indiana. The key objectives of this III technology transfer program are to produce: (i) research innovations with commercial potential; (ii) market strategies and business plans; (III) graduates with joint expertise in both basic research and in the economic principles required for technology transfer. In other words, the aim is to create new technologies of economic value, and to produce technically proficient Ph.D.s with the professional and personal skills needed to succeed in industry, be it as entrepreneurs in Indiana start-up companies or as entrepreneurs in existing companies.

♦ Tools and Services for CNS Research

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Introduction

Bioanalytical Systems has been providing products and services for neuroscience for over 25 years. We provide tools and methodology that help biologists make better chemical measurements—easier, faster, cheaper. We have organized symposia, provided hundreds of workshops and we try to keep the state of the art moving, often in collaboration with our academic and industry partners. CNS drugs developed, in part, using BAS products and services (including support for clinical trials), now have annual sales of just under $10 billion.

Thousands of dedicated individuals have made this possible. Millions of individuals are living better lives because of this effort. Many know BAS for only a small part of what we do, whether it be liquid chromatography, contract research, toxicology support or dialysis probes. While we can't review here all we do in CNS research, let's take a quick look.

Brain Microdialysis

Microdialysis allows extracellular analytes to be monitored in discrete areas of the brain. In this technique, a probe is inserted into the desired region. A perfusing solution is pumped slowly through the probe. Analytes pass from the extracellular fluid into the perfusing solution by crossing a semipermiable membrane. The collected analytes can then be quantitated by means such as liquid chromatography/ electrochemistry or liquid chromatography/mass spectrometry. It is even possible to infuse drugs directly into the region while the microdialysis experiment proceeds. Compounds common to neuroscience (i.e. dopamine, serotonin, norepinephrine, acetylcholine, glutamate, aspartate, GABA, etc.) have been monitored by this method. Bioanalytical Systems manufactures an extensive line of precision microdialysis products to meet your in vivo-sampling needs.

The Raturn™

Designed as an awake animal containment system for microdialysis, the RATURN offers several advantages to the neuroscientist. First, it increases the reliability of the microdialysis experiments by eliminating the need for liquid swivels. Swivels prevent the tubing which connects microdialysis probes to stationary apparatus from becoming twisted. However, they frequently leak and fail. The RATURN allows multiple microdialysis probes to be connected to apparatus by contiguous lengths of tubing. But it does much more than this.

To prevent twisting, the RATURN rotates the animal in the direction opposite to its travel. If the animal walks clockwise in the RATURN's animal bowl, one of two optical sensors is engaged. The bowl will rotate counterclockwise until the sensor disengages. Each time a sensor is activated, associated software records the event. Hence, the frequency and duration of animal movement (clockwise or counterclockwise) is recorded. If the animal is being dosed with an experimental drug, the RATURN can provide preliminary data about the effect of the drug on the animal's behavior.

The Culex™

The CULEX is an automated blood-sampling system for pharmacokinetic and metabolic studies. It was designed with input from scientists at some of the nation's leading pharmaceutical companies.

Employing the RATURN, the CULEX allows blood to be sampled from active rodents in a time- and volume-independent manner. Blood samples are kept refrigerated by CULEX after collection. Because the RATURN is an integral part of the CULEX system, microdialysis experiments can be conveniently conducted while blood is being collected. Hence, a drug can be administered to a rodent. Then, unbound analyte concentrations (of neurotransmitters, the drug and its metabolites) can be continuously monitored, along with animal behavior, while blood samples are collected to monitor drug/metabolite levels. With CULEX, very elegant but complex pharmacodyamic and pharmacokinetic experiments are made easy.

To learn more about CULEX, please visit its website at *www.culex.net.*

Liquid Chromatography/ Electrochemistry

Electrochemistry is the preferred method of detection for many neuroactive compounds, Catecholamines (i.e. norepinephrine and dopamine) are oxidized at an electrode surface. Amino acids (i.e. glutamate, aspartate, and GABA) can be precolumn derivatized to form electrochemically active conjugates. Acetylcholine is detected indirectly as hydrogen peroxide after a two-step process involving acetylcholine esterase and choline oxidase. Bioanalytical Systems, first to commercialize LCEC, manufactures a complete line of liquid chromatography equipment for quantitation of such compounds at their low, endogenous levels.

Contract Analytical Services

Bioanalytical Systems is now offering contract services for the quantitation of many neuroactive compounds. All of these compounds are determined by our original LCEC methods: acetylcholine, dopamine, serotonin, norepinephrine, aspartate, glutamate, GABA, neuroactive amino acids and other related compounds.

Quantitation limits for these analyses will vary depending on sample type and the number of analytes to be determined in a single chromatographic injection. All of these analyses are done on a non-GLP basis. The following typical values are presented as a guide only and cannot be guaranteed for every matrix:

- acetylcholine ... 20 femtomoles injected
- dopamine ... 100 femtograms injected
- serotonin ... 150 femtograms injected
- norepinephrine ... 500 femtograms injected
- aspartate/glutamate/neuroactive amino acids ... 0.5 micromolar
- GABA ... 50 femtomoles injected

In addition to these endogenous compounds, our Analytics Division has extensive experience in monitoring CNS drugs using liquid chromatography/mass spectrometry. These analyses are performed under GLP conditions for preclinical pharmacokinetics and all phases of clinical trials. A list of validated assays is available.

Contract In-Vivo Sampling

Finally, our team of neuroscientists is ready to assist you in the design and execution of in vivo-sampling (microdialysis) experiments to meet your research needs.

♦ INSURE 2001

The International Conference on Advances in Surface Science and Engineering (INSURE 2001) will be held in Chennai (Madras), India on 21 - 23 February 2001. The aims of this conference are as follows:

- To create an interactive forum for multi-disciplinary discussion and to exchange expertise and technology between scientists/engineers and personnel from industrial organizations.
- To identify new processes and important areas of research in traditional and advanced surface modification and analysis.
- To discuss future trends relating to surface modification and analysis.
- Contributions are invited for the following topics:
- PVD,CVD, DLC, biomedical, polymer, high temperature coatings.
- Electroplating, electroless plating, anodizing.
- Painting, galvanizing, hard facing, weld cladding and overlay, nitriding, organic and chemical conversion coatings.
- Plasma, ion implantation, electron beam and laser based coatings.
- Thin and thick film preparation and characterization.
- Surface analysis and investigations using optical microscopy, SEM, TEM,XRD, EPMA, XPS, AES, SIMS, NDT techniques, etc.
- Surface electrochemistry.
- Testing of coatings - traditional and modern evaluation methods: corrosion, wear, tribology, mechanical behavior, erosion, adhesion, magnetic, electronic and semiconducting properties.
- Application of coatings - conventional and special applications in automobile, space/aerospace, nuclear/defense, marine, electronics, construction, chemical processing, etc.

Abstracts should be sent to the address below by November 30, 2000. For further information, please contact:

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