GROUP PROJECT I

"Gang of Three"

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Group Meetings

The group met together twice a week, usually at 6:00 PM in the Chemistry Reading Room. These meetings lasted from thirty to forty-five minutes each, except for the first, which lasted for two hours, and included a trip to the UMC Library to look up resource materials. We also met at least one other time per week, usually on Monday or Wednesday afternoon, at 2:00 PM to assign tasks for individual members to perform between meetings, and to review progress made since the last get-together. Tasks included locating and contacting vendors; reviewing materials provided by vendors; writing the various parts of the assignment; and collating the information so as to make decisions concerning purchase options.

PUTTING A NEW SPIN ON DRUGS

ELECTRON SPIN RESONANCE ANALYSIS OF PHARMACEUTICALS STERILIZED BY RADIATION

The sterilization of many drugs and delivery packages by exposure to gamma rays from a ^{60}Co source has become a major approach to the problem of drug safety and efficacy. This method, if properly applied, meets the criteria for a good sterilization method: it does not significantly raise the temperature of the materials, nor does it introduces any harmful byproducts. The products so irradiated have been shown in many cases to retain their viability and sterility for long periods, under normal conditions of storage. Moreover, the method's cost, even in small lots, may often be measured in pennies per sample (Bogl, 1985.) However, in order to be accepted, a proven method for analyzing and assessing the characteristics of these materials as a result of their sterilization must be used (Gopal, 1988).

Since the materials used exhibit characteristic free-radical profiles, and since these patterns are often reproducibly altered as a result of irradiation, electron spin resonance spectroscopy is a logical technique to analyze these products, and has in fact been used exactly for this purpose. (Duroux, 1996; Mader, 1996; Onori,1996) A single dose of 25 kGy (2.5 mRad) of radiation is usually sufficient to render the material sterile without undue degradation, and to introduce characteristic changes in the free radical profile of the material, which may be evaluated with a proper choice of instrumentation. This instrumentation must at a minimum be capable of variable temperature (77K - 373K)

operation, ability to handle both solid and aqueous samples, and sophisticated data handling to interpret data obtained under a wide range of conditions, and over long periods of time.

The companies we contacted are:

(1) Varian Associates
3120-T Hansen Way,0-120
Palo Alto
Fax: 415-493-0307
Ph: 415-429-4819

(2) Bruker Instruments
Manning Park
19 Fortune Drive
Billerica, MA 01821-3991
Ph: 978-663-7406
Fax:508-667-3954

e-mail: mac@bruker.com
Internet: www.bruker.com

(3) Research Specialties
5629 N.Maplewood
Chicago IL 60659
Ph:773-728-6570

(4) Jeol USA
P.O Box 6043, 11 Dearborn Rd
Peabody MA 01961-6043
Ph: 508-535-5900
Fax: 508-536-2205

(5) Resonance Instruments Inc.
9054 Terminal Ave.
Skokie IL 60077
Ph: 847-583-1000
Fax: 847-583 -1021
e-mail: rii@wwa.com

Instrument Specifications:

On the basis of information received we selected the following two instruments for further consideration.

(1) Bruker ESP 300E/EMX series (Enhanced performance computer aided spectroscopy)**:**

This product lines has the benefits gained from the use of digital electronics functions, new measuring techniques and ESP 3220 series and data processing system
The important features of this instrument are:

Standard hardware:

ESP 3220 multiprocessor acquisition series with 32 bit architecture, 32 bit bus.
2 input 3 out put lines(TTL- level) for process control

3 programmable pulse output lines(1MHz-30MHz)
MHz-12 bit digitizer with sample hold, on board accumulator and memory with 10ns access time.
ESP 1600-1074 digital rapid acquisition scan(50G/200G)

Hardware options:

Computer controlled ganiometer accessory with resolution of 0.125degree
ESP 385 ultra fast programmer with 12 Ns res. and 8 digital channels with 16K per channel available for user programmable pulses.
FT ,ESE,ESEEM accessories
ENDOR/TRIPLE accessories
Low Q resonators with extremely high power/field conversion factors

Standard software:

Spectrometer control
Signal channel calibrations
Acquisition with automatic calibration and scaling
Baseline correction
Dual display
Automatic routines
TCP/IP
Fast fourier transformation

BRUKER EMX system

A) Basic instrument package with 6 inch magnet
40000 sampling rate,6400G max, 1.0 kW ----------**$125,000.00**
B) Aqueous cavity,ER41037M ---------- **-$11,350.00**
C) Variable temperature access.,ER423NT ----------**$13,000.00**
D) PCbased data package include
E) Accessory set, ER176TM-SET ----------**$ 4,730.00**

TOTAL $154,080.00

Resonance Instruments (Model 8400)

A truly portable X-band ESR spectrometer. It consists of a compact electromagnet and power supply which utilizes air or water cooling. The important features of this instrument are:

* automatic tuning of its balanced bridge
* Automatic baseline correction
* Thermostabilization of the Hall probe and field regulator.
* Complete computer control of all bridge and field parameters.
* Software package which provides for comprehensive data manipulation including output to a digital plotter and comprehensive mathematical modeling

The components of this 8400 ESR spectrometer are:

Microwave Bridge:

The solid- state signal source , Gunn oscillator provides an extremely stable frequency (9.6 Hz) and power output has low voltage power requirements. The circulator provides good isolation and low signal loss.

Microwave Cavity :

Rectangular TE102 Cavity of approximately 9.6GHz and unloaded Q of 6000. Variable iris aperture matches a wide range of sample holder and dewars with a maximum sample diameter of 9.5mm

Lock-In amplifier:

Operates at 100KHz and performs the signal processing function. The initial amplification and impedance matching between the microwave detector and the lock-in amplifier is provided by a fixed gain preamplifier in the microwave bridge.

Gain, phase and time constant are all controlled by means of setup menu in the data acquisition software.

Field Controller:

Sets and maintain the level of the magnetic field to the sample. Field center point , scan width and scan duration are all set from the external computer.

Electromagnet:

Hardchromed four inch diameter pole caps which provide a field of up to 700 gauss. The pole caps are shimmed to provide a homogeneous field over the entire sample area of the cavity.

Magnet Power Supply:

Well regulated solid- state supply, air water cooled that can deliver up to 16 amperes. It is regulated by field controller and is temperature protected against cooling system failure.

Plotter:

Hewlett Packard model is recommended by the company but older analog X-Y recorders can also be driven from the front panel XY recorder interface.

Basic Instrument
$63,000.00

Accessories Available:

* Variable temperature controllers (-150°C to +200°C)	**$9,718.00**
*NMR Guassmeter(Range 1 to 52 Kiloguass)	**$ 3.300.00**
*Magnetic Field Controller	**$ 8,500.00**
Total	**$84,518.00**

COMPARISON:

Bruker EMX: Water cooled 6-18 inches magnet system, air gap 62-160 mm with power supply 1-40 KW.
Use of parallel transputers in each of the spectrometer units makes it possible to operate EMX via a standard PC. Where PC serves primarily as the user interface.
The variable temperature range from 77-373K

RI I MODEL 8400: A fixed 4 inches air and water cooled magnet that has well regulated solid state supply capable of delivering up to 16 amperes.
Data read out through Hewlett -Packard digital plotter.
The variable temperature range from 277-373K.

FINAL DECISION:

After considerable discussion as to the needs of this project, we decided to specify the Bruker package. The reasons are many, and both overt and implied advantages went into the decision.

The Bruker instrument offers a larger magnet with better field homogeneity and the ability to handle samples of larger size. Its temperature range is better(77K- lower limit Vs 277K) and its data handling package is more versatile allowing a broader range of possible applications.

In addition the Bruker corporation offers in house workshops, full technical and product support and a long history of leadership in the field of ESR. While this may also be true of RI I they were not forthcoming in providing full information in some of these regards.

In short the combination of capabilities, support and proven history made Bruker instruments offering a better choice inspite of its higher initial cost.

GROUP DYNAMICS:

This group had mixed feelings about the project, as probably do all such groups. On the good side were the chance to interact with other students to an extent which would have been difficult ordinarily, given the pressure of graduate study. We also were able to view points from differing vantages, giving us a better perspective on what others are going through, and discovering every one has the same type of frustrations as ourselves. We also were able to get a better feel for what is involved in picking an instrumentation package, and kinds of decision that go into such a move. For those who had gone through this procedure before, experience was enlightening; and even those of us who did not suffer from the review.

On the bad side, the difficulty of intertwining three very busy schedule so as to met at times agreeable to all, and then to construct a single document which everyone had a chance to provide input into, were at times almost insurmountable. Most graduate students are by nature or by training selfmotivated, and desirous of laying their fortunes on themselves; linking the academic success of three people, who may each be quite competent,to the styles and schedules of the others, was at times difficult to justify.

As to whether we would willingly undergo the experience again, we generally would answer y es, but with some modifications, and some what better guidance as to what is expected.