

15:31:25

OCA PAD AMENDMENT - PROJECT HEADER INFORMATION

10/21/93

Active

Project #: G-33-615
Center # : R6021-OA0

Cost share #:
Center shr #:

Rev #: 15
OCA file #:
Work type : RES
Document : GRANT
Contract entity: GTRC

Contract#: DE-FG05-85ER13435
Prime #:

Mod #: M009

Subprojects ? : N
Main project #:

CFDA: 81.043
PE #: N/A

Project unit:
Project director(s):
BROWNER R F

CHEMISTRY
CHEMISTRY

Unit code: 02.010.136
(404)894-4020

Sponsor/division names: US DEPT OF ENERGY
Sponsor/division codes: 141

/ DOE OAK RIDGE - TN
/ 017

Award period: 860901 to 931231 (performance) 940331 (reports)

Sponsor amount	New this change	Total to date
Contract value	0.00	556,409.00
Funded	0.00	556,409.00
Cost sharing amount		0.00

Does subcontracting plan apply ? : N

Title: FUNDAM'L STDY W/MONODISPERSE AEROSOL BASED LIQUID CHROMATOGRAPHY/MASS SPECTRO

PROJECT ADMINISTRATION DATA

OCA contact: E. Faith Gleason

894-4820

Sponsor technical contact

Sponsor issuing office

DR. JOHN L. BURNETT, OFFICE OF BASIC
(301)894-5802

MELISSA Y. JOHNSON, CONTRACT SPECLST
(615)576-7599

ENERGY SCIENCES, US DOE
19901 GERMANTOWN ROAD
GERMANTOWN, MD 20874

US DOE OAK RIDGE OPERATIONS
SPECIAL ACQUISITIONS BRANCH
P.O. BOX 2001
OAK RIDGE, TN 37831-8757

Security class (U,C,S,TS) : U

ONR resident rep. is ACO (Y/N): N

Defense priority rating : N/A

N/A supplemental sheet

Equipment title vests with: Sponsor

GIT X

Administrative comments -

* AMENDMENT M009 PROVIDES A NO-COST EXTENSION TO DECEMBER 31, 1993.

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 05/09/95

Project No. G-33-615

Center No. R6021-0A0

Project Director BROWNER R F

School/Lab CHEMISTRY

Sponsor US DEPT OF ENERGY/DOE OAK RIDGE - TN

Contract/Grant No. DE-FG05-85ER13435

Contract Entity GTRC

Prime Contract No.

Title FUNDAM'L STDY W/MONODISPERSE AEROSOL BASED LIQUID CHROMATOGRAPHY/MASS SPE

Effective Completion Date 931231 (Performance) 940331 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	Y	940309
Final Report of Inventions and/or Subcontracts	Y	
Government Property Inventory & Related Certificate	Y	
Classified Material Certificate	N	
Release and Assignment	N	
Other	N	

Comments

USE SPONSOR FORMS FOR PATENT AND PROPERTY

Subproject Under Main Project No.

Continues Project No.

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Management	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other	N
	N

NOTE: Final Patent Questionnaire sent to PDPI.

U.S. DEPARTMENT OF ENERGY
NOTICE OF ENERGY RD&D PROJECT

G-33-615
1

APPROVED FOR USE BY
SMITHSONIAN SCIENCE INFORMATION EXCHANGE

OMB Approval
No. 1901-0021

1. Descriptive title of work Development of a Monodisperse Aerosol Generation Interface for Coupling Liquid Chromatography and Mass Spectrometry

2. Performing organization control number G33-615

3. Contract or grant number

Work status ☒ New ☐ Continuing ☐ Terminated

DE-FG05-85E13435

4. Contractor's principal investigator/project manager and address where work is performed

A. Name (Last, First, MI) Browner, Richard F.

B. Phone: FTS- (404) 894-4020

C. Research organization Georgia Tech Research Corporation

business address: Street Georgia Institute of Technology

Com.-

City Atlanta

State GA

Zip 30332

5. A. Name of performing organization Georgia Institute of Technology

School of Chemistry

(Organization)

(Department)

B. Mailing address (If different from 4C)

C. Circle only one code for TYPE OF ORGANIZATION PERFORMING R&D
(See instructions):

CU

FF

IN

NP

ST

TA

US

XX

EG

D. Location where the work is being performed

Boggs Chemistry Building, Georgia Institute of Technology

E. Country sponsoring research

USA

6. Supporting organization

A. Program division or office (Full name) Office of Basic Energy Sciences

B. Technical monitor (Last, First, MI) Stevenson, F. Dee

C. Phone: FTS- (202) 353-5802

D. Address (If different from DOE Hqs.)

Com.-

E. Administrative monitor (Last, First, MI) Cansler, Marlena

7. Project schedule

A. Start date September 1985
(Month) (Year)

B. Expected completion date August 1988
(Month) (Year)

8. Funding in thousands of dollars (Funds represent budget obligations for operating and capital equipment)

	Funding organization(s)	Current FY <u>85</u>	Next FY <u>86</u>
A.	<u>DOE</u>	<u>80</u>	<u>67</u>
B.			
C.			

D. For DOE projects, enter budgeting and reporting classification code

E. Interagency agreement (Specify funding agency)

F. Agency in-house effort (Check if applicable) ☐

G. EPA "pass-thru" funding (Check if applicable) ☐

Note: Funding Section utilization is optional on Federal Financial Assistance Programs: grants, direct payments, cooperative agreements, loan guarantees, and other related programs.

9. Descriptive summary of work (Limit to 200 words. Include objective, approach, results to date and their significance, and expected product. Quantify where possible).

The research to be carried out is aimed at investigating the behavior of aerosols formed in the interfaces between liquid chromatographs and mass spectrometers. Liquid chromatography (LC) has become the method of choice for separating large molecules, such as those found in fossil fuels and materials of biological origin. When combined with the powerful technique of mass spectrometry (MS), the hybrid technique of LC/MS gives unique selectivity to the analysis of complex mixtures.

The research to be carried out involves fundamental studies of aerosol generation, evaporation and transport in a unique aerosol-based LC/MS interface. The interface uses a monodisperse aerosol generator (MAG) which produces a stream of drops from the chromatography effluent. The drops evaporate under controlled pressure conditions to leave essentially dry analyte particles, which then pass through a two-stage aerosol beam separator, to the ionization chamber region of the mass spectrometer.

10. List the five most descriptive publications in the last year that are available to the public which have resulted from the project (Please give a complete bibliographic citation. Use additional sheets if necessary).

R. C. Willoughby and R. F. Browner, Monodisperse Aerosol Generation Interface for Combining Liquid Chromatography with Mass Spectrometry, Anal. Chem. 1984, 56, 2626.

11. General technology categories (Enter applicable code of codes from instructions).

F	2												
---	---	--	--	--	--	--	--	--	--	--	--	--	--

12. Type of research activity (Check applicable activities)

- | | |
|---|--|
| A. <input checked="" type="checkbox"/> Basic research | H. <input type="checkbox"/> Mathematical model development |
| B. <input type="checkbox"/> Applied research | I. <input type="checkbox"/> Data analysis/assessments |
| C. <input type="checkbox"/> Laboratory scale R&D | J. <input type="checkbox"/> Information systems management |
| D. <input type="checkbox"/> Technology development | K. <input type="checkbox"/> Policy analysis |
| E. <input type="checkbox"/> Field study | L. <input type="checkbox"/> Socioeconomic |
| F. <input type="checkbox"/> Pilot plant scale R&D | M. <input type="checkbox"/> Other (Specify) _____ |
| G. <input type="checkbox"/> Full scale demonstration | N. <input type="checkbox"/> Not applicable |

13. keywords (Please list 5 keywords).

Mass spectrometry, liquid chromatography, aerosol, monodisperse, organic analysis

14. Is this research project solely an ANALYTICAL/PAPER STUDY?
(Non-experimental, paper and pencil, computer analysis, etc.).

YES _____ NO X

15. Respondent's Name: Browner, Richard F. Phone No.: (404) 894-4020 Date: 9/5/85
Street: School of Chemistry, Georgia Institute of Technology
City: Atlanta State: GA Zip: 30332

Georgia Tech

G-33-615
NIA

Office of Grants and Contracts Accounting

Georgia Institute of Technology

Hinman Building

Atlanta, Georgia 30332-0259

404.894.4624; 2629

Fax: 404.894.5519

February 6, 1990

Ms. Melissa Y. Johnson, Contract Specialist
U. S. Department of Energy-Oak Ridge Operations
Contract Management Branch
P. O. Box 2001
Oak Ridge, Tn 37831-8758

REFERENCE: Grant #DE-FG05-85ER13435

Dear Ms. Johnson,

Enclosed in triplicate is the Financial Status Report (SF-269) for Grant No. DE-FG05-85ER13435 covering the period September 1, 1988 through November 30, 1989.

If you should have questions or need additional information, please contact Geraldine Reese of this office at (404) 894-2629.

Sincerely,

David V. Welch
Director

DVW/GMR/djt

Enclosures

cc: Dr. R. F. Browner, Chemistry 0400
Dr. E. K. Barefield, Chemistry 0400
Ms. Mary Wolfe, OCA/CSD 0420 ✓
File G-33-615/R6021-0A0

FINANCIAL STATUS REPORT

(Short Form)

(Follow instructions on the back)

1. Federal Agency and Organizational Element to Which Report is Submitted U. S. Department of Energy		2. Federal Grant or Other Identifying Number Assigned By Federal Agency DE-FG05-85ER13435		OMB Approval No. 0348-0039	Page 1	of 1 page
3. Recipient Organization (Name and complete address, including ZIP code) Georgia Tech Research Corporation P. O. Box 100117 Atlanta, GA 30384						
4. Employer Identification Number 58-0603146		5. Recipient Account Number or Identifying Number G-33-615/R6021-0A0		6. Final Report <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		7. Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual
8. Funding/Grant Period (See Instructions) From: (Month, Day, Year) September 1, 1986		To: (Month, Day, Year) November 30, 1992		9. Period Covered by this Report From: (Month, Day, Year) September 1, 1988		To: (Month, Day, Year) November 30, 1989
10. Transactions:				I Previously Reported	II This Period	III Cumulative
a. Total outlays				\$ 212,000.00	\$ 88,932.15	\$ 300,932.15
b. Recipient share of outlays				-0-	-0-	-0-
c. Federal share of outlays				212,000.00	88,932.15	300,932.15
d. Total unliquidated obligations						162.50
e. Recipient share of unliquidated obligations						-0-
f. Federal share of unliquidated obligations						162.50
g. Total Federal share (Sum of lines c and f)						301,094.65
h. Total Federal funds authorized for this funding period						301,999.00
i. Unobligated balance of Federal funds (Line h minus line g)						904.35
11. Indirect Expense						
a. Type of Rate (Place "X" in appropriate box) <input type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input checked="" type="checkbox"/> Fixed						
b. Rate See Below		c. Base MTDC		d. Total Amount		e. Federal Share
12. Remarks: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation. GEORGIA TECH'S FISCAL YEAR ENDS JUNE 30 <div style="float: right; text-align: right;"> Questions pertaining to this report should be directed to: Geraldine Reese (404) 894-2629 </div>						
13. Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.						
Typed or Printed Name and Title David V. Welch, Director, Grants and Contracts Accounting					Telephone (Area code, number and extension) (404) 894-2629	
Signature of Authorized Certifying Official <div style="border: 1px solid black; height: 20px; width: 100%;"></div>					Date Report Submitted February 6, 1990	

Previous Editions not Usable

FY86 @ 63.5%	FY89 @ 60.0%
FY87 @ 63.5%	FY90 @ 62.5%
FY88 @ 60.0%	

Standard Form 269A (REV 4-88)
Prescribed by OMB Circulars A-102 and A-110

GRANT # DE-FG05-85ER13435

September 1 , 1988 - November 30, 1989

	<u>Direct Costs</u>	<u>Indirect Costs</u>	<u>Equipment</u>
FY'86	\$ 47,877.56 @ 63.5% =	\$ 15,415.97	\$ 23,600.42
FY'87	43,589.43 @ 63.5% =	27,107.16	901.00
FY'88	43,981.24 @ 60.0% =	25,897.11	819.40
FY'89	51,818.94 @ 60.0% =	31,091.36	.00
FY'90	8,976.54 @ 62.5% =	5,176.84	.00

Report Period

09/01/88 - 06/30/89	\$ 46,736.73 @ 60.0% =	\$ 28,042.04
07/01/89 - 11/30/89	8,976.54 @ 62.5% =	5,176.84

ADMINISTRATIVE
OFFICE OF CONTRACTS
WASHINGTON, D.C. 20540

FEB 8 - 1990

RECEIVED

Georgia Institute of Technology
Hinman Building
Atlanta, Georgia 30332-0259
404-894-4624; 2629
Fax: 404-894-5519

July 15, 1991

Ms. Melissa Y. Johnson, Contract Specialist
U. S. Department of Energy-Oak Ridge Operations
Procurement and Contracts Division
P. O. Box 2001
Oak Ridge, TN 37831-8758

REFERENCE: Contract # DE-FG05-85ER13435

Dear Ms. Johnson,

Enclosed in triplicate is the Financial Status Report (SF-269A) for Contract No. DE-FG05-85ER13435 covering the period December 1, 1989 through December 30, 1990.

If you should have questions or need additional information, please contact Geraldine Reese or me at (404) 894-2629.

Sincerely,

David V. Welch
Director

DVW/GMR/djt

Enclosures

cc: Dr. R. F. Browner, Chemistry 0400
Dr. E. K. Barefield, Chemistry 0400
Ms. Mary Wolfe, OCA/CSD 0420 ✓
File: G-33-615/R6021-0A0

FINANCIAL STATUS REPORT

(Short Form)

(Follow instructions on the back)

1. Federal Agency and Organizational Element to Which Report is Submitted U. S. DEPARTMENT OF ENERGY		2. Federal Grant or Other Identifying Number Assigned By Federal Agency DE-FG05-85ER13435		OMB Approval No. 0348-0039	Page 1	of 1 page
3. Recipient Organization (Name and complete address, including ZIP code) GEORGIA TECH RESEARCH CORPORATION P. O. BOX 100117 ATLANTA, GA 30384						
4. Employer Identification Number 58-0603146		5. Recipient Account Number or Identifying Number G-33-615/R6021-OAO		6. Final Report <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		7. Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual
8. Funding/Grant Period (See Instructions) From: (Month, Day, Year) September 01, 1986		To: (Month, Day, Year) December 31, 1992		9. Period Covered by this Report From: (Month, Day, Year) December 01, 1989		To: (Month, Day, Year) December 30, 1990
10. Transactions:				I Previously Reported	II This Period	III Cumulative
a. Total outlays				300,932.15	84,876.85	385,809.00
b. Recipient share of outlays				-0-	-0-	-0-
c. Federal share of outlays				300,932.15	84,876.85	385,809.00
d. Total unliquidated obligations						-0-
e. Recipient share of unliquidated obligations						-0-
f. Federal share of unliquidated obligations						-0-
g. Total Federal share (Sum of lines c and f)						385,809.00
h. Total Federal funds authorized for this funding period						385,809.00
i. Unobligated balance of Federal funds (Line h minus line g)						-0-
11. Indirect Expense						
a. Type of Rate (Place "X" in appropriate box) <input type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input checked="" type="checkbox"/> Fixed						
b. Rate		c. Base		d. Total Amount		e. Federal Share
SEE ATTACHED		MTDC		\$30,836.68		\$30,836.68
12. Remarks: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation. <div style="text-align: right;"> QUESTIONS PERTAINING TO THIS REPORT SHOULD BE DIRECTED TO: GERALDINE REESE (404) 894-2629 </div> GEORGIA TECH'S FISCAL YEAR ENDS JUNE 30						
13. Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.						
Typed or Printed Name and Title David V. Welch, Director, Grants and Contracts Accounting					Telephone (Area code, number and extension) (404) 894-2629	
Signature of Authorized Certifying Official <div style="border: 1px solid black; height: 20px; width: 100%;"></div>					Date Report Submitted July 15, 1991	

Attachment
 07/15/91
 Contract # DE-FG05-85ER13435
 Financial Status Report
 Period Covering: 12/01/89 - 12/30/90

	<u>Direct Costs</u>	<u>Indirect Costs</u>	<u>Equipment</u>
FY'86	\$47,877.56 @63.5% = \$15,415.97		\$23,600.42
FY'87	43,589.43 @63.5% = 27,107.16		901.00
FY'88	43,981.24 @60.0% = 25,897.11		819.40
FY'89	51,818.94 @60.0% = 31,091.36		.00
FY'90	60,976.71 @62.5% = 34,738.52		5,395.06
FY'91	2,040.00 @62.5% = 1,275.00		

RECEIVED
 OFFICE OF CONTRACT ADMINISTRATION
 305-553381

<u>REPORT PERIOD</u>	<u>Direct Costs</u>	<u>Indirect Costs</u>	<u>Equipment</u>
12/01/89 - 06/30/90	\$ 52,000.17	\$ 29,561.68	\$4,701.48
07/01/90 - 12/30/90	2,040.00	1,275.00	

Georgia Institute of Technology

190 Bobby Dodd Way
Atlanta, Georgia 30332-0259
USA

404•894•4624; 2629

Fax: 404•894•5519

March 22, 1994

Ms. Melissa Y. Johnson, Contract Specialist
Special Acquisitions Branch
U. S. Department of Energy
Procurement and Contracts Division
P. O. Box 2001
Oak Ridge, TN 37831-8757


REFERENCE: Grant # DE-FG05-85ER13435

Dear Ms. Johnson,

Enclosed in triplicate is the Financial Status Report (SF-269A) for Grant Number DE-FG05-85ER13435 covering the period January 01, 1991 through December 31, 1991.

If you should have questions or need additional information, please contact Geraldine Reese of this office at (404) 894-2629.

Sincerely,


David V. Welch
Director

DVW/GMR/djt

Enclosures

c: Dr. R. F. Browner, Chemistry 0400
Dr. L. M. Tolbert, Chemistry 0400
Ms. Wanda Simon, OCA/CSD 0420 ✓
File: G-33-615/R6021-OA0

FINANCIAL STATUS REPORT

(Short Form)

(Follow instructions on the back)

1. Federal Agency and Organizational Element to Which Report is Submitted U. S. DEPARTMENT OF ENERGY		2. Federal Grant or Other Identifying Number Assigned By Federal Agency DE-FG05-85ER13435		OMB Approval No. 0348-0039	Page 1	of 2 pages													
3. Recipient Organization (Name and complete address, including ZIP code) GEORGIA TECH RESEARCH CORPORATION P. O. BOX 100117 ATLANTA, GA 30384																			
4. Employer Identification Number 58-0603146		5. Recipient Account Number or Identifying Number G-33-615/R6021-0A0		6. Final Report <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		7. Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual													
8. Funding/Grant Period (See Instructions) From: (Month, Day, Year) September 01, 1986		To: (Month, Day, Year) December 31, 1992		9. Period Covered by this Report From: (Month, Day, Year) January 01, 1991		To: (Month, Day, Year) December 31, 1991													
10. Transactions:				I Previously Reported	II This Period	III Cumulative													
a. Total outlays				385,809.00	84,599.98	470,408.98													
b. Recipient share of outlays				-0-	-0-	-0-													
c. Federal share of outlays				385,809.00	84,599.88	470,408.98													
d. Total unliquidated obligations						-0-													
e. Recipient share of unliquidated obligations						-0-													
f. Federal share of unliquidated obligations						-0-													
g. Total Federal share (Sum of lines c and f)						470,408.98													
h. Total Federal funds authorized for this funding period						470,409.00													
i. Unobligated balance of Federal funds (Line h minus line g)						.02													
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td rowspan="2" style="width: 15%; vertical-align: top;">11. Indirect Expense</td> <td colspan="6" style="vertical-align: top;"> a. Type of Rate (Place "X" in appropriate box) <input checked="" type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed </td> </tr> <tr> <td style="width: 20%; vertical-align: top;"> b. Rate SEE ATTACHED </td> <td style="width: 20%; vertical-align: top;"> c. Base MTDC </td> <td style="width: 20%; vertical-align: top;"> d. Total Amount \$32,507.76 </td> <td colspan="3" style="width: 45%; vertical-align: top;"> e. Federal Share \$32,507.76 </td> </tr> </table>							11. Indirect Expense	a. Type of Rate (Place "X" in appropriate box) <input checked="" type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed						b. Rate SEE ATTACHED	c. Base MTDC	d. Total Amount \$32,507.76	e. Federal Share \$32,507.76		
11. Indirect Expense	a. Type of Rate (Place "X" in appropriate box) <input checked="" type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed																		
	b. Rate SEE ATTACHED	c. Base MTDC	d. Total Amount \$32,507.76	e. Federal Share \$32,507.76															
12. Remarks: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation. <div style="text-align: right;"> Questions concerning this report should be directed to: Geraldine Reese (404) 894-2629 </div> GEORGIA TECH'S FISCAL YEAR ENDS JUNE 30																			
13. Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.																			
Typed or Printed Name and Title David V. Welch, Director, Grants and Contracts Accounting					Telephone (Area code, number and extension) (404) 894-2629														
Signature of Authorized Certifying Official <div style="background-color: black; width: 300px; height: 20px; margin-top: 10px;"></div>					Date Report Submitted March 9, 1994														

U. S. Department of Energy
 Financial Status Report (03/09/94)
 Grant No. DE-FG05-85ER13435 G-33-615/R6021-OA0
 Period Covering: 01/01/91 - 12/31/91

	<u>Direct Costs</u>		<u>Indirect Costs</u>	<u>Equipment</u>
FY86	\$47,877.56 @63.5%	=	\$15,415.97	\$23,600.42
FY87	43,589.43 @63.5%	=	27,107.16	901.00
FY88	43,981.24 @60.0%	=	25,897.11	819.40
FY89	51,818.94 @60.0%	=	31,091.36	.00
FY90	63,016.71 @62.5%	=	36,013.52	
FY91	47,104.05 @62.5%	=	29,440.03	
FY92	4,988.17 @61.5%	=	3,067.73	

<u>REPORT PERIOD</u>	<u>Direct Costs</u>	<u>Indirect Costs</u>	<u>Equipment</u>
01/01/91 - 06/30/91	\$47,104.05	\$29,440.03	
07/01/91 - 12/31/91	4,988.17	3,067.73	

Georgia Institute of Technology

190 Bobby Dodd Way
Atlanta, Georgia 30332-0259
USA
404•894•4624; 2629
Fax: 404•894•5519

March 22, 1994

Ms. Melissa Y. Johnson, Contract Specialist
Special Acquisitions Branch
U. S. Department of Energy
Procurement and Contracts Division
P. O. Box 2001
Oak Ridge, TN 37831-8757

REFERENCE: Grant # DE-FG05-85ER13435

Dear Ms. Johnson,

Enclosed in triplicate is the Financial Status Report (SF-269A) for Grant Number DE-FG05-85ER13435 covering the period January 01, 1992 through December 31, 1992.

If you should have questions or need additional information, please contact Geraldine Reese of this office at (404) 894-2629.

Sincerely,

David V. Welch
Director

DVW/GMR/djt

Enclosures

c: Dr. R. F. Browner, Chemistry 0400
Dr. L. M. Tolbert, Chemistry 0400
Ms. Wanda Simon, OCA/CSD 0420 ✓
File: G-33-615/R6021-0A0

FINANCIAL STATUS REPORT

(Short Form)

(Follow instructions on the back)

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3. Recipient Organization (Name and complete address, including ZIP code) GEORGIA TECH RESEARCH CORPORATION P. O. BOX 100117 ATLANTA, GA 30384							
4. Employer Identification Number 58-0603146		5. Recipient Account Number or Identifying Number G-33-615/R6021-0A0		6. Final Report <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		7. Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual	
8. Funding/Grant Period (See Instructions) From: (Month, Day, Year) September 01, 1986		To: (Month, Day, Year) December 31, 1992		9. Period Covered by this Report From: (Month, Day, Year) January 01, 1992		To: (Month, Day, Year) December 31, 1992	
10. Transactions:				I Previously Reported	II This Period	III Cumulative	
a. Total outlays				470,408.98	86,000.02	556,409.00	
b. Recipient share of outlays				-0-	-0-	-0-	
c. Federal share of outlays				470,408.98	86,000.02	556,409.00	
d. Total unliquidated obligations						-0-	
e. Recipient share of unliquidated obligations						-0-	
f. Federal share of unliquidated obligations						-0-	
g. Total Federal share (Sum of lines c and f)						556,409.00	
h. Total Federal funds authorized for this funding period						556,409.00	
i. Unobligated balance of Federal funds (Line h minus line g)						.00	
11. Indirect Expense							
a. Type of Rate (Place "X" in appropriate box) <input checked="" type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed							
b. Rate SEE ATTACHED		c. Base MTDC		d. Total Amount 32,748.69		e. Federal Share 32,748.69	
12. Remarks: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation. <div style="text-align: right; padding-right: 50px;"> Questions concerning this report should be directed to: Geraldine Reese (404) 894-2629 </div> GEORGIA TECH'S FISCAL YEAR ENDS JUNE 30							
13. Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.							
Typed or Printed Name and Title David V. Welch, Director, Grants and Contracts Accounting					Telephone (Area code, number and extension) (404) 894-2629		
Signature of Authorized Certifying Official <div style="background-color: black; width: 150px; height: 20px;"></div>					Date Report Submitted March 9, 1994		

U. S. Department of Energy
 Financial Status Report (03/09/94)
 Contract # DE-FG05-85ER13435 (G-33-615/R6021-OA0)
 Period Covering: 01/01/92 - 12/31/92

	<u>Direct Costs</u>		<u>Indirect Costs</u>	<u>Equipment</u>
FY86	\$47,877.56 @63.5%	=	\$15,415.97	\$23,600.42
FY87	43,589.43 @63.5%	=	27,107.16	901.00
FY88	43,981.24 @60.0%	=	25,897.11	819.40
FY89	51,818.94 @60.0%	=	31,091.36	.00
FY90	66,486.32 @62.5%	=	38,182.02	4,701.48
FY91	43,634.44 @62.5%	=	27,271.53	
FY92	58,239.50 @61.5%		35,816.42	

<u>REPORT PERIOD</u>	<u>Direct Costs</u>	<u>Indirect Costs</u>	<u>Equipment</u>
01/01/92 - 06/30/92	\$53,251.33	\$32,748.69	
07/01/92 - 06/30/93	-0-	-0-	
07/01/93 - 12/31/93	-0-	-0-	

G-33-615
2

DOE/ER/13435-1

**FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED
LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE (MAGIC-LC/MS)**

Progress Report

September 1, 1985 - August 31, 1986

Richard F. Browner

**School Of Chemistry
Georgia Institute Of Technology
Atlanta, GA 30332-0400**

May 1986

**PREPARED FOR THE U.S. DEPARTMENT OF ENERGY
UNDER GRANT NUMBER DE-FG05-85ER13435**

ACCOMPLISHMENTS DURING YEAR 1985-86

INTERFACE DESIGN

Considerable progress has been made on the design and characterization of the MAGIC interface during the current grant period. A completely new interface has been developed, following the basic principles determined during investigations with the earlier design, and preliminary tests with the interface indicate a substantial improvement in performance over the previous design. The principle advances are listed below, under headings of mechanical and optical studies.

Mechanical

The primary improvements have been made through a careful examination of the basic properties of the interface, in terms of aerodynamic behavior of gas and particle streams. The design of all parts of the system has been improved. Of particular note are improvements that have been made in the aerosol generator and in the aerosol beam separator.

Monodisperse Aerosol Generator. The aerosol generator construction has been drastically simplified in the present design. The original orifice was made from conically-tapered, drawn capillary tube. The current model is constructed from cylindrical-bore fused silica capillary tubing. The fused silica capillary shows much superior freedom from blockage, may be interchanged with capillary of other sizes, and may be readily connected to a zero-dead-volume fitting for minimal peak broadening.

Aerosol Beam Separator. The construction of the aerosol beam separator has been made much more rigid. Studies with the variability of the separator's performance showed that the threaded design used lead to misalignment of the critical nozzle/skimmer arrangement. This could lead to significant signal loss from particle impaction on misaligned surfaces. A new design with pre-aligned components has shown great robustness in operation, with much improved operational reliability. The pumping capacity of the separator has been improved by the addition of a turbomolecular pump in place of one rotary backing pump. This allows much better operating pressures in the mass spectrometer, while increasing analyte throughput through the use of larger skimmer orifice diameters.

Optical studies

A laser Fraunhofer light-scattering system has been used to provide size characterization of both the initial drop stream issuing from the aerosol generator, and the evaporation characteristics of this stream while passing through the evaporation chamber. This information has helped develop a better understanding of the optimum drop size and evaporation time for a number of solvents (e.g. water, acetonitrile, methanol, hexanes and various binary mixtures.)

GRADIENT AND MICROBORE WORK

Gradient Elution

A number of different normal and reversed-phase solvent mixtures have been examined, and the interface has proved to be very insensitive to solvent composition. In the most testing situation, with a methanol/water gradient, a signal change of $<2.5\times$ was observed for a gradient from 100% MeOH to 50% MeOH/50% H₂O. A similar experiment with a Thermospray interface would result in a signal change of approximately 200x.

Even the 2.5x signal loss with the MAGIC interface appears to be a transport phenomenon, and as such should be capable of considerable reduction.

Microbore Separations

The system has been tested with microbore columns, and found to perform excellently. The only limitation is found result from the limited scanning rate of the magnetic sector instrument, which causes some peak broadening and response loss. This should not occur with a quadrupole mass spectrometer.

APPLICATIONS

Pesticides and Herbicides

A number of pesticides, both carbamate and triazine types, have been tested with the system, and both E.I. and C.I. spectra have been demonstrated to be exact matches for reference spectra. Similar experiments with several herbicides proved equally successful.

Epoxy Resins

The successful separation and identification of a number of components of a reaction mixture from the synthesis of an epoxy resin was accomplished, as an operational test for the system. A similar experiment with a Thermospray interface was unable to identify any of the mixture components.

PUBLICATIONS

Journals

No papers have yet been published on this work, but three papers have been submitted, and a further two are in preparation.

Conferences

A total of five presentations on the research have been given at National Meetings. Three of these talks were invited.

RESEARCH GOALS FOR 1986-87

FURTHER INTERFACE DESIGN AND CHARACTERIZATION

The studies with the mechanical design of the interface will be continued. In particular, the optical studies of aerosol evaporation and transport phenomena will be continued. A special chamber, fitted with optically flat side windows has been constructed for this purpose. The precise configuration of the interface, particularly with regard to the aerosol beam separator geometry and orifice dimensions, still requires further study. Basic laws of aerosol evaporation and transport will need to be developed for a better understanding of the interface operation.

Transport Efficiency

A critical parameter in the interface design is the efficiency of the interface when operating under a wide range of conditions. We have developed a method for measuring the transport efficiency accurately can by

collecting injected analyte on a specially designed probe in the mass spectrometer ionization chamber. We propose to use this method to optimize the interface for uniform throughput for all solvent systems, including gradient work.

The experiments will focus on careful quantitative measurements with the injection of a series of compounds of varying density and volatility. This will give a good indication of the system to provide quantitative response to a number of compound types. Additionally, the quantitative response range of several key compounds will be determined. It is a matter of some interest as to the precise relationship between mass of analyte injected and ion count at the detector. There is a possibility that there may be a particle momentum related, and hence injected mass related, response dependence. Clearly, this is of the greatest importance for practical analytical determinations. The MAGIC-LCMS interface has the potential to be a powerful quantitative detector for LC, and so this study is of the utmost importance.

Aerosol Generation: Drop Size

As yet, full characterization of the monodisperse aerosol generator has not been attempted. However, such a study is essential for a proper understanding of its properties, which in turn are a key to the successful operation of the interface. We propose to carry out a systematic study of the properties of the generator, using a range of solvents of known physical properties, such as viscosity and surface tension. By controlling both gas and liquid flow rates to the monodisperse generator, it should be possible to produce a complete description of the aerosol generator. This will be an invaluable aid to understanding its operation, and ensuring that it is operated under optimum conditions with the wide range of solvent types normally encountered in LC separations.

Evaporation Chamber Design

The optical studies with the interface will be continued, using the laser scattering system. The precise evaporation rates for a number of solvents will be determined, and the particle trajectories monitored by following the particle densities in the system. Various designs of chamber will be tested, in order to determine the optimum configuration. It is of major importance to determine the configuration of the evaporation chamber that will ensure *complete* evaporation for even the least volatile solvent mixtures (e.g. acetonitrile/water).

Aerosol Beam Separator

The geometry of the aerosol beam separator will be further investigated. The optimum nozzle/skimmer separation is dependent on the skimmer dimensions and the operating pressures of the chambers. This requires a complex iterative optimization procedure. The newly installed higher capacity pumping system calls for a careful re-examination of this part of the system.

Dual/single stage design. The greater pumping capabilities of the turbomolecular pump recently installed on the interface open the possibility of operating with a single-stage aerosol beam separator. This exiting possibility will be investigated. The potential benefits of such an interface would include much greater analyte transport efficiency, with a consequent improvement in detection capability.

Continuing Studies with Gradient and Microbore Separations

As yet, only a relatively limited experience has been gathered with the use of various gradient systems, and also with microbore columns. We intend during the next year to gain a great deal more experience in working with these important separation approaches. In particular, the full range of response variations that are observed with microbore vs. packed column operation, and gradient operation vs. isocratic will be examined. This information will be used to help understand the operation of the interface, as an aid to interface design improvement.

Applications to Energy-related Samples

As part of the continuing evaluation of the interface for practical analytical use, selected groups of compounds will be tested thoroughly, in order to determine the range and scope of the interface. This will provide a measure of the evolving capabilities of the system. Selected groups of compounds will include polynuclear aromatic compounds, and other compounds of practical interest in fossil fuel analysis.

BUDGET

YEAR 2. 1986/1987

1. Personal Services

(i) Richard F. Browner, 2 months @ \$4,750.00/month \$ 9,500

(ii) 1.5 Research Assistants @ \$11,500 for 45% time
(0.68 FTE) \$ 17,250

TOTAL SALARIES and WAGES \$ 26,750

3. Fringe Benefits @ 21.8% of \$9,500 \$ 2,071

TOTAL SALARIES, WAGES and FRINGE BENEFITS \$ 28,821

4. Permanent Equipment

TOTAL PERMANENT EQUIPMENT \$

5. Travel

Participation in 2 major meetings to present results
of research \$ 1,500

6. Materials and Supplies \$ 6,903

7. Publication Costs for Research Articles \$ 350

TOTAL DIRECT COSTS \$ 37,574

8. Indirect costs, as established by ONR auditors,
@ 69% of Total Modified Direct Costs (\$37,574) \$ 25,926

TOTAL DIRECT and INDIRECT COSTS \$ 63,500

* Rates utilized above are estimated for the 7/1/86 - 6/30/87 and are subject to change pending negotiation.

YEAR 3. 1987/1988

1. Personal Services

(i) Richard F. Browner, 2 months @ \$5,333.00/month \$ 10,666

(ii) 2.0 Research Assistants @ \$11,500 for 45% time
(0.90 FTE) \$ 23,000

TOTAL SALARIES and WAGES \$ 33,666

3. Fringe Benefits @ 21.8% of \$10,666 \$ 2,325

TOTAL SALARIES, WAGES and FRINGE BENEFITS \$ 35,991

4. Permanent Equipment

TOTAL PERMANENT EQUIPMENT \$

5. Travel

Participation in 2 major meetings to present results
of research \$ 1,500

6. Materials and Supplies \$ 2,692

7. Publication Costs for Research \$ 350

TOTAL DIRECT COSTS \$ 40,533

**8. Indirect costs, as established by ONR auditors,
@ 69.0% of Total Modified Direct Costs (\$40,533) \$ 27,967**

TOTAL DIRECT and INDIRECT COSTS \$ 68,500

Richard F. Browner,
Principal Investigator

May 1, 1986

Jerry L. Goldbaugh
Contracting Officer

* Rates utilized above are estimated for the 7/1/86 - 6/30/87 and are subject to change pending negotiation.

G-33-615
3

DOE F 1332.16 (10-84)
(Formerly RA-427)

OMB Approval
No. 1910-1400

U. S. DEPARTMENT OF ENERGY

UNIVERSITY CONTRACTOR, GRANTEE, AND COOPERATIVE AGREEMENT
RECOMMENDATIONS FOR ANNOUNCEMENT AND DISTRIBUTION OF DOCUMENTS

See Instructions on Reverse Side

1. DOE Report No. DOE/ER/13435-2	3. Title FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL- BASED LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE (MAGIC-LC/MS).	
2. DOE Contract No. DE-FG05-85ER13435		
4. Type of Document ("x" one) <input type="checkbox"/> a. Scientific and technical report <input type="checkbox"/> b. Conference paper: Title of conference _____ Date of conference _____ Exact location of conference _____ Sponsoring organization _____ <input type="checkbox"/> c. Other (Specify) _____		
5. Recommended Announcement and Distribution ("x" one) <input checked="" type="checkbox"/> a. Unrestricted unlimited distribution. <input type="checkbox"/> b. Make available only within DOE and to DOE contractors and other U. S. Government agencies and their contractors. <input type="checkbox"/> c. Other (Specify) _____		
6. Reason for Recommended Restrictions _____		
7. Patent and Copyright Information: Does this information product disclose any new equipment, process, or material? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, identify page nos. _____ Has an invention disclosure been submitted to DOE covering any aspect of this information product? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, identify the DOE (or other) disclosure number and to whom the disclosure was submitted. Are there any patent-related objections to the release of this information product? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, state these objections. Does this information product contain copyrighted material? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, identify the page numbers _____ and attach the license or other authority for the government to reproduce.		
8. Submitted by Richard F. Browner, Professor of Chemistry Organization School of Chemistry, Georgia Institute of Technology Signature _____ Phone (404) 894-4020 Date June 17, 1987		

FOR DOE OR OTHER AUTHORIZED
USE ONLY

9. Patent Clearance ("x" one)
☐ a. DOE patent clearance has been granted by responsible DOE patent group.
☐ b. Report has been sent to responsible DOE patent group for clearance.

**FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED
LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE
(MAGIC-LC/MS)**

Progress Report

September 1, 1986 - August 31, 1987

Richard F. Browner

**School Of Chemistry
Georgia Institute Of Technology
Atlanta, GA 30332-0400**

June 1987

**PREPARED FOR THE U.S. DEPARTMENT OF ENERGY
UNDER GRANT NUMBER DE-FG05-85ER13435**

ACCOMPLISHMENTS DURING YEAR 1986-87

A number of major accomplishments have been made during the last year. These include both technical aspects of the project, and developments associated with commercial exploitation of MAGIC-LC/MS.

Technical advances have been made through a number of careful and detailed studies of fundamental processes occurring within the interface. These have led to great improvements in the performance of the interface, many of which are detailed below. Of particular importance has been an improvement in detection capabilities, allowing full-scan (40 - 400 daltons) electron impact mass spectra to be obtained with only approximately 5 ng of material injected on column. Selected ion monitoring gives detection limits in the range of 100 pg. These figures are particularly noteworthy because they represent values within a factor of 3 of the lowest detection limits possible with the same instrument when used in a GC/MS mode. This is a truly remarkable accomplishment, and one which might not have been anticipated at the outset of the project.

From an industrial perspective, a licensing agreement has been signed between Hewlett-Packard and the Georgia Tech Research Corporation providing an exclusive license for Hewlett-Packard to explore the commercial possibilities of the interface. The research leading to the MAGIC-LC/MS patent preceded the DOE research support for this project. However, DOE support has contributed greatly to the improvement of the interface from an early developmental model with relatively poor performance, to the current state-of-the-art interface which is of great interest commercially.

Interface Characterization

Substantial progress has been made on characterization of the interface, in terms of the aerosol generation and transport mechanisms that control the throughput of the system. The relationships that exist between analyte transport and signal magnitudes have also been studied, in an attempt to generate a preliminary understanding of the relationship between the three variables of aerosol transport, analyte volatility, and mass spectrometer ion count. This is of key interest because of the need to characterize the response sensitivity of the mass spectrometer to compounds of widely different volatilities.

Aerosol Generation. The characteristics of the aerosol generated by the monodisperse aerosol generator (MAG) have been determined, using laser Fraunhofer scattering, in order to determine the influence of important parameters, such as solvent flow, He gas dispersal flow, and solvent type on the properties of the generated aerosol. The detailed studies have demonstrated that while there is a significant difference in the primary (unevaporated) drop size between pure aqueous and pure organic solvents, there is very little difference between the primary drop sizes of aerosols generated from different organic solvents, even those of widely different volatilities, such as acetonitrile and hexanes. This is attributed to the predominance in the aerosol formation process of surface tension-related properties. The primary difference between the solvent types is therefore between water, with a surface tension around 80 dyne/cm, and organic solvents with surface tensions in the region of 30 dyne/cm.

The slightly larger diameters of the aqueous aerosols compared with the pure organic aerosols make efficient solvent removal somewhat harder for high percentage aqueous solutions. This is not very important at low solvent flow rates, but becomes increasingly important at flow rates in excess of 0.5 mL/min. Current studies

are centering on means to overcome this limitation, and ensure that solvents up to 100% aqueous buffers may be used routinely under normal liquid chromatography flow conditions.

Interface Transport Processes. The transport of analyte through the interface has been the subject of a preliminary study, to be expanded upon shortly. A test device has been constructed, based on a specially designed test chamber. The chamber is evacuated with a turbomolecular pump to simulate the pressures normally encountered in the ion source area of a mass spectrometer, and includes a valve system which allows the collection of analyte test aerosol on a removable probe. The probe can be removed through a butterfly valve and O-ring seals. This allows a number of samples to be collected in sequence, without the need to pump down the chamber between runs.

Preliminary data have shown that the current model of the interface is substantially more efficient in analyte throughput than earlier models. The current (Mark IV) model gives approximately 17% throughput, compared to 5% with the previous (Mark III) model. This mass transport improvement of 3.5 x leads to corresponding signal enhancements, which is clearly of analytical importance. Tests have shown that the majority of the remaining aerosol is lost in the two stages of the momentum separator. Detailed studies have also been made to determine at what precise positions the losses occur in the interface. It is anticipated that further design improvements will allow the further reduction in loss processes in the interface, with resultant signal enhancement.

Chromatographic Studies

The practical utility of the interface has been determined by its performance when coupled to a liquid chromatograph. In this regard, the MAGIC-LC/MS interface performs with much fewer restrictions than all other types of LC/MS interface. We have carried out extensive tests of the interface operated with both reversed phase and normal phase separations. Solvent systems tested include MeOH/H₂O; MeOH/H₂O with ammonium acetate buffer; CH₃CN; and C₆H₁₄. All of these solvent systems have proved to be essentially trouble free, and have required no alteration of operating conditions. It has also proved possible to run gradients, up to 50% H₂O composition at 0.5 mL/min solvent flow, without any difficulty. With a higher H₂O percentage in the solvent, or at liquid flows > 0.5 mL/min, the current interface has some difficulty in coping with the very heavy solvent loading imposed on it. This tends to lead to problems of condensation build-up in the evaporation chamber, which can sometimes lead to blockage in the interface. We are currently working on means to improve the water evaporation process for pure aqueous buffers, and feel confident that significant improvements can be made.

A number of solvent and analyte systems have been tried, in an attempt to test the practical performance of the system. These include both reversed phase and normal phase systems. Sample types examined include antioxidants, pesticides, and bis-phenol A dimers, of a type of great interest to the polymer industry. In addition, the interface has been used very successfully with 2.1 mm bore i.d. columns, with no loss of performance, and no detectable peak broadening. This is a truly remarkable feature of the interface, in comparison with the highly noisy peaks characteristic of Thermospray LC/MS. With the Thermospray interface considerable difficulty is also found in performing separations with small-bore columns.

PUBLICATIONS

Journals

1. "Aerosols as Microsample Introduction Media for Mass Spectrometry", R. F. Browner, P. C. Winkler, D. D. Perkins and L. E. Abbey, *Microchem. J.*, **34**, 15 (1986).
2. "An Improved Interface Design for MAGIC-LC/MS", Paul Winkler and Richard F. Browner, *Anal. Chem.*, (1987), in press.

Patents

1. "Monodisperse Aerosol Generator," US Patent No. 4,629,478, issued December 16, 1986.
2. "Monodisperse Aerosol Generation Interface for Chromatography," patent granted, waiting issuance (1987).

Conferences

1. "Aerosol Characteristics of MAGIC-LC/MS," Paul C. Winkler and Richard F. Browner, American Society of Mass Spectroscopists Meeting, Cincinnati, Ohio (1986).
2. "Gradient Elution Liquid Chromatography/Mass Spectrometry Using a Monodispersed Aerosol Generation Interface," American Society of Mass Spectroscopists Meeting, Cincinnati, Ohio (1986).
3. "Studies with Compounds of Environmental and Biological Interest Using MAGIC-LC/MS," Lawrence E. Abbey, David Bostwick, Paul Winkler and Richard F. Browner, American Society of Mass Spectroscopists Meeting, Cincinnati, Ohio (1986).
4. "MAGIC-LC/MS - A Powerful Detector for Liquid Chromatography," Richard F. Browner, Oak Ridge National Laboratories, Analytical Chemistry Division Seminar (1986), invited talk.
5. "Gradient Elution Studies with MAGIC-LC/MS", Richard F. Browner, Deborah D. Perkins, Paul C. Winkler, and Lawrence E. Abbey, 3rd International Symposium on LC/MS Interfacing, Montreux, Switzerland (1986), invited talk.
6. "A Study of Selected Compound Classes and Their Response for the MAGIC-LC/MS Interface" Deborah D. Perkins, Paul C. Winkler, and Richard F. Browner, Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Atlantic City, NJ (1987).
7. "LC/MS: Will it MAGICally Change our View of Mass Spectrometry?" Richard F. Browner, Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Atlantic City, NJ (1987), invited talk.
8. "Transport Properties, Loss Mechanisms and Signals in MAGIC-LC/MS," Richard F. Browner, J. Daniel Kirk, Debbie A. Garrett, and Deborah D. Perkins, American Society of Mass Spectroscopists Meeting, Cincinnati, Ohio (1987).

Symposia Organized

"LC/MS and SFC/MS: Will they replace GC/MS?", Conference Symposium at 1987 Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy.

RESEARCH GOALS FOR 1986-87

Interface Characterization and Development

Transport of Buffers. The flow dynamics of the interface are not fully understood yet. This has a negative impact on certain specific aspects of practical operation of the device. In particular, the tendency of the interface to clog after extended use with high concentration buffer solutions is a problem which must be addressed. It is hoped that further studies of aerosol deposition and transport will enable this difficulty with the interface to be resolved.

Solvent Evaporation Properties. As yet, the rates and degree of completion of solvent evaporation are not fully understood, particularly for the all-important aqueous solvent systems. As a consequence, studies will be conducted to further investigate the influence of various instrument operating parameters, such as aerosol dispersion gas, evaporation chamber temperature, momentum separator operating pressures and orifice sizes on the transport efficiency of the interface.

Particle Characterization. The precise nature of the desolvated particles reaching the ion source area of the mass spectrometer has not yet been properly characterized. We propose to collect representative portions of the aerosol for scanning electron microscope studies. The studies will be carried out for different solvents, and with different analyte concentrations. This will give valuable information regarding the relationship between initial analyte concentration, diameter of the resultant desolvated particle, and the magnitude of the ion count in the mass spectrometer.

Ion Generation

Study of Vaporization and Ionization Mechanisms in the Mass Spectrometer. To date, there is only available a relatively imprecise understanding of the vaporization and ionization processes which occur in the ion source region of the mass spectrometer. We propose to study systematically the relationship between compound type, particularly compound volatility, source temperature, and ion count. This is most important as part of gaining a more complete understanding of the processes leading to ion formation.

Fast Atom Bombardment Studies. We have been able to obtain on loan a fast atom bombardment (FAB) source from Hewlett-Packard, and propose to use this for FAB studies compounds introduced with the MAGIC-LC/MS interface. We will attempt two types of studies. In the first, the particle beam will impinge on a flat surface in the particle beam path. The impacted particles will then be subjected to FAB bombardment, and the spectra observed. In a second, and potentially more far-reaching study, a crossed-beam experiment will be attempted in which the fast atom beam will intersect the desolvated particle beam in the ion source area of the mass spectrometer. It is hoped that FAB spectra will be generated by this means, thus providing a rapid "on-the-fly" means of generating mass spectra for those compounds incapable of

generating EI or CI spectra with the interface. This will extend the molecular weight range of compounds accessible with the interface very greatly.

Tests of the Interface with Selected Compounds

As a continuing component of the project, selected types of compounds of particular interest to energy-related processes will be examined using the interface, to determine the MAGIC-LC/MS interface's applicability to such samples. Samples to be examined will include certain coal extracts, whose chromatographic separations have already been substantially investigated.

LIBRARY DOES NOT HAVE

Progress Report

September 1987 - November 1989

U. S. DEPARTMENT OF ENERGY

UNIVERSITY CONTRACTOR, GRANTEE, AND COOPERATIVE AGREEMENT
RECOMMENDATIONS FOR ANNOUNCEMENT AND DISTRIBUTION OF DOCUMENTS

See Instructions on Reverse Side

1. DOE Report No. DOE/ER/13435-5	3. Title "FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE." Program Report	
2. DOE Contract No. DE-FC-05-85ER 13435		
4. Type of Document ("x" one) <input checked="" type="checkbox"/> a. Scientific and technical report <input type="checkbox"/> b. Conference paper: Title of conference _____ Date of conference _____ Exact location of conference _____ Sponsoring organization _____ <input type="checkbox"/> c. Other (Specify) _____		
5. Recommended Announcement and Distribution ("x" one) <input checked="" type="checkbox"/> a. Unrestricted unlimited distribution. <input type="checkbox"/> b. Make available only within DOE and to DOE contractors and other U. S. Government agencies and their contractors. <input type="checkbox"/> c. Other (Specify) _____		
6. Reason for Recommended Restrictions _____		
7. Patent and Copyright Information: Does this information product disclose any new equipment, process, or material? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, identify page nos. _____ Has an invention disclosure been submitted to DOE covering any aspect of this information product? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, identify the DOE (or other) disclosure number and to whom the disclosure was submitted. Are there any patent-related objections to the release of this information product? <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If so, state these objections. Does this information product contain copyrighted material? <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes If so, identify the page numbers _____ and attach the license or other authority for the government to reproduce.		
8. Submitted by Richard F. Browner, Regents Professor Organization GEORGIA INSTITUTE OF TECHNOLOGY		
Signature _____	Phone (404) 894-4020	Date 8-17-90

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USE ONLY

9. Patent Clearance ("x" one)
☐ a. DOE patent clearance has been granted by responsible DOE patent group.
☐ b. Report has been sent to responsible DOE patent group for clearance.

FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED
LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE
(MAGIC-LC/MS)

Progress Report

December 1, 1989 – November 30, 1990

Richard F. Browner

School Of Chemistry and Biochemistry
Georgia Institute Of Technology
Atlanta, GA 30332-0400

October 1990

PREPARED FOR THE U.S. DEPARTMENT OF ENERGY
UNDER GRANT NUMBER DE-FG05-85ER13435

ACCOMPLISHMENTS DURING GRANT PERIOD DECEMBER 1, 1989 to
NOVEMBER 30, 1990

Studies with Thermal Vaporization Properties of Particle Beam Interface

One of the most important aspects of particle beam LC/MS is the interaction of the solvent free particle with the heated ion source chamber. Our studies have demonstrated that the particles reaching the ion source region of the mass spectrometer are typically in the size range of 20-100 nm diameter. Particles of this size vaporize rapidly at the temperature of the ion source, after collision with a heated wall surface. However, the precise nature of this interaction, the time period for which the particle adheres to the wall, the rate of energy transfer from the wall to the particle and the subsequent transfer of the molecular species into the vapor phase are not well characterized. Consequently, we have carried out a series of studies with a various test compounds in order to determine the influence of temperature on the vaporization and decomposition properties of these molecules.

We have selected both thermally stable and thermally labile molecules in order to establish a framework for estimating the competitive rates at which molecules are thermally desorbed from a heated surface and at which they absorb internal energy. The absorption of thermal energy solely in the molecule/surface bonds will result in production of intact vapor phase species, whereas absorption of energy into the internal (vibrational) states of the molecule will result in substantial decomposition of the molecule, and probable loss of the molecular ion. The test compounds used were a series of polynuclear aromatic (PAH) compounds covering a wide range of molecular weights from two-ring naphthalene (128 amu) to twelve-ring perylene (531 amu). The vaporization properties of these compounds show little evidence of thermal degradation under any conditions, as they are extremely thermally stable, and so make an excellent reference point for comparison with less thermally stable species. The less thermally stable species examined were aldicarb, a highly thermally labile pesticide and cholesterol, which readily loses water when subjected to high temperatures. The appearance of the mass spectra of these two molecules under conditions of thermal decomposition are for aldicarb the decrease in the magnitude of the molecular ion peak, and for cholesterol a reduction in the ratio of the intact molecular ion (386 amu) to the intensity of the molecule minus a water molecule (368 amu). The ratio for a near ideal situation would have a 386/368 ratio of approximately 4:1.

Our studies have show some very interesting trends to date. While we have not as yet explored the situation at very high temperatures, and have run only at temperatures of < 325 °C, nevertheless, the extent of thermal decomposition has been shown to have a direct relationship to the mass loading of material on the heated ion source surface. Mass loading is controlled by varying the mass of analyte species injected into the LC injection loop. As the mean diameter of the generated aerosol is known, this allows the calculation of the mean diameter of the desolvated particle reaching the heated ion source of the mass spectrometer. It has been shown by these studies that the production of intact molecular ions from thermally labile species bears a direct relationship to the particle size reaching the heated surface, which in turn is directly related to the effective film thickness on the surface. The thinner the film thickness, the faster the vaporization process which occurs, and so the more rapidly the molecule/surface bonds are broken and the

less prevalent thermal decomposition of the molecular species becomes. This has been demonstrated to lead to a remarkable reduction in, for example, the ratio of 386/368 ions for cholesterol. At high mass loadings (1 μ g injected) and high temperatures (325 °C) the 386/368 ratio may be as low as 2.0, whereas at lower mass loadings (100 ng injected) the 386/368 ratio is close to the "ideal" value of 4.0.

Further studies are being pursued in which a new, externally heated probe, which can be raised to temperatures as high as 500 °C will be used. It is hoped that by increasing the rate of desorption from the heated surface to even high values that the time of residence of thermally labile species on the high temperature surface will be further reduced, and will allow the production of relatively intact vapor phase molecules from higher molecular weight species than had been thought possible previously using EI or CI mass spectral generation. Additional studies in this area will also examine the very interesting observation that the vaporization of high molecular weight species, such as Gramicidin S (m.w. 1152 amu) are significantly enhanced in the CI mode compared to the EI mode of ionization. The primary difference between these two modes of ionization is the pressure in the ion source. For EI spectral generation it is typically 2×10^{-5} torr, whereas for CI mode it will be in the high millitorr to low torr range. We believe that the enhancement of signal in CI mode for highly involatile species is primarily due to this pressure increase, and we intend to investigate whether control of pressure may be a major factor in which could be used in enhancing the vaporization of involatile, high molecular weight species. This is an aspect of particle beam LC/MS which is receiving particular attention, as attempts are being made to extend its range of applicability to ionic compounds of environmental and biological interest.

Fast Atom Bombardment Particle Beam LC/MS

Combining particle beam mass spectrometry with FAB mass spectrometry has proved to be a promising approach for the generation of spectra from non-volatile compounds.¹ The great potential for on-line HPLC FAB mass spectrometry system has created the need for better understanding of the fundamental processes which occur in the particle beam LC/FAB MS system. The role of the matrix has been, and will continue to be, a major point of investigation. One specific area of concern is matrix loading. Interest in the influence of matrix loading on FAB signals achieved stimulus when Caprioli reported a significant improvement in S/N with continuous flow FAB using low percentages of matrix, e.g.(5%-20%).² Since that time, Heine has studied matrix loading in static FAB, again finding improvements in S/N with low percentages of matrix.³ During the last year, our research has addressed matrix loading effects for a range of surface active and non-surface active compounds in three different matrices: glycerol, 3-nitrobenzyl alcohol, and thioglycerol. Additionally, the time dependence of FAB spectra generation in the particle beam system has been examined and contrasted with ion generation in normal probe FAB work.

PB LC/FAB MS provides a valuable approach for the analysis of non-volatile compounds. Compounds are ionized by the FAB beam, and spectra result which are similar to spectra produced using classic techniques. Samples are introduced into the source of the mass spectrometer in a relatively straightforward manner. Also, the ability to control the amount of matrix added not only reduces the amount of background due to the matrix, but also decreases contamination of the source. When the presence of matrix with the sample is detrimental to the chromatography, post column addition of matrix may be

performed with little loss of chromatographic integrity. Addition of matrix through the target produces higher sensitivity and no corruption of the chromatography; however, the frequency of source maintenance will increase due to contamination from continual bombardment of the matrix.

Under flow injection conditions, the system displays a high degree of stability over several hours. The degree of stability is, however, dependent on the mode of matrix addition, the type of matrix used and the amount and type of sample used. When matrix is added to the sample, stability is affected by three things, type of matrix, amount of matrix, and number of injections. The more involatile matrices like glycerol tend to collect on the skimmers in the momentum separator, reducing transport efficiency. The end result is that signal decreases as the number of injections increases. More volatile matrices like thioglycerol and 3-nitrobenzyl alcohol are less likely to collect on the skimmers and this gives better stability for a given number of injections; however, some form of blockage is eventually likely to occur, ultimately leading to a reduction in analyte transport. In this situation the matrix loading will determine how many injections are possible before stability suffers. Experimentally, it is observed that after several injections, the target becomes stained. This is a result of matrix interaction with the FAB beam. It is not clear whether this process affects the signal stability; however, background was observed to increase slightly during this period.

PB LC/FAB MS is useful for a wide range of compounds, although there is considerable variation in response between them. Response is dependent on the choice of compound, matrix, and ionizing gas, as well as the performance of the interface, and the condition of the mass spectrometer. Response varies greatly with compound type. Aerosurf (a quaternary ammonium salt) deposited on the matrix gave a detection limit of 50 ng, while several micrograms of the azo dyes were necessary to produce useful spectra when deposited onto the matrix. This behavior may be related to a number of factors, including surface activity, gas-phase basicity, and insolubility in the matrix. Response is also dependent on the matrix used. This was evident with erythromycin, which showed relatively good response using "magic bullet" as matrix, poor response with NBA, and no response with glycerol. The performance of the interface will also affect response through changes in transport efficiency. The condition of the mass spectrometer may also exert a major effect on response. Specifically, the tune of the mass spectrometer is critical, and varies considerably from matrix to matrix, especially when matrix is placed on the target. For example, thioglycerol requires a completely different set of tune values compared to glycerol. This is most likely explained by the difference in vapor pressure of the two compounds.

Results from studies involving matrix loading showed that response is dependent upon the ratio of matrix to analyte. An order of magnitude increase in signal was observed when the optimum amount of matrix was used. Quantitative response was found to be dependent upon available surface area. It was shown that a 50% reduction in the amount of matrix resulted in a substantial decrease in linearity. A linear plot of concentration vs. peak area for the matrices studied showed a concentration effect similar to that seen with Beer's law. At higher concentrations the surface area was insufficient to accommodate additional analyte, and so the curve bent back towards the concentration axis.

It was also observed that better sensitivity was obtained when matrix was placed on the target, rather than combined with the sample. There are two explanations which can account for the observed results. When matrix is mixed with the sample, the viscosity of the sample is changed. Changes in the viscosity will produce changes in the drop size distribution upon sample nebulization. If the droplet size is increased significantly, then analyte transport will be decreased, causing a reduction in sensitivity. A second possibility is that the particle beam from the interface is deposited on the surface of the matrix only, with no penetration of the surface. On the surface, analyte is independent of diffusion processes and is more readily ionized by the FAB beam. Because Aerosurf is a surfactant it will inherently tend to reside on the matrix surface, and so it is difficult to determine whether or not it penetrates the surface of the matrix. Erythromycin, which has much less surface activity, was therefore used to compare its properties with those of Aerosurf. When injections were made onto the NBA matrix, initially very small signals were seen. After 5 minutes of fast atom bombardment, the signal increased to a maximum and then rapidly decreased. Apparently the erythromycin was able to diffuse to the surface only when a substantial amount of matrix had evaporated. These findings indicate that the particle beam penetrates the surface of the matrix; however, earlier studies using "magic bullet" produced well defined peaks immediately after injection. Further study is necessary to determine the interaction which is occurring between the particle beam and the surface of the matrix. This type of phenomenon must be explained in order to produce the performance and predictability necessary for on line chromatographic analysis.

Future FAB LC/MS Research

At the present state of development of the FAB work, a number of general conclusions may be drawn: 1) PB LC/FAB MS is a novel and versatile approach for the production of ions from semi-volatile and non-volatile compounds. 2) Spectra produced with LC/FAB MS are similar to, if not always identical to spectra obtained using classic or static FAB MS. 3) There are two viable ways to operate PB LC/FAB MS (a) with matrix added to the sample or mobile phase, and (b) with matrix placed directly on the target. 4) The system shows acceptable stability over the time periods necessary for chromatographic runs, although the lifetime of volatile matrices placed directly on the target may not be adequate. 5) PB LC/FAB MS is applicable to a wide range of compounds. However, response varies significantly, depending on the nature of both the compound and the matrix. 6) Chromatographic separations are possible, however, greater response per mass of analyte injected is necessary to avoid poor chromatographic peaks due to overloading the column. 7) Response is dependent on the ratio of analyte to matrix. 8) Quantitative response is dependent on the available matrix surface area and the concentration of analyte on the surface. 9) Mechanistically, it appears that the particle beam penetrates the surface of the matrix material collected on the probe. Analyte must therefore, diffuse back to the surface before it can be ionized by interaction with the atom beam.

A second interesting observation related to ionization involves an observed time lag between the appearance of the analyte ion signal and the matrix ion signal. With the mass spectrometer set to monitor both a matrix ion and an analyte ion in rapid sequence, samples containing matrix and analyte were injected and analyzed. Upon integration it was noticed that the initial appearance of the analyte signal always preceded the matrix signal. Sometimes the time lead was much as 1 second. This phenomenon merits further study for a wide range of analyte and matrix species. PB LC/FAB MS itself provides a unique way to study FAB mechanisms. While the ultimate goal of this research project is to produce a system which is

capable of on-line chromatographic analysis, a better understanding of the nature of the FAB process is central to successful development. To this end, rigorous experiments need to be carried out to determine the precise role of the matrix in the ionization process. Ideally, a number of species with widely different surface activities and gas-phase basicities should be studied. Novel approaches to the delivery of matrix to the target should also have a high priority. A probe similar to a continuous flow FAB probe has been built, which allows matrix to be added to the target without interrupting the experiment. A heater controller has also been built, so that the temperature of the probe may be controlled, thus controlling the evaporation rate of the matrix. A number of different matrices should also be explored, including the use of novel species such as liquid metals, (e.g. gallium). The enhancement of sensitivity should also have high priority. As more is understood about interactions of matrix and analyte, better sensitivity may result. Additionally, significant improvements may be expected from improvements in source design and in development of ion optics more suitable for particle beam/FAB of high molecular weight species.

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PUBLICATIONS UNDER PRESENT GRANT

Reviewed Journals (Citing DOE Support)

"Reversed phase and gradients separations capabilities of the particle beam LC/MS interface," D.D. Perkins, W.E. Harris and R.F. Browner, *Anal. Chem.*, in press 1990.

"Transport Properties of the Particle Beam LC/MS Interface," J.D. Kirk, K. Edman and R.F. Browner, *J. Amer. Soc. Mass Spectrom.*, submitted for publication 1990.

"Vaporization Processes for Involatile and Thermally Labile Species in Particle Beam Liquid Chromatography/mass Spectrometry," W.E. Harris, J. Small and R.F. Browner, *Anal. Chem.*, submitted for publication 1990.

Conference Presentations

"The Next Logical Step: LC/MS in Environmental Analysis," Richard F. Browner, 6th Waldbronner Themen, Enklosterle, West Germany, 1990 (invited talk).

"Particle Beam LC/MS for Environmental Monitoring," Environmental Teleconference, San Jose, CA, 1990 (invited talk).

"Particle Beam LC/MS Interfacing of Environmentally Important Compounds," W. Eric Harris and Richard F. Browner, American Society of Mass Spectroscopists Meeting, Tucson, AZ 1990.

"Fast Atom Bombardment Studies using Particle Beam LC/MS," J. Daniel Kirk and Richard F. Browner, American Society of Mass Spectroscopists Meeting, Tucson, AZ 1990.

"Supercritical Fluid Particle Beam Mass Spectrometry Interfacing for Biologically Important Compounds," American Society of Mass Spectroscopists Meeting, Tucson, AZ 1990.

"LC/MS Interfacing: a Marriage of Particle Dynamics and Particle Ionization"
Richard F. Browner, J. Daniel Kirk, W. Eric Harris and Katherine Edman, Eastern Analytical Symposium, Somerset, N.J. 1990 (invited talk).

"An Overview of Particle Beam LC/MS," Richard F. Browner, J. Daniel Kirk and W. Eric Harris, LC/MS Symposium, Montreux, Switzerland 1990 (invited talk).

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**FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED
LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE
(MAGIC-LC/MS)**

Progress Report

December 1, 1990 - November 30, 1991

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AEROSOL GENERATION AND TRANSPORT PROPERTIES OF PARTICLE BEAM INTERFACE

The operation of the particle beam interface, using either electron impact (EI) or chemical ionization (CI), depends on a five-stage process: (1) aerosol generation (2) solvent evaporation (3) particle beam enrichment (4) particle vaporization and (5) ionization. If ionization is through fast atom bombardment (FAB), then steps (4) and (5) are replaced with the impact of high energy Xe atoms which both vaporize and ionize molecules from the desolvated particles reaching the ion source. The drop size distribution of the initial aerosol plays a critical role in the operation of the entire interface for the following reasons: (1) it determines the rate of solvent evaporation in the desolvation chamber (2) it determines the size of the particles remaining after solvent removal (3) it determines the analyte transport efficiency through the interface and (4) it determines the rate of analyte vaporization from the heated source area into the electron beam. The combined effect of these factors impacts both the qualitative and quantitative nature of the mass spectral information obtained from the interface.

We have carried out an extensive study of the particle beam interface from several aerosol-related perspectives. First, we have studied the characteristics of the aerosol as a function of the operating parameters of the nebulizer. Second, we have attempted to correlate the aerosol characteristics with the *quality* of the mass spectra resulting from several different classes of compounds, covering a wide range of volatility and thermal lability.

1. Primary Drop Size Distribution and Signal.

The nebulizer in the Hewlett Packard particle beam interface is adjustable, by moving the 100 μm fused silica capillary in and out of the He gas jet outlet. Adjustment of the capillary position changes the analytical response from the system, producing a series of peaks and troughs (Figure 1). We have correlated the signal variation as a function of capillary position with the characteristics of the aerosol produced, using a Fraunhofer laser scattering system to measure the aerosol drop size distribution. The influence of nebulizer operation on the aerosol primary drop size distribution is shown in Figure 2 for acetonitrile solvent and Figure 3 for water.

The first characteristic of real note is that the capillary position which gives rise to a *minimum* in response also corresponds to an aerosol with a *smaller* mean drop size than the aerosol which gives rise to the two local maxima. This is indicative that from the perspective of analyte mass transport to the ion source, the production of an aerosol with a significant fraction of drops $< 20 \mu\text{m}$ diameter produces dry particles which are too small to pass efficiently through the momentum separator. The exact nature of the aerodynamic forces which limit the passage of these small particles through the momentum separator, and the extent and nature of the laminar and turbulent flow patterns established, is as yet unknown. We intend to study the particle flow patterns in the interface using laser doppler velocimetry at a later stage of the project.

The shape of the signal response vs. capillary position curve (Fig. 1) is typical for all solvents. However, the exact size distribution of the aerosol formed shifts significantly with solvent type. A comparison of Figures 2 and 3 shows how changing the solvent influences the variation of drop size with capillary position. There is clearly a very significant difference between the behavior of water and of acetonitrile from this perspective. The water aerosol tends to have a preponderance of large drops compared to the acetonitrile aerosol. The drop size

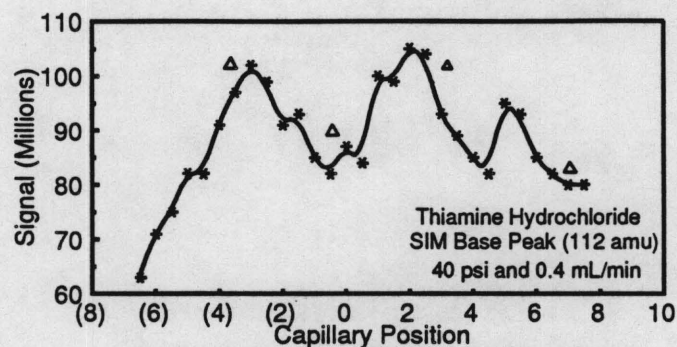


Fig. 1 Response vs. Capillary Position for Particle Beam Nebulizer Δ Position of Capillary for Drop Size Experiments

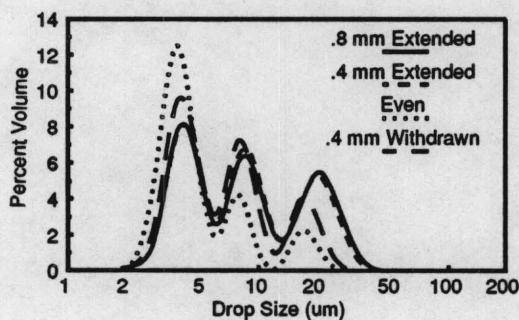


Fig. 2. Variation of Drop Size Distribution with Capillary Position for Acetonitrile

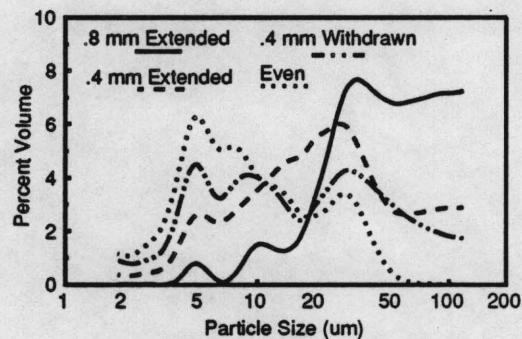


Fig. 3. Variation of Drop Size Distribution with Capillary Position for Water

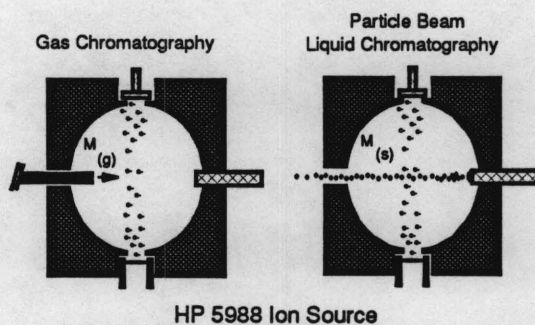


Fig. 4 GC/MS and PB-LC/MS Sample Introduction Paths

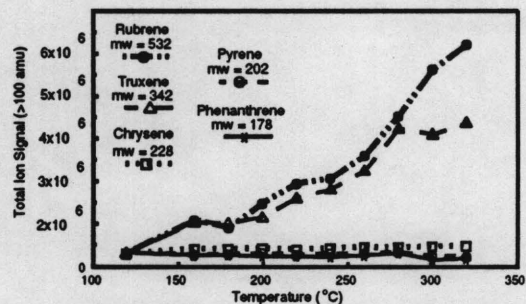


Fig. 5 Response vs. Temperature for PAH (Normalized signal)

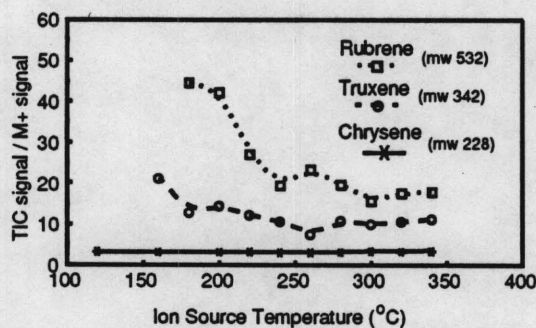


Fig. 6. Total Ion Current/Molecular Ion Signal for Several Polycyclic Aromatic Hydrocarbons

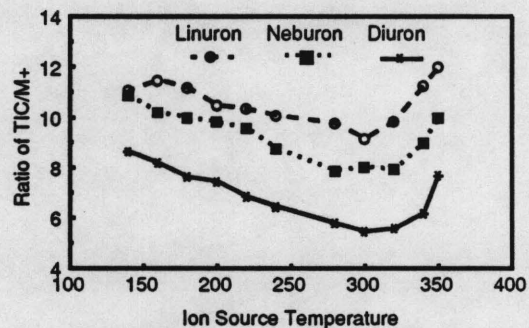


Fig. 7. Total Signal/Molecular Ion Signal for Phenyl Urea Herbicides

distribution of the acetonitrile aerosol is typical of all organic solvents tested, including methanol and hexanes. The size distribution seems to be determined primarily by the surface tension, σ , of the solvent, and all the common LC solvents have surface tension values in the range 30-45 dyn/cm, compared with the water value of 72 dyn/cm. This difference in surface tension between water, on the one hand, and all the organic solvents on the other hand, seems to be quite general, and similar behavior has been observed in studies carried out in our group with pneumatic nebulizers used for atomic emission and elemental mass spectrometry.¹ From our present studies it is not yet clear just precisely what the optimum drop size would be for maximum efficiency of transport through the interface. The size of the particles remaining after solvent evaporation may be related, using a simple model assuming spherical particles, to the original aerosol drop size with the relationship:

$$d_x^3 = d_0^3 \cdot (C/\delta) \cdot 10^{-6} \quad \text{----- (1)}$$

where d_x is the final (spherical) particle diameter (μm), d_0 is the initial drop diameter, C the analyte concentration ($\mu\text{g/mL}$) and δ is the final particle density (g/cm^3). This relationship also demonstrates how the final particle diameter, d_x , is related to the original solution concentration. For an initial injection of 50 ng of analyte in 5 μL , it may be calculated that drops initially smaller than approximately 20 μm will not contribute usefully to the signal, because the desolvated analyte particles coming from these smaller drops will not pass through the system efficiently. It is probably the predominant loss of these smaller drops which accounts for the majority of the analyte transport loss in the interface. With the present interface, a typical transport efficiency is 20%.

2. Differences in Crystalline Structure of Analytes

Our work has also involved generating scanning electron microscope (SEM) measurements of particles collected at the point where they would normally strike the heated mass spectrometer source volume and flash vaporize into the electron beam. We have constructed a test chamber, pumped with a 100 L/s turbo pump, which allows us to carry out these measurements without the need to use the mass spectrometer itself. This test chamber also includes a collection plate mounted on an arm which may be inserted and removed through a vacuum inlet to the collection chamber. This allows the rapid cycling of the collection process, without the need to repeatedly pump down the vacuum chamber. Collection of the desolvated particles has allowed us to both roughly check the accuracy of the predicted dry particle size of the particles reaching the ion source and to determine whether the shape of the particles follows the simple spherical model used for prediction of transport properties of the interface.

Preliminary studies with two chemically similar compounds, tetrahydroxybenzidine (THB) and dimethoxybenzidine (DMB) has revealed some very interesting data. First, the appearance and size of the collected particles does not differ greatly with either water or methanol solvents. This might be considered surprising in view of the greatly different size distributions of the original aerosol drops. However, if the remainder of the interface is considered to act as essentially a high-pass filter, then the similarity in the size distributions of the collected dry particles reaching the ion source region is less surprising. What will be the major difference between the aerosols from organic and aqueous solvents will then be the *fraction* of the initial primary aerosol reaching the source region, which will be greater for the highest percentage of initial drops in the correct size range. If the initial aerosol has drops which *exceed* a certain value, these will also not pass through the interface efficiently. The very large drops, probably those above approximately 70 μm , will be lost by collisions with the walls of the chambers, as their momentum will be too great for them to follow the rapidly changing gas flow patterns.

Of great interest, and somewhat unexpectedly, the different compounds produced particles of entirely different crystalline structure. The DMB particles were largely spherical in shape, apparently made up of a large number of smaller, but uniform sub-units. By contrast, the THB particles were each made up of three or four rod-like crystals joined together in a cluster. It is not yet clear exactly what influence the shapes of these crystals may have on the transport properties of the analyte. However, it may reasonably be assumed that the aerodynamic properties of rod-like crystals will be significantly different from those of spherical crystals. Consequently, it is quite possible that the *transport efficiencies* with which compounds which produce markedly different crystalline forms pass through the interface will differ. This may possibly result in differences in the slopes of the calibration curves for different compounds, due to differences in mass transport efficiency, rather than to differences in either vaporization or ionization efficiency.

VAPORIZATION PROCESSES IN THE ION SOURCE REGION

One of the most important, but frequently neglected, differences between GC/MS and particle beam LC/MS is the vaporization step which must precede ionization in particle beam LC/MS. In GC/MS, the analyte enters the ion source already in the vapor phase, and so is ionized as it passes through the electron beam. By contrast, in particle beam LC/MS, the particle beam must cross the electron beam on its way to collision with the chamber walls, but the molecules will not interact with the beam while they remain in the condensed phase (Fig. 4). When the particles reach the chamber walls, they initially impact with them and momentarily adhere. The individual particles will then absorb energy from the heated surface. Depending on the relative energies of the surface/molecule and intramolecular bonds, the absorbed energy will eventually break one or the other of these bonds, leading in one instance to vaporization and in the other to pyrolysis. Consequently, the generation of intact, vapor phase molecules will depend on both the relative bond strengths of surface/molecule bonds and intramolecular bonds and also on the rate at which energy is fed to the molecule on the surface.

In GC/MS, the ion source temperature is normally set to just exceed the column temperature, and its primary function is to ensure that condensation of the eluting molecules onto cooler surfaces does not occur. As a consequence of these differences in mechanisms, the temperature of the ion source assumes a role of much greater importance in PB-LC/MS than in GC/MS. Some specific ways in which source temperature may influence both signal response and also the *quality* of the mass spectrum is shown in Figures 5 and 6. Figure 5 shows the variation in response for several polycyclic aromatic hydrocarbons (PAH) covering a wide range of molecular weights, from chrysene at 228 Da to rubrene at 532 Da. The response for relatively volatile molecules, such as chrysene is largely temperature independent, and similar signals are observed at temperatures from 150-350 °C. On the other hand, the response variation with temperature for more involatile molecules such as rubrene is far greater, and a high source temperature (> 300 °C) will be essential to obtain a good response from such molecules. The behavior of polycyclic aromatic compounds reflects their relatively high thermal stability. By contrast, many molecules have much lower thermal stabilities than PAH, and so when their source vaporization temperature is raised, they have a tendency to thermally decompose. In this situation, there may exist a competitive tendency for higher temperatures to lead to enhanced vaporization of less volatile species, but this may also be accompanied by greater thermal degradation. This type of trend may be followed by observing the change in the ratio of molecular ion peak to the total ion current generated from all ions in the mass spectrum. The ratio (M^+/TIC) should provide a clear indication of the extent of thermal decomposition of the molecule. Figure 7 shows the situation for several phenoxy ether pesticides, and shows that an optimum temperature of approximately 325 °C should be selected for a combination of best response and best mass spectral quality.

PUBLICATIONS UNDER PRESENT GRANT
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Reviewed Journals (Citing DOE Support)

"Chromatographic Evaluation of the Particle Beam LC/MS Interface," W.E. Harris, D.D. Perkins and R.F. Browner, *Journal of the American Society for Mass Spectrometry*, submitted for publication.

"Transport Characteristics of the Particle Beam LC/MS Interface," K. Edman and R.F. Browner, *Analytical Chemistry*, submitted for publication.

"Aerosol Properties of the Particle Beam LC/MS Interface," W. Eric Harris and R.F. Browner, *Analytical Chemistry*, submitted for publication.

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"Particle Beam LC/MS in Environmental Analysis: Considerations for Vaporization and Ionization of Thermally Labile Species," Richard F. Browner and W. Eric Harris, 8th Montreux LC/MS Meeting at Cornell, Cornell, NY, July 1991, invited talk.

"Particle Size Effects In Aerosol Generation, Transport and Vaporization for Particle Beam LC/MS," Richard F. Browner, W. Eric Harris and Katherine Edman, 202nd ACS Meeting, New York, NY, August 1991, invited talk.

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**FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED
LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE
(MAGIC-LC/MS)**

FINAL REPORT

September 1, 1985 - November 30, 1989

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ACCOMPLISHMENTS DURING GRANT PERIOD SEPTEMBER 1, 1985 to NOVEMBER 30, 1989

Note: This report attempts only to summarize the accomplishments made during the term of the present DOE grant. More detailed descriptions of many projects are contained in publications in the open literature. Research material relevant to ongoing and proposed research projects is also described in the attached proposal requesting renewal of support.

A number of accomplishments have been made during the term of this grant. These include both technical aspects of the project, and developments associated with commercial development of the MAGIC-LC/MS interface.

Technical advances have been made through a number of detailed studies of fundamental processes occurring within the interface. These have led to substantial improvements in the performance of the interface, many of which are detailed below. Of particular importance has been a major improvement in detection capabilities. At beginning of this grant period, sensitivity for many compounds was in the high μg to low mg range. Presently, full-scan (40-400 daltons) electron impact mass spectra may be obtained for many compounds with typically 10-50 ng of material injected on column. Selected ion monitoring gives detection limits in the range of 100-1,000 pg. These figures are particularly noteworthy because they represent values which fall between 3-10x the lowest detection limits possible with the same instrument when used in a GC/MS mode.

From a practical perspective, a licensing agreement signed between Hewlett-Packard and the Georgia Tech Research Corporation led to the development of a commercial version of the interface, which was introduced to the market on July 1, 1988. To date, there are approximately 100 interfaces installed worldwide. The research leading to the original MAGIC-LC/MS patent preceded the DOE research support for this project. However, the metamorphosis of the interface from a laboratory concept to a working reality has taken place entirely under DOE support, during the current grant period. The main thrust of this research has been the study of fundamental aspects of the interface, in order to better understand basic processes occurring in the interface operation.

The MAGIC interface was specifically designed to overcome a number of the functional problems experienced with other LC/MS approaches. MAGIC-LC/MS can be used to generate either EI and/or CI spectra of compounds that are either too involatile or too thermally labile to allow their direct analysis by GC/MS. While early designs of the interface have proved successful in generating EI spectra of involatile compounds and in producing detection limits in the nanogram range, a number of features were in need of improvement.

Problems with earlier models of the interface included: (1) difficulty of maintaining accurate nozzle/skimmer alignment (2) poor reproducibility (3) inadequate sensitivity for many separations, and (4) undesirably large dead volumes in both aerosol generator and aerosol evaporation chamber. Based on this need, and following principles of aerodynamics and particle dynamics, an improved MAGIC-LC/MS interface has been developed. This interface overcomes many of the limitations of earlier models.

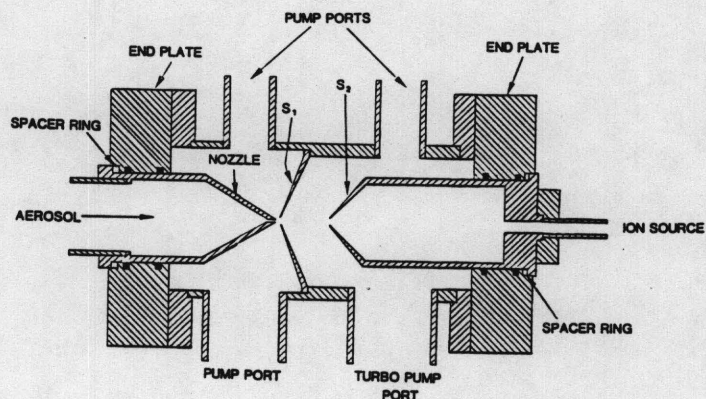


Figure 1: Schematic of Redesigned MAGIC Momentum Separator

Improvements in Interface Design

Aerosol generator. The newly designed aerosol generator uses cylindrical bore fused silica capillary tubing in place of the conical glass tip of the earlier aerosol generator. The fused silica capillary is of the type used routinely for capillary GC applications, and has a polyimide coating. In the new aerosol generator design, a short length of 25 μm i.d. fused silica is connected to a length of 200 μm i.d. fused silica, using a zero dead volume fused silica connector (Valco). The 200 μm capillary tube is used to connect the aerosol generator with the LC column. The liquid jet is formed at the tip of the 25 μm i.d. tube. This aerosol generator is much simpler than the previous design, and seldom clogs.

Momentum separator. Transport efficiency studies have indicated that analyte loss in the MAGIC interface occurs primarily in the momentum separator. The most important analyte loss processes are the result of particle sedimentation, poor nozzle/skimmer alignment and turbulence loss. The earlier MAGIC interface incorporated two cylindrical-bore tubes in the nozzle/skimmer design, with each tube capable of adjustment in the x-y plane at one end only. This approach suffered from two major disadvantages. First, accurate alignment was difficult, because only one end of the tube could be moved during the adjustment process. This tended to cause the axial alignment of the skimmer and nozzle tubes to be disturbed during adjustment. Second, the tubes were typically several centimeters long, which resulted in substantial particle loss due to particle impaction from the expanding beam onto the tube walls.

The improved MAGIC momentum separator (Figure 1) is substantially shorter than the original version, and the nozzle and skimmers are fixed in place radially for proper alignment. The momentum separator body is made from stainless steel. Nozzles and skimmers are machined from 6010 grade aluminum. The nozzle has a 0.5 mm orifice at the apex of a 60° cone. The separation between the nozzle and first skimmer is continuously variable from 0 to 10 mm through the use of shims. Vacuum seals between the various chambers are with Viton O-rings. The first skimmer has a 100° exterior angle and a 95° interior angle, with a 0.5 mm orifice at the tip. The second skimmer has a 45° exterior angle and a 30° interior angle, with a 1.0 mm orifice. The separation between the skimmers is adjustable from 0 to 10 mm. Both vacuum chambers are pumped with mechanical vane (hot oil) pumps of 21.6 m³/h capacity. A tubular vacuum inlet, with the same dimensions as a direct inlet probe (DIP) or standard GC interface probe, is bolted directly to the second skimmer. This allows the interface to be connected rapidly and simply to the mass spectrometer

directly through the DIP vacuum lock. Accurate alignment of the probe to the ion source is then provided by locating the probe tip against the ion source inlet.

The improved design has many advantages over the previous design: (1) it is easier to set up and operate, resulting in less down time of the mass spectrometer (2) the alignment between nozzle and skimmers is fixed and its accuracy depends only on the quality of the component machining (3) the skimmer design is aerodynamically superior, resulting in a less turbulent gas flow through the interface (4) the new momentum separator has higher transport efficiency than the previous design, which results in improved detection limits (5) the lower dead volume in the aerosol evaporation chamber causes less peak broadening, which improves both interface chromatographic resolution and analyte detection limits.

Interface Characterization

Substantial progress has been made on characterization of the interface, in terms of the aerosol generation and transport mechanisms that control the throughput of the system. The relationships that exist between analyte transport and signal magnitudes have also been studied, in an attempt to generate a preliminary understanding of the relationship between the three variables of aerosol transport, analyte volatility, and mass spectrometer ion count. This is of key interest because of the need to characterize the response sensitivity of the mass spectrometer to compounds of widely different volatilities.

Aerosol Generation. The characteristics of the aerosol generated by the monodisperse aerosol generator (MAG) have been determined, using laser Fraunhofer scattering, in order to determine the influence of important parameters, such as solvent flow, He gas dispersal flow, and solvent type on the properties of the generated aerosol. The detailed studies have demonstrated that while there is a significant difference in the primary (unevaporated) drop size between pure aqueous and pure organic solvents, there is very little difference between the primary drop sizes of aerosols generated from different organic solvents, even those of widely different volatilities, such as acetonitrile and hexanes. This is attributed to the predominance in the aerosol formation process of surface tension-related properties. The primary difference between the solvent types is therefore between water, with a surface tension around 80 dyne/cm, and organic solvents with surface tensions in the region of 30-40 dyne/cm.

The slightly larger diameters of the aqueous aerosols compared with the pure organic aerosols make efficient solvent removal somewhat harder for high percentage aqueous solutions. This is not very important at low solvent flow rates, but becomes increasingly important at flow rates in excess of 0.5 mL/min. Current studies are centering on means to overcome this limitation, and ensure that solvents up to 100% aqueous buffers may be used routinely under normal liquid chromatography flow conditions.

Interface Transport Processes. The transport of analyte through the interface has recently been studied in detail using a specially designed test device. This has a great advantage over the direct use of the interface with our own mass spectrometer, through allowing unrestricted access to the instrument for mass spectral studies and through avoiding the high possibility of source contamination. The setup is based on a test chamber which is evacuated with a turbomolecular pump to simulate the pressures normally encountered in the ion source volume of a mass spectrometer. It also includes a valve system which allows the collection of analyte test aerosol on a removable probe. The probe can be removed through a butterfly valve and O-ring seals. This allows a number of samples to be collected in sequence, without the need to pump down the chamber between runs.

The performance of the interface has been characterized very precisely using different solvent types, ranging from the highly volatile hexanes to the least volatile solvent used, namely water.

Preliminary data have shown that the current model of the interface is substantially more efficient in analyte throughput than earlier models. The current model gives approximately 17% throughput, compared to 5% with the previous model. This mass transport improvement of 3.5 x leads to corresponding signal enhancements, which is clearly of analytical importance. Tests have shown that the majority of the remaining aerosol is lost in the two stages of the momentum separator. Detailed studies have also been made to determine at what precise positions the losses occur in the interface. It is anticipated that further design improvements will allow the further reduction in loss processes in the interface, with resultant signal enhancement.

Chromatographic Studies

A number of solvent and analyte systems have been tried, in an attempt to test the practical performance of the system. These include both reversed phase and normal phase systems. Sample types examined include antioxidants, pesticides, and bis-phenol A dimers, of a type of great interest to the polymer industry. In addition, the interface has been used very successfully with 2.1 mm bore i.d. columns, with no loss of performance, and no detectable peak broadening.

It was previously believed that the factor determining the maximum flow rate would be solvent evaporation rate. If the mobile phase has a high evaporation rate, all solvent droplets would be expected to desolvate before reaching the momentum separator. Heptane ($165 \mu\text{m}^3/\text{sec}$), for instance, would peak at a higher flow rate than methanol ($47.2 \mu\text{m}^3/\text{sec}$). This, however, is not found experimentally. It was also predicted that perhaps the total volume of solvent vapor played a key role. Calculations show that the total volume of heptane at 0.5 mL/min would be 0.0766 L/min and methanol would be 0.280 L/min. One can see that the methanol produces a far greater volume of gas phase molecules. In reality, however, the use of heptane affects the response more dramatically than methanol. The total volume of solvent vapor after evaporation does not therefore appear to account for the apparent trend.

Another possible explanation is that those solvents with higher vapor pressures saturate the atmosphere in the desolvation chamber and produce inefficient evaporation of the remaining droplet. The droplets, instead of desolvating, would impact on the nozzle of the momentum separator. The vapor pressure of heptane < toluene < 2-propanol < acetonitrile < benzene < ethyl acetate < methanol. The observed trend of peak flow rates does not follow the vapor pressure order given above. In addition, there was no visible evidence of impacted solvent to confirm this possibility.

Mobile phases utilized with the MAGIC-LC/MS interface have a useful flow rate range from 0.2 mL/min to approximately 1.2 mL/min. A flow rate of at least 0.2 mL/min is necessary to form an adequate liquid jet with the nebulizer. At high flow rates, solvent will begin collecting on the glass desolvation chamber and on the inside of the nozzle thus incurring losses.

Gradient Elution. There is not a great change in either intensity or peak shape as the solvent composition is changed from 100% hexane to 100% ethyl acetate. The observed change in intensity is cyclical in nature. This phenomena has been described previously. As the peak is sampled by the ion source, it is scanned and then the scan is reset. Because it is not continuous, one may or may not sample the actual peak top. From the data shown here it may be concluded that normal phase gradients may be utilized without concern for significant changes in spectral features or response.

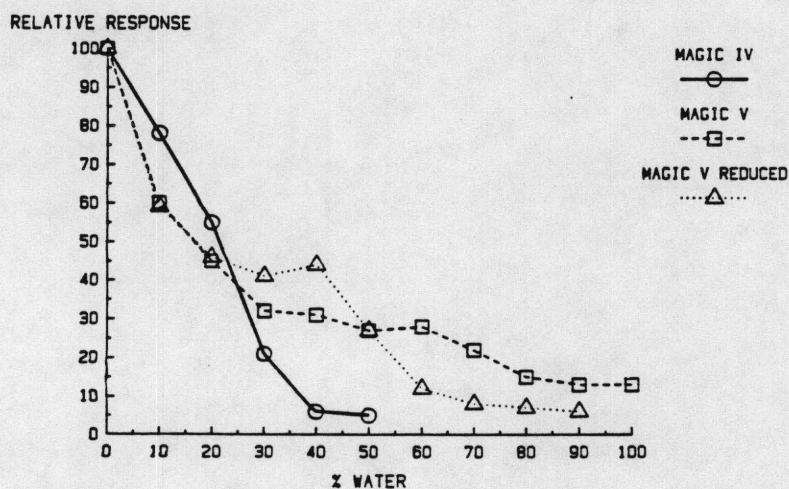


Figure 2: Mass Spectrometer Response vs. Solvent Composition

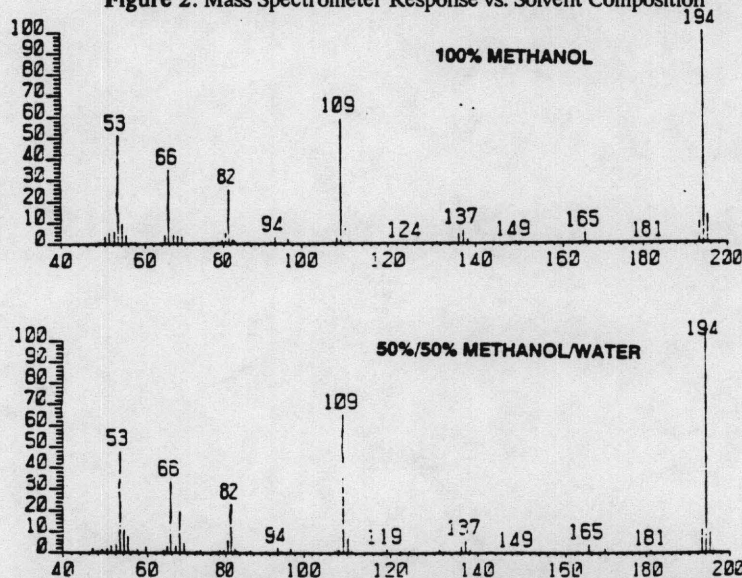


Figure 3: EI Mass Spectra of Caffeine at 100% MeOH and 50/50 MeOH/H₂O

A reversed-phase gradient involves the combination of water with some organic modifier, where the concentration of the organic modifier is gradually increased to bring all compounds in the separation off the column. Unfortunately, the presence of water is a more difficult situation with the MAGIC-LC/MS interface. From Figure 2, it can be seen that the response increases as the organic modifier concentration increases during a reversed-phase gradient. The increase in response from 50/50 methanol/water to 100% methanol will be approximately two and one-half times. These data are promising however, because no modifications were performed such as extraneous heating of interface parts or solvent.

Figure 3 is an example of the spectra obtained while changing the mobile phase composition. The spectra were obtained at 50/50 methanol/water and 100% methanol solvent compositions. Both spectra are nearly identical and also agree with the NIH spectrum. It is noteworthy that no solvent cluster ions are observed in the spectra obtained with the MAGIC-LC/MS interface.

External Variance. In conventional high performance liquid chromatography systems, external variance is caused by an increase in volume between the injector and the detector. External variance can also result

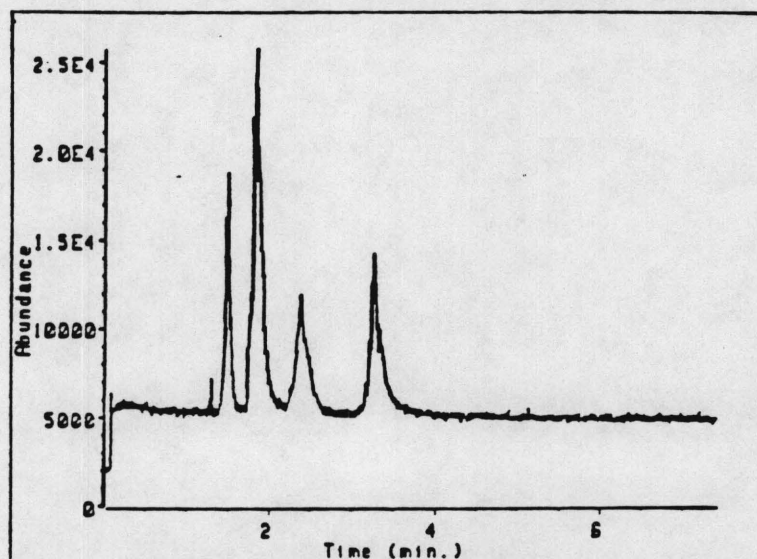


Figure 4: Total Ion Chromatogram Used for Measurement of Peak Variance

from an increase in the sample volume injected. The sources of external variance include large diameter or extra lengths of tubing, fittings which do not meet zero-dead volume requirements, and detector flow cells. In addition, the detector electronics and recording systems may contribute to the overall external variance.

In conventional liquid chromatography, liquid dispersion in the tubing is a consequence of a parabolic velocity profile across the tubing and turbulent rather than laminar flow. The MAGIC-LC/MS interface is an aerosol-based interface and the peak dispersion should be minimal as long as the flow is laminar and not turbulent. The velocity profile should largely be eliminated because less drag will occur against the gas phase and in partial vacuums than along a stainless steel surface of the tubing. In addition, dispersion will be reduced because the sample band will have reduced residence time as compared to a sample passing through the same length of tubing. It appears from the above discussion that the only point where variance may occur appreciably in the MAGIC-LC/MS interface is at the point where vaporization takes place.

The variance of a chromatographic band is measured by calculating the second statistical moment, M_2 , of an eluting band. The total peak variance is a measure of the contribution of independent factors which can be treated as additives in their second moments or variances, σ^2 .

$$\sigma_{\text{ext}}^2 = \sigma_{\text{col}}^2 + \sigma_{\text{inj}}^2 + \sigma_{\text{det}}^2 + \sigma_{\text{conn}}^2 + \sigma_{\text{oth}}^2$$

These independent factors include contributions from the column variance, σ_{col}^2 , the injector variance, σ_{inj}^2 , the detector variance, σ_{det}^2 , any variance that results from connections, σ_{conn}^2 , and other factors, σ_{oth}^2 . Extra-column effects lead to $\sigma_{\text{tot}}^2 > \sigma_{\text{col}}^2$ and this additional band spreading causes the chromatographic resolution to fall short of the inherent column capability.

The method chosen here is that of the exponentially modified Gaussian (EMG) as the skewed peak model. This is a graphical method based on measurement of the retention time, t_R , peak width at 10% peak height, $w_{0.1}$, and the empirical asymmetry factor, B/A . The second statistical moment, M_2 , which gives the total variance, σ_{tot}^2 is given by the equation below.

$$M_2 = w_{0.1}^2 / 1.764(B/A)^2 - 11.15(B/A) + 28$$

This equation is accurate to within $\pm 1.5\%$ for $1.00 < B/A < 2.76$. All experimental values were within these limits.

Figure 4 shows the total-ion-chromatogram collected at 300 °C. Similar chromatograms were obtained for the other experiments. The retention times were obtained from the mass spectrometer data station. Table 1 contains the calculated values for σ_{ext}^2 , the total variance; r , the correlation coefficient; and σ_{ext} , the external variance.

For conventional and fast liquid chromatography columns, the MAGIC-LC/MS interface system appears to be completely compatible at both 300 °C and 220 °C with the capillary tubing transfer line. The maximum allowable external variance for a conventional column is 15 μl . The values for MAGIC at 220 °C and 300 °C are 10.60 μl and 3.84 μl respectively, well below the limit. The MAGIC-LC/MS interface compares favorably to other LC/MS interfaces. The DLI interface has a reported variance of 10-40 μL . Most of this is attributable to the long length of tubing necessary to reach the ion source (at least 40 cm) utilized in most commercial DLI systems. The moving-belt interface has a reported value for fluorene at 1 mL/min of 15.8 μL . The reported variance for the moving-belt interface is compound dependent, however, and significant skewing is reported for polar compounds.

Table 1
Values calculated from linear regression analysis of variance and retention data.

Capillary Transfer Line

Temperature	$r_{\text{ext}}^2(\text{sec}^2)$	r	$r_{\text{ext}}(\text{uL})$
300° C	0.59	.9789	3.84
220° C	4.49	.9077	10.60

Temperature Effects and Compound Response for the MAGIC-LC/MS Interface

The temperature of various components in many LC/MS interfaces has often played a crucial role. For instance, in thermospray LC/MS, a change in the vaporizer temperature of just 10 °C to 20 °C in either direction can modify signal levels by as much as an order of magnitude (1). Temperature control in the moving-belt interface is also crucial to vaporize the analyte off the belt itself; and in DLI, the ion source temperature can have profound effects on both spectra and intensity. Often, complicated means are necessary to control the temperature of LC/MS interface components.

Desolvation Chamber Temperature Studies. Figure 5 shows the results obtained as the desolvation chamber temperature was varied for three different solvent compositions. For a methanol mobile phase, the optimal performance corresponds to a temperature setting of between 27-32 °C measured at the wall. The center of the chamber had a temperature of between 18-26 °C.

As water is added to the mobile phase, the optimum desolvation chamber temperature increases. For a mobile phase consisting of 90% methanol/10% water, the most useful desolvation chamber temperature exists between 34 °C to 36°. An even higher water composition requires more desolvation chamber heating. At 50% methanol/50% water, the best temperature setting was approximately 39 °C.

An important observation of this experiment is that as the percentage of water is increased, the temperature of the desolvation chamber becomes more and more important. A variation in desolvation chamber temperature of 5 °C at 100% methanol causes only a 25% decrease in signal. At 50% methanol/50% water, however, the signal decreases by 65%. The implication of this observation appears

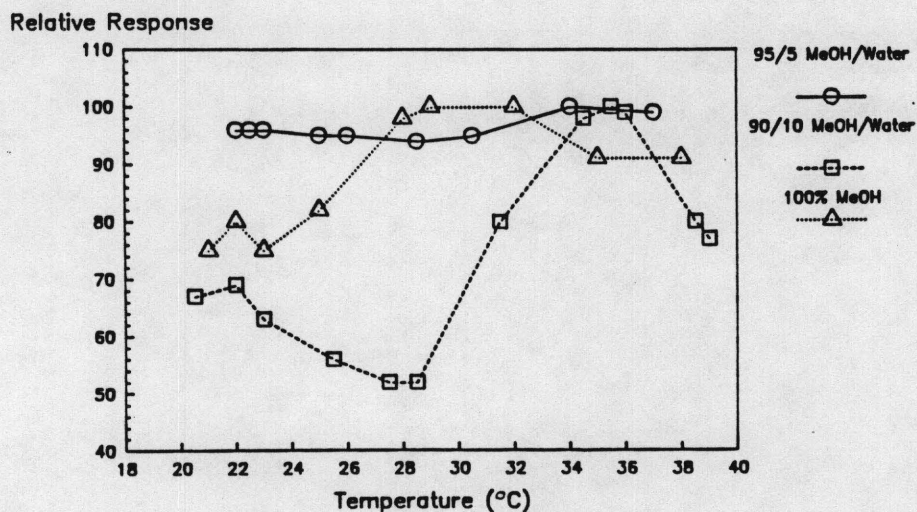


Figure 5: Influence of Desolvation Temperature on Response

to be that some of the problems of reversed-phase gradients can be solved with a variably thermostated desolvation chamber.

Ion Source Temperature Effects. The proposed mechanism for ionization with the MAGIC-LC/MS interface involves vaporization of the analyte particles off the walls of the ion source. It is therefore apparent that the ion source temperature is expected to play an important role in the signal production.

The ion source temperature of the mass spectrometer was varied while all other parameters were held fixed. An easily volatilized compound, methyl stearate, was tested along with some less volatile fatty acids. The results of the test appear in Figure 6. Finally, a thermally labile and involatile compound, glucose, was studied. It may be observed that the more volatile compound is best run at a lower ion source temperatures than the less volatile compound. However, temperatures between 180-280 °C, give good results without affecting the signal by more than 20% for both volatile and involatile compounds. The response of the labile sugar, glucose, peaks at a somewhat lower temperature than the fatty acid response due to the decomposition which occurs at high temperatures producing fragments which appear below the solvent cutoff and are thus not recorded.

Thermally Labile Compounds

Aldicarb. Many compounds are precluded from gas chromatography/mass spectrometry analysis not by their volatility, but by their thermal lability. In other words, these compounds decompose rapidly when exposed to thermal energy. Such a group of compounds is the carbamate pesticides which find much current use due to their effectiveness and low mammalian toxicity. Liquid chromatography is highly suited for thermally labile compounds and its combination with mass spectrometry should give sensitive, specific detection.

Many LC/MS interfaces, unfortunately, utilize heat in the process of transforming the mobile phase and analyte into vapor and analyte gas molecules. Thermal degradation of compounds has been reported with moving-belt LC/MS, as well as, thermospray LC/MS.

In order to test the MAGIC-LC/MS interface capabilities with thermally labile compounds, a sample of aldicarb, was obtained from the U.S. EPA Pesticides and Industrial Chemicals Repository (MS-8)(Research Triangle Park, NC). Aldicarb is a carbamate pesticide sold under the name of Temik. It rapidly degrades in

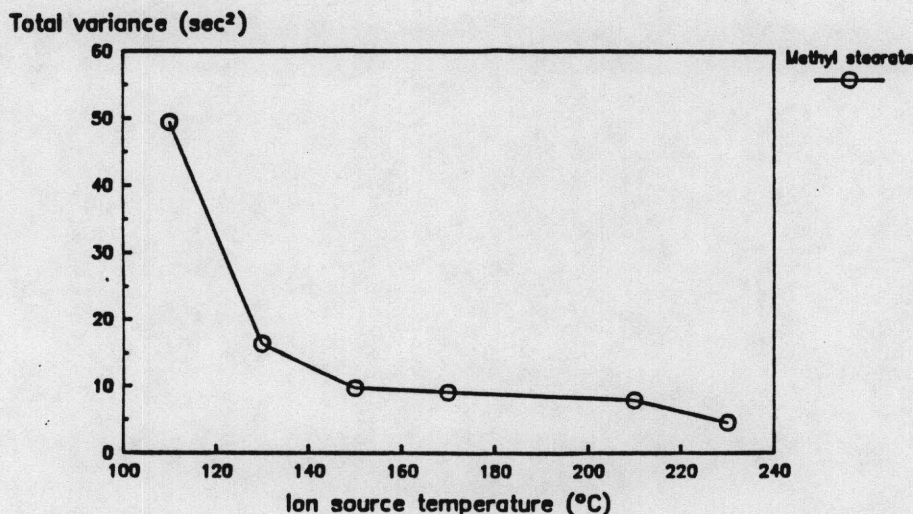


Figure 6: Influence of Ion Source Temperature on Response for Methyl Stearate

the injection port or on the column during gas chromatographic methods. The degradation product of aldicarb is aldicarb nitrile. Aldicarb would produce a molecular ion at m/z 190, whereas the molecular ion for aldicarb nitrile would appear at m/z 115.

At an ion source temperature of 82 °C, enough of the aldicarb molecule remains intact to give a molecular ion at m/z 190. As the ion source temperature is increased to 250 °C, degradation of the compounds clearly occurs. The spectrum obtained at 250 °C resembles the NIH spectrum reported for aldicarb.

Note that it was possible to obtain the intact molecular ion by lowering the ion source temperature. This illustrates that alternate ionization sources which do not require molecules in the gas phase can be utilized with this interface to obtain intact molecules of thermally labile compounds. The degradation of the compound is not significant in the interface itself, but occurs in the ion source.

Fast Atom Bombardment Ionization

The MAGIC-LC/MS interface has been used in an on-line mode to generate fast atom bombardment (FAB) spectra from a range of solvent types. By a relatively simple modification of the instrument, the fast atom beam is directed on the surface of a probe in the ion source of the mass spectrometer. Matrix material (e.g. glycerol) is combined with the analyte, either by post column addition or by placing the matrix directly on the probe. The particle beam then interacts with the analyte suspended in the matrix surface.

Classical FAB spectra are generated in this mode. These compare exactly with probe FAB spectra generated on the quadrupole, and also with spectra generated from a probe using a magnetic sector instrument. The important conclusions which may be drawn from this preliminary study are the following: (1) FAB spectra may be generated with a particle beam interface without any changes from its normal mode of operation for EI and CI spectral generation, with only the addition of a suitable collection surface in the mass spectrometer (2) The FAB mass spectra generated are independent of solvent type (e.g. hexanes, acetonitrile, MeOH, H₂O and gradients of these show no differences). This is because the solvent is removed very efficiently in the interface (3) Solvent flow rates which may be used are typical for EI/CI particle beam mass spectrometry, and are in the range 0.3-1.0 mL/min. (4) Matrices used for normal FAB probe work are also

suitable for on-line particle beam use (5) Signal responses for the same mass of analyte generated directly from the probe and obtained with the particle beam interface are generally comparable.

Selected Applications of MAGIC-LC/MS Interfacing

The optimum columns for use with MAGIC-LC/MS interfacing are: (1) small bore columns with an internal diameter of 2.1 mm i.d., packed with 5 μ m particles. Typically, flow rates range from 0.2 mL/min to 0.6 mL/min. (2) 4.6 x 60 mm columns, packed with 3 μ m particles. Although these columns are usually employed at high flow rates (3-6 mL/min) they also work well at MAGIC's flow rates of 0.2-1.2 mL/min because their small particle size provides fast analysis time and little dilution. They are also ideal for high sample throughput.

Fatty Acids. A number of fatty acids were measured. All spectra showed the molecular ion peak as well as characteristic fragment ions. All peaks contained a base peak at m/z 129. This is not the normal base peak of a free fatty acid. Normally, the base peak is at m/z 74, the McLafferty rearrangement. Due to an impurity, however, the scan began at m/z 80. The base peak at m/z 129 is the fragment $[\text{HOCO}(\text{CH}_2)_6]^+$. Other prominent peaks represented include fragments formed from losses of $[\text{CH}_2]$.

Phenyl Urea Herbicides. Diuron, neburon and metoxuron show significant degradation in gas chromatography/mass spectrometry analyses. Electron impact spectra collected with the MAGIC-LC/MS interface were observed to contain the molecular ion as well as an abundance of structurally significant fragment peaks. The base peaks in all four spectra represent the cleavage of the nitrogen-carbonyl bond which is secondary to the phenyl ring. The appearance of isotope peaks which are indicative of chlorine presence are easily identified in the spectra.

CI spectra showed the $(\text{M}+\text{H})^+$ ion as the base peak. The identification of a chlorine containing compound was again evident with the $(\text{M}+\text{H}+2)^+$ isotope peaks. This class of compounds is one of the most successful yet found to display the capabilities of MAGIC with low nanogram detection limits comparable to thermospray. The spectra are also much more informative than those of thermospray due to the presence of significant fragment ions.

Antioxidants. Antioxidants are commonly used as additives in plastics to enhance their lifetime and physical properties. A mixture of such compounds was readily measured using MAGIC-LC/MS. Elution was in order of molecular weight and all compounds analyzed displayed a molecular ion. BHT showed a base peak at m/z 205, an obvious loss of 15 mass units, the CH_3 moiety. The second eluting compound 2-hydroxy-4(octyloxy)-benzophenone showed a base peak at 213 Da. This fragment is left after the loss of the alkane C_8H_{17} . The 4-4'-methylene-bis-(2-6-di-t-butylphenol) also gave a base peak which results from the loss of a CH_3 group. The final compound octadecyl-3-5-di-t-butyl-4 hydroxycinnamate gave a base peak from a much smaller fragment, m/z 73. Detection limits were in the hundreds of nanograms for this type of compound on the MAGIC interface.

Appendix VIII Compounds. Appendix VIII is a list of chemical constituents which have been shown in scientific studies to have toxic, carcinogenic, mutagenic or teratogenic effects on humans and other life forms.

Appendix VIII compounds are found in Part 261: Identification and Listing of Hazardous Wastes of the Federal Registry. The compounds examined included some benzidine compounds which cannot be analyzed

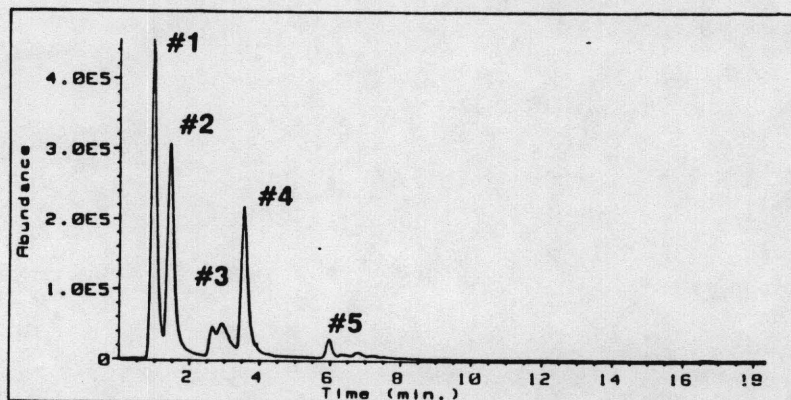


Figure 7: Total Ion Chromatogram for Selected EPA Appendix VIII Compounds. Solvent System pH5 Buffer

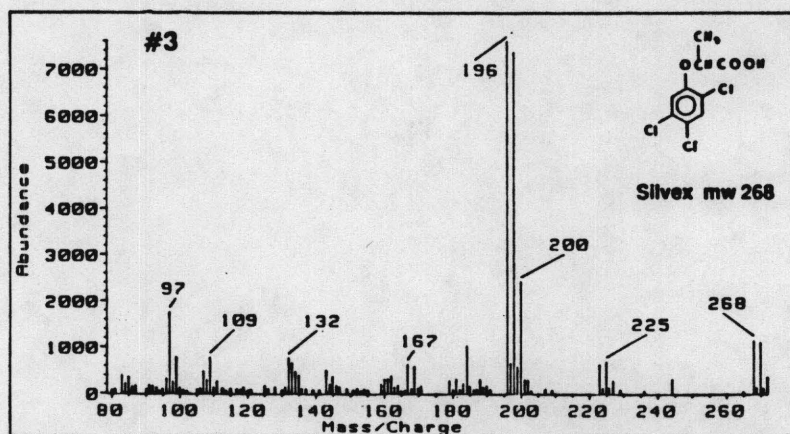


Figure 8: EI Spectrum for Silvex. (Peak #3 of TIC from Fig.7)

by gas chromatography, silvex which is a chlorphenoxy acid herbicide and reserpine, an indole alkaloid tranquilizer which is difficult to characterize by mass spectrometry.

The total-ion-chromatogram for the separation of Appendix VIII compounds appears in Figure 7. The elution order was benzidine, dimethoxybenzidine, silvex, dichlorobenzidine and reserpine. Spectra for silvex and reserpine are shown in Figures 8 and 9. The base peak for all benzidine related compounds was the molecular ion. A molecular ion for silvex is present along with isotope peaks indicative of three chlorine atoms. The base peak for silvex at m/z 196 is the $[Cl_3C_6H_2OH]^+$ fragment. Reserpine displays a considerable molecular ion at m/z 608 and a base peak at m/z 195, the $[^+OC(C_6H_2)(OCH_3)_3]$ fragment ion.

Summary

Scope of the MAGIC-LC/MS interface. As yet, the full range of compound types accessible with the MAGIC-LC/MS interface has not been fully investigated. In general terms, all compounds which are known to be capable of generating EI and CI spectra and which have been tried with the interface have generated

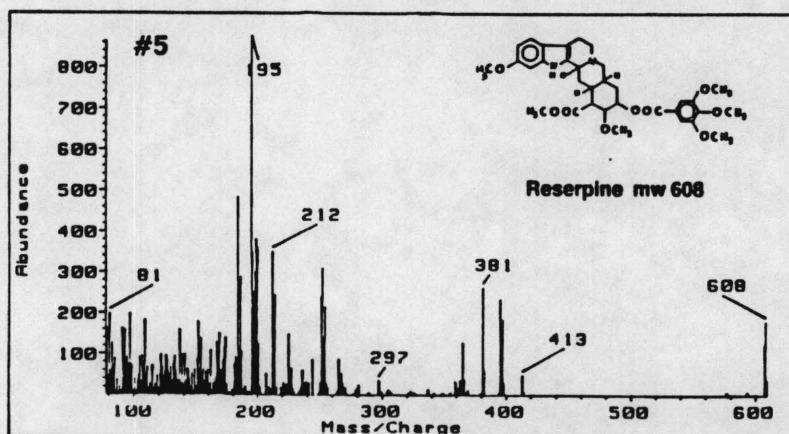


Figure 9: EI Spectrum for Reserpine. (Peak #5 from Fig.7)

good quality spectra. These include carbamate and triazine pesticides, phenyl urea herbicides, polynuclear aromatic hydrocarbons, plant alkaloids, antioxidants and EPA Appendix 8 compounds. Compounds known *not* to generate EI spectra, such as simple sugars and certain azo dyes, predictably do not generate spectra with the current system. The primary mode of ion formation appears to be through a flash vaporization step in the ion source, followed by EI or CI ionization, as selected. Any limitation on compound type accessible with MAGIC-LC/MS will be influenced by: (1) whether the molecule is functionally capable of generating an EI spectrum (2) whether the compound is sufficiently volatile to be capable of forming an adequate vapor pressure in the ion source. This latter property will ultimately represent the interface limitation for generation of EI and CI spectra, rather than the molecular weight of the species. Nevertheless, it is possible to generate good searchable EI spectra with strong molecular ions even for quite involatile species. An example is provided by reserpine, with a molecular weight of 608 daltons, which generates a searchable EI spectrum with a strong molecular ion at m/z 608. Very recently, good CI spectra have been generated of quite high molecular weight species. An excellent CI spectrum of Gramicidin-S (mw 1154) has recently been obtained.

Additionally, the recent work with FAB generation of spectra using on-line MAGIC-LC/MS has been extended to include environmentally important classes of compounds, such as azo dyes. The potential for FAB is to extend the MAGIC-LC/MS mass range initially to values in the 1,000-2,000 Da range, and ultimately well above this value.

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OMB Approval
No. 1910-1400

U. S. DEPARTMENT OF ENERGY

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1. DOE Report No. DOE/ER/13435-8	3. Title "FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE." Final Program Report	
2. DOE Contract No. DE-FC-05-85ER 13435		

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**FUNDAMENTAL STUDIES WITH A MONODISPERSE AEROSOL-BASED
LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY INTERFACE
(MAGIC-LC/MS)**

Final Progress Report

December 1, 1989 - December 31, 1992

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One of the most dramatic developments in mass spectrometry in the last fifteen years has been the evolution of versatile and powerful interfacing approaches that allow direct chromatographic coupling of separations techniques to mass spectrometers. Separations techniques successfully coupled include normal bore and micro-bore reversed phase chromatography and more recently, capillary electrophoresis. The most successful of these approaches have been aerosol-based. Aerosols provide a unique means of converting column effluent into a form that allows ion production in the mass spectrometer. At the present time, the dominant forms of chromatographic interfacing are Thermospray (TSP), Particle Beam (PB) and Electrospray (ES). Each of these techniques compliments the others, and together they have become a rapidly growing field with wide practical applications in environmental, biomedical and energy-related problems of analysis.

This report describes the research carried out under DOE support directed toward fundamental studies with the Particle Beam LC/MS interface (also known as the MAGIC LC/MS interface). The primary goal has been to gain a better understanding of aerosol generation, transport, vaporization, and ionization processes which forms the basis of the technique. Gaining a deeper understanding of the basic physical processes on which particle Beam LC/MS is based provides the most direct way to improve performance benchmarks, such as (1) detection limits (2) quality of mass spectra (3) range of compound types possible, and (4) the ability to interface with all types of separation technique.

Although on-line LC interfacing techniques have been available since the pioneering direct liquid introduction (DLI) work of McLafferty in 1974, it is only really in the last fourteen years that LC/MS has experienced significant growth, following the introduction of Thermospray interfacing (Vestal *et al.*, 1978). In the last few years the pace of growth has accelerated considerably, since the introduction of Particle Beam LC/MS in 1984 (PB-LC/MS) (Willoughby *et al.*) and Electrospray (ES/MS) in 1989 (Fenn *et al.*). PB-LC/MS and ES/MS have been rapidly adopted and have achieved remarkable growth in industrial and governmental laboratories. Numerous conference presentations and research publications have followed, and these techniques are now being used to support much forefront biomedical and environmental research.

In light of this rapid growth, our research effort has been devoted to developing a fundamental understanding of the basic physical process which underlie aerosol mass spectrometry interfacing approaches.

Chromatographic Peak Broadening Studies

Particle beam LC/MS interfacing allows mass spectrometry to be coupled to liquid chromatography separations using a wide range of solvents, with relatively little change necessary from normal LC operating conditions. Although there are some slight response variations when different solvents are used, solvent flows in the range 0.3 to 0.5 mL/min give optimum results. Measurement of external variance produced by the interface shows peak broadening to be negligible for normal bore (4.6 mm i.d.) packed columns, but to be detectable, though relatively slight, for small bore (2.1 mm i.d.) packed columns. Microbore (≤ 1 mm i.d.) columns are unsuitable for present systems both because the liquid flow is inadequate for efficient aerosol generation without addition of a makeup stream, and because excessive band broadening occurs in the interface. The use of solvent gradients causes no significant change in the quality of mass spectra produced by electron impact or chemical ionization. However, the use of 100% water is

found to cause a decrease in response of approximately a factor of 2 compared to other solvents. Separations may readily be carried out in buffer solutions, but buffers must be volatile (e.g. $\text{CH}_3\text{COOH}/\text{NH}_4\text{COOCH}_3$) in order to avoid contamination of the ion source and possible blockage of the momentum separator

Gradient Elution.

Many separation problems in liquid chromatography require gradient elution for adequate resolution. The ability of an interface to work readily with gradients is therefore a very important feature in LC/MS. However, gradient elution has often proved to be a major obstacle in the design of working interfaces. Generally, the problem has arisen because a change in properties of the solvent influences either the aerosol formation process, as with Thermospray, or the ionization process, as with DLI.

LC/MS interfaces in which solvent participates in the ionization process will be affected by solvent composition. For instance in Thermospray LC/MS, operation with gradient elution is only practical with inverse temperature programming of the Thermospray source [1] in order to maintain vaporization of a constant fraction of the solvent. The fraction of solvent vaporized is related to the specific heat of the solvent, and so will vary as the mobile phase composition changes. The nature of Thermospray spectra also changes as the water content of the mobile phase is reduced. Spectra which consist initially primarily of $(\text{M}+\text{H})^+$ ions gain an increasing fraction of $(\text{M}+\text{solvent})^+$ ions as the organic content of the solvent rises.

Solvent elimination interfaces, such as the moving-belt interface, do not appear to experience as much difficulty with gradient separations as do DLI and Thermospray. However, difficulty has been reported in working with high water content solvents at the initiation of a reversed-phase gradient separation [2].

Quality of Mass Spectra Observed with Different Solvents.

In spite of the 2x signal loss found with water, the quality of the EI mass spectra generated with both types of particle beam interfaces showed no detectable differences. Electron impact mass spectra generated for caffeine $\text{C}_8\text{H}_{10}\text{N}_4\text{O}_2$ and thiamine, using the both types of particle beam interface and thiamine, and using three solvents of different composition: (1) 100% methanol (2) 50% methanol/50% water and (3) 100% water appear identical in all important respects. They all gave comparable molecular ions at m/z 194 and m/z 264 respectively, structurally meaningful fragmentation patterns, and correspond closely to the EPA/NIH reference spectra. It is also noteworthy that no solvent cluster ions were observed in any of the spectra obtained with either of the particle beam interfaces, irrespective of solvent composition.

Use of Buffer Solutions.

All practical methods of LC/MS interfacing developed to date require the use of volatile buffers. The particle beam LC/MS interface is no different in this regard, and for much the same reasons as those found with the other systems. The use of involatile buffers, such as phosphate buffers, with the interface results in the presence of an involatile residue which will pass into the mass spectrometer, and rapidly lead to serious contamination of the ion source. Additionally, if high concentrations of such buffers are used, there will be some build up of material around the skimmers in the momentum separator, which in time can lead to partial or total blockage of the orifices.

Particle beam interfaces work well with volatile buffers, and a number of separations have been carried out using ammonium acetate/acetic acid mixtures. The performance of the interface

when used with these buffers appears to be largely unaffected by their presence in terms of both system response and quality of mass spectra generated.

External Variance Measurements.

Adequate chromatographic resolution between adjacent peaks is clearly an important criterion in any LC/MS interface, and is related directly to the peak variance. In a well designed system, the width of the final bands should be due almost entirely to intra-column band broadening, resulting from eddy diffusion, longitudinal diffusion and mass transfer processes taking place on the column.

In a conventional LC system, band broadening external to the column, or external variance, may result from a variety of sources, including an increase in volume between the injector and the detector and an increase in the sample volume injected. Common sources of external variance include large diameter or extra lengths of tubing, fittings which do not meet zero-dead volume requirements, and detector flow cells. In addition, the detector electronics and recording systems may contribute to the overall external variance [3].

The processes which may lead to band broadening in the particle beam type interfaces are more complex than in a traditional liquid chromatograph equipped with a flow cell detector. First, an eluting band must exit the fused silica capillary and form an aerosol which will travel to the ion source of the mass spectrometer in a stream of helium gas. Then, the analyte particles contained in the band passing through the interface must vaporize off the walls of the ion source. The analyte gas phase components will then diffuse back into the electron beam, where they will be ionized and ultimately travel to the detector.

In conventional liquid chromatography, liquid dispersion in the tubing is a consequence of a parabolic velocity profile across the tubing and turbulent rather than laminar flow [4]. Particle beam interfaces are aerosol-based and the peak dispersion should be minimal as long as the flow is laminar and not turbulent. The velocity profile should largely be eliminated because less drag will occur against the gas phase and in partial vacuums than along a stainless steel surface of the tubing. In addition, dispersion will be reduced because the sample band will have reduced residence time as compared to a sample passing through the same length of tubing [5]. It appears from the above discussion that the main site for band broadening should occur in the ion source region at the point of final particle vaporization.

Attention to external variance is particularly important in particle beam LC/MS because of the optimum flow rates of the interface, which match small bore and fast liquid chromatography columns in a nearly ideal manner. These columns place high demands on the liquid chromatography system as they necessitate low external variances in the total system. Visual comparisons between HPLC chromatograms obtained with a UV detector and the total ion chromatogram from the mass spectrometer are often quoted in the literature. This procedure, however, lacks any reliable quantitation which can be used to compare various systems.

Interface Performance.

A series of total ion chromatograms were obtained for a test mixture of carboxylic acids, with retention times measured using the mass spectrometer data station. The total dispersion for each peak was calculated and plotted against the square of the retention time. Table I contains the calculated values for σ_{ext}^2 , the total variance; r , the correlation coefficient; and σ_{ext} , the external variance. In Table II, the maximum external dispersion allowed in order to maintain chromatographic integrity is listed for four types of columns. A comparison between the values of external variance measured for the particle beam interface and the values in Table II reveal the extent of particle beam's compatibility with various column types.

Table I. Variance values calculated from linear regression analysis of variance and retention data.

Type #1 PB Interface			
Temperature (°C)	r_{ext}^2 (s ²)	r	r_{ext} (μL)
300	0.59	0.9789	3.84
220	4.49	0.9077	10.60

Type #2 PB Interface			
Temperature (°C)	r_{ext}^2 (s ²)	r	r_{ext} (μL)
300	0.48	0.9970	4.62
220	3.17	0.9616	11.86

The maximum allowable external variance for a conventional column is 15 μl. The values for particle beam at 220 °C and 300 °C are 10.60 μl and 3.84 μl respectively, which are well below the upper limit.

For conventional and fast liquid chromatography columns, the particle beam LC/MS interface system appears to be completely compatible at both 300 °C and 220 °C, when using the capillary tubing transfer line. The lowest external variance found for the particle beam interface was 3.84 μl. This value exceeds slightly the maximum tolerable limit of 3.1 μl for small bore columns. The use of these columns with the particle beam interface will therefore result in measurable, if slight, band broadening. The maximum permissible external variance for microbore (≤ 1 mm i.d.) columns is 0.7 μl, which is well below the best external variance value found with particle beam. At present, therefore, use of the particle beam interface with these columns would lead to significant loss of chromatographic resolution.

Table II. Maximum allowable external dispersion (μL) for various columns, defined by $\sigma_{\text{ext}} = 0.5\sigma_{\text{col}}$

Column type	σ_{ext} $k' = 1$ [20]
Conventional 4.6 x 100 mm 5 μm packing	15.0
Fast 5.0 x 60 mm 3 μm packing	10.6
Small bore 2.1 x 100 mm 5 μm packing	3.1
Microbore 1 x 100 mm 5 μm packing	0.7

The relationship between external variance and ion source temperature for the particle beam interface demonstrates that dispersion is quite high at low ion source temperatures, but drops to reasonable values at normal ion source operating temperatures. The rate of analyte vaporization from the ion source is an issue of great interest in particle beam LC/MS, as it influences both band breadth and the quality of the mass spectrum produced for thermally labile compounds. The factors involved in these processes are quite complex, and related to both the compound type and the nature of the vaporization surface, in addition to the source temperature. From the perspective of the present study, the need to maintain a source temperature in excess of the minimum value necessary to produce sufficiently rapid analyte vaporization to avoid band broadening is clear. There will be a minimum source temperature necessary to ensure rapid vaporization without band broadening, which will be a direct function of the compound volatility. This factor, which is not normally of importance in GC/MS work, must be taken into account to ensure optimum chromatographic performance.

Dispersion performance of the particle beam interface compares quite favorably with other LC/MS interfaces. The DLI interface has a reported variance of 10-40 μL [6]. Most of this is attributable to the long length of tubing necessary to reach the ion source (at least 40 cm) utilized in most commercial DLI systems. The moving-belt interface has a reported value for fluorene at 1 mL/min of 15.8 μL [7]. The reported variance for the moving-belt interface is compound dependent, however, and significant skewing is reported for polar compounds [8]. The possibility of similar effects occurring with the particle beam interface has not yet been investigated.

Carrier Effects with the Particle Beam Interface

A major issue with particle beam LC/MS is the so-called "carrier effect." This describes the influence of concentration on particle size, and hence particle mass, and its influence on the transport efficiency of analyte passing through the interface. In a negative connotation, this can lead directly to non-linearity in the calibration graphs for species. The "carrier effect" is the effect of adding mass to the solvent-free particles through the medium of a high concentration of matrix added to the analyte solution. After solvent evaporation, the more massive particle remaining reaches a higher momentum in the interface, and so has a higher probability of traversing the momentum separator than the matrix-free particle. This increases the analyte transport, and leads to higher analyte signal in the detector.

However, the influence of analyte volatility could be quite significant in influencing the mass, and hence the momentum of the dried particle as it passes through the interface. Consequently, it might be anticipated that for a series of compounds of varying volatility, the more volatile species would tend to have a lower analyte transport efficiency, and so lead to a lower response in the mass spectrometer than a less volatile homologue, on a mass normalized basis. This should also lead to non-linear calibration curves for volatile species, which should become more linear with the addition of less volatile matrix species.

Calibration curves for naphthalene with pyrene carrier are shown in Figure 1.1. Each curve in the figure represents a different amount of carrier added, from zero to $13.5\mu\text{g}$. Similar curves for anthracene and naphthacene appear in Figures 1.2 and 1.3. (Error bars included in Figure 1.2 represent the greatest RSD observed; RSD's never exceeded 10%.) After analysis of the data, several trends can be observed. Considering first the calibration curves *without* carrier, become clear through the generation of analytical curves for a homologous series of compounds, such as the polynuclear aromatics. These are particularly suitable, as they have simple mass spectra, are unreactive and thermally stable, and cover a very wide range of vapor pressures at room temperature. In these experiments, therefore, naphthalene, anthracene, naphthacene and pyrene were used as model compounds. from the range of 200 to 1500ng, it is observed that linearity increases with decreasing volatility (naphthalene $r^2=0.9536$, anthracene $r^2=0.9797$, and naphthacene $r^2=0.9896$). The sublimation rate of a solid particle is mainly dependent on two factors: the volatility of the species and the surface area to volume ratio (SA/V). Figure 1.4 below illustrates the effect of increasing injection amount on the surface area to volume ratio. The naphthalene suffers from decreased transport efficiencies at lower concentrations, most likely due to a combination of high volatility and high SA/V ratios. In contrast, while anthracene and naphthacene experience almost identical increases in SA/V ratios at the lower concentrations, their decreased volatility limits sublimation and subsequent losses in the momentum separator. At low injection masses ($<1\mu\text{g}$), the SA/V ratio increases very rapidly, leading to greatly enhanced sublimation rates for volatile species.

Figure 1.1 Naphthalene Calibration Curves with Additions of Pyrene Carrier

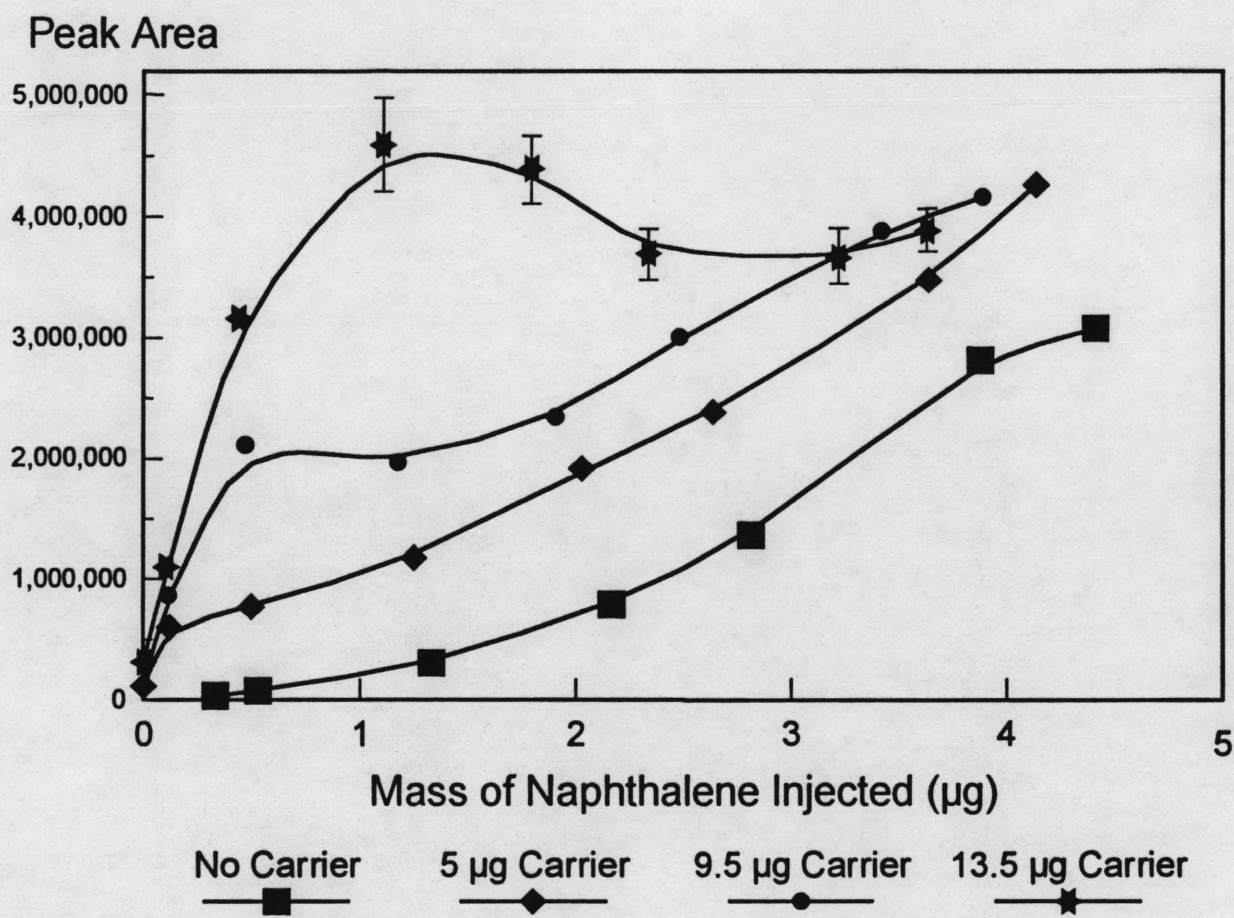


Figure 1.2 Anthracene Calibration Curves with Additions of Pyrene Carrier

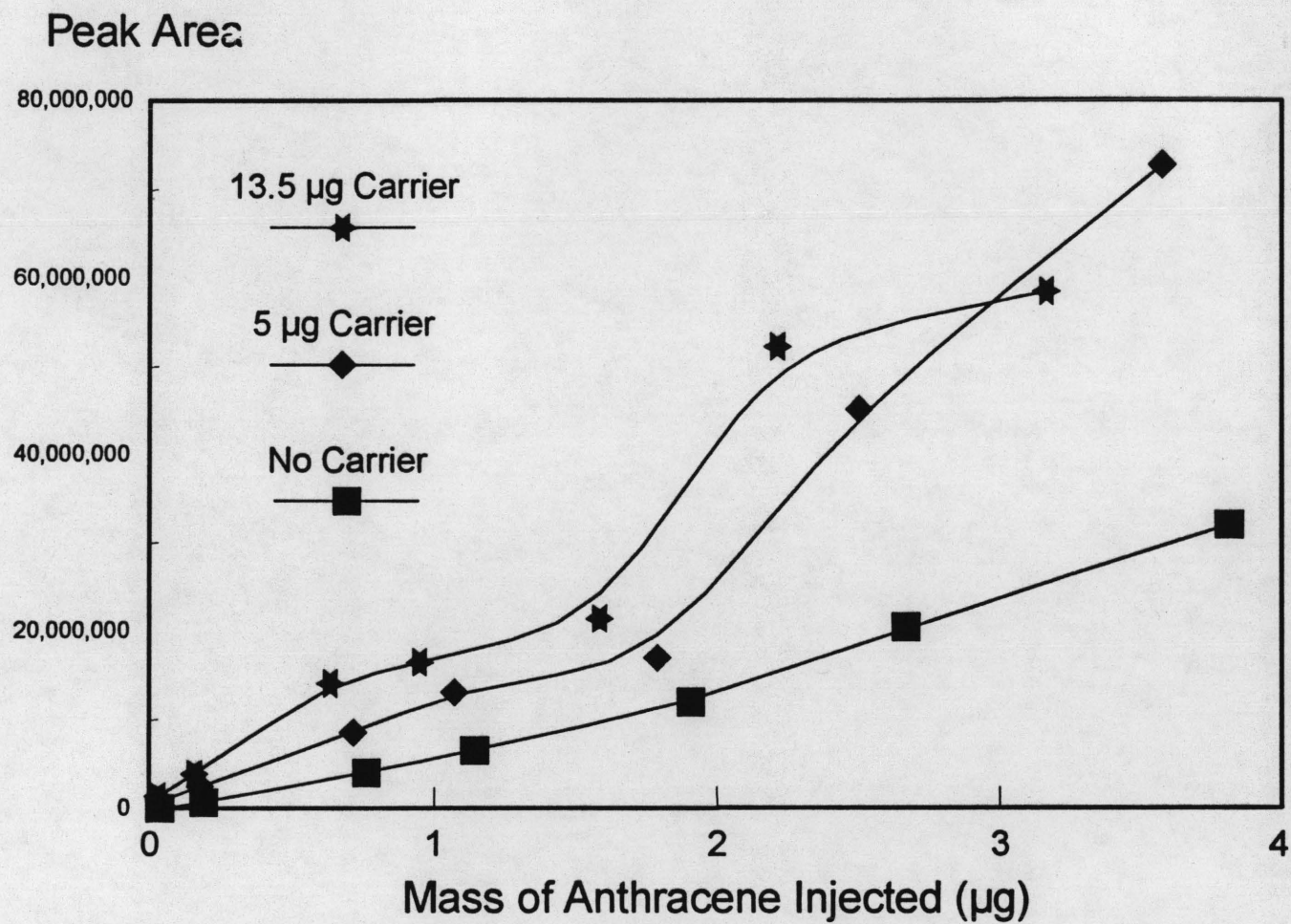
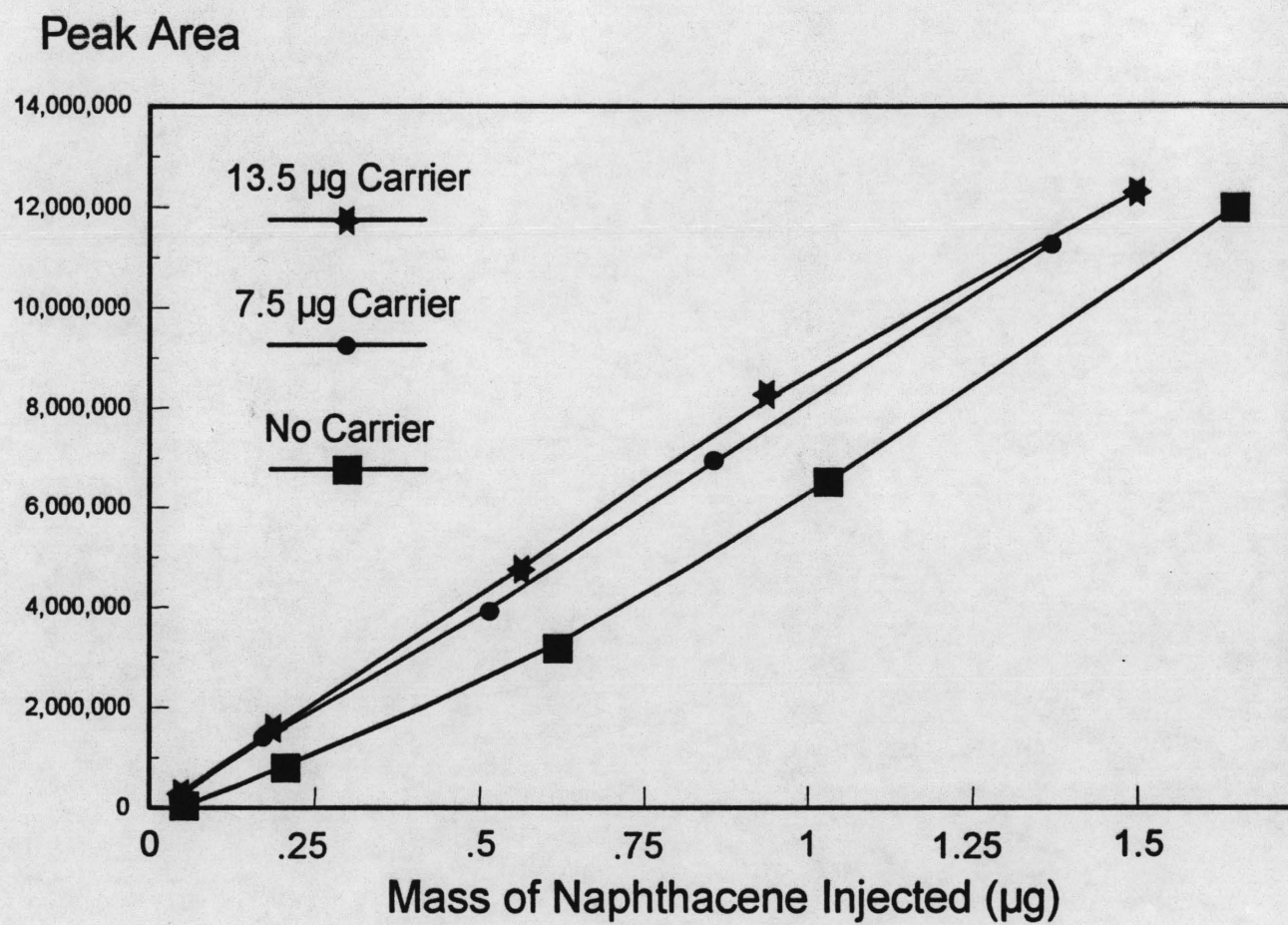


Figure 1.3 Naphthalene Calibration Curves with Addition of Pyrene Carrier



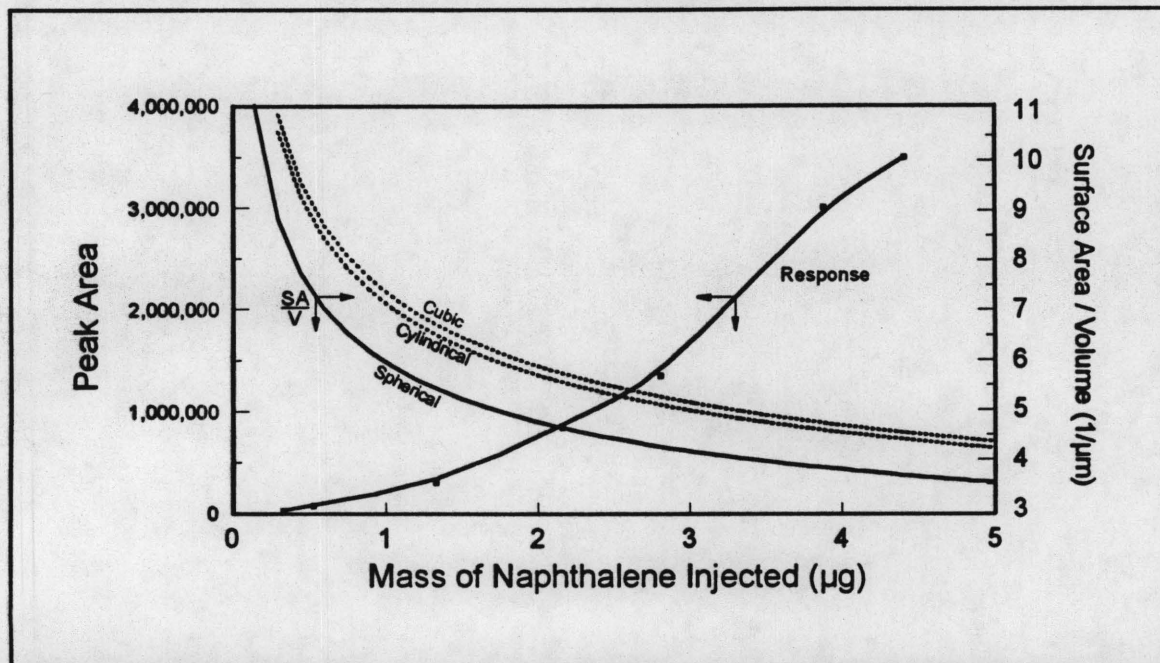


Figure 1.4 Surface Area to Volume Ratio & MS Response vs. Amount of Naphthalene Injected

Naphthalene, being highly volatile, gave relatively low response per mass injected, with a detection limit of only 200ng (without carrier). However, after the addition of nonvolatile pyrene carrier, the detection limit decreased by an order of magnitude (20ng with 13.5μg carrier). Anthracene gave a higher response per unit mass than naphthalene, with a pure compound detection limit of 35ng. After the addition of 13.5μg carrier, the detection limit decreased to 5ng. The highly involatile compound naphthacene gave the greatest response per mass injected, with a detection limit of 500pg. In this case the addition of a nonvolatile carrier had almost no effect on the naphthacene response, even at values near the detection limit. Further experiments were carried out over a narrower injected mass range (near the detection limit), and are presented in Figure 1.5. As can be seen, no significant enhancement in signal was observed after the addition of various amounts of pyrene carrier, even down to 500pg. At the 500pg level, the addition of 13.5μg of pyrene carrier should produce particles with approximately 27,000 times greater mass, yet no enhancement in signal was observed. These data seem to discount the existence of a dominant mass transport effect as suggested by many researchers. Under normal operating conditions, the momentum separator separates gas (solvent and other volatiles) from solid (analyte and other nonvolatiles). This corresponds to a difference in momentum of greater than ten orders of magnitude. Knowing this, it seems difficult to believe that doubling the mass of a particle could increase MS signal by any significant amount. Instead, it seems likely that volatility and the SA/V ratio of the particles play the major role during transport through the interface.

The shapes of some of the curves in Figures 1.1, 1.2, and 1.3 might initially seem to be rather complex. Clearer trends emerge, however, when the data are presented as in Figure 3.10, which shows a plot of enhancement factor (signal with carrier / signal without carrier) versus mass of analyte injected, for the three analytes. This graph clearly shows that the highly volatile naphthalene is greatly affected by the addition of nonvolatile pyrene. The analyte of medium volatility, anthracene, exhibits a medium signal enhancement, and the nonvolatile naphthacene is almost totally unaffected by the presence of carrier. Furthermore, the enhancements for naphthalene and anthracene become much greater at lower injected mass of analyte. Generally, anthracene would not be considered a compound of medium volatility, especially at temperatures near room temperature. However, the path that the particles travel on their way through the interface involves both reduced pressure and highly turbulent zones. While passing into the

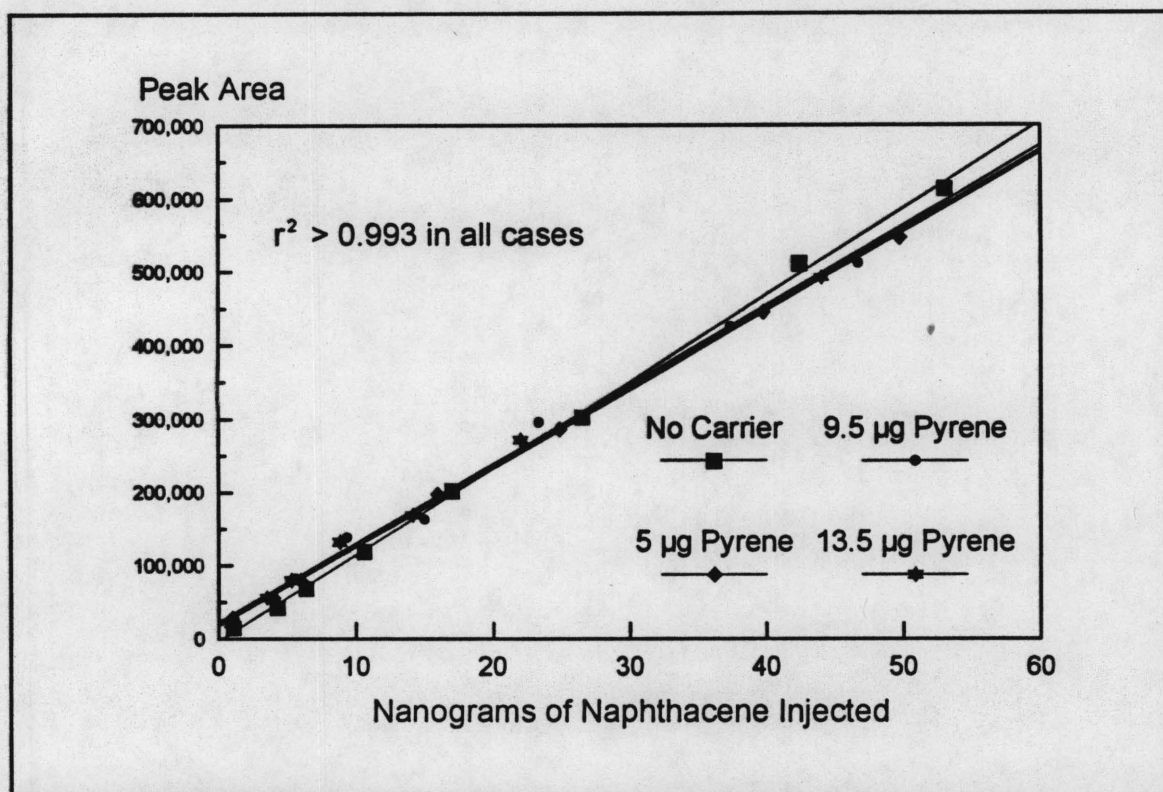


Figure 1.5 Naphthacene with Pyrene Carrier (Near the Detection Limit)

momentum separator, the particles undergo supersonic expansion into a low pressure region, resulting in great turbulence and the formation of a Mach disc. Under these conditions it is not unrealistic to propose that losses due to volatility may occur for anthracene and other compounds of similar volatility.

After examination of Figure 1.1, it is important to note that in the presence of pyrene carrier, as the mass of the naphthalene is increased, the mass of the pyrene remains constant. At low naphthalene concentrations, the pyrene carrier is present in much greater abundance than the naphthalene, resulting in dramatic increases in sensitivity. However, as the mass of the naphthalene increases, the mass of naphthalene in the particle becomes comparable to the mass of pyrene present. Consequently, the naphthalene response approaches that of pure naphthalene. This behavior is similar to a Raoult's Law relationship in which the partial pressure of a liquid is proportional to the mole fraction of that liquid in solution. However, in the case of naphthacene, the addition of pyrene carrier does not produce any significant decrease in the volatility of the already nonvolatile naphthacene particles, so no enhancement is observed.

Conclusions

Based on these experiments, the carrier effect seems to be largely the result of a combination of particle volatility and surface-area-to-volume ratios. The addition of a nonvolatile carrier can, in certain situations, greatly improve PB-LC/MS sensitivity for volatile (even slightly volatile) analytes. However, the addition of such a carrier seems to be effective only when the carrier is less volatile than the analyte. Also, while the effect of particle mass may play a greater role at lower concentrations (e.g. $< 0.1 \text{ ng}/\mu\text{L}$), the mass of the particles seems to have little effect on transport through the interface within the range of 500pg to 13.5µg injected ($\sim 100\text{-}2,800 \text{ nm}$ dry

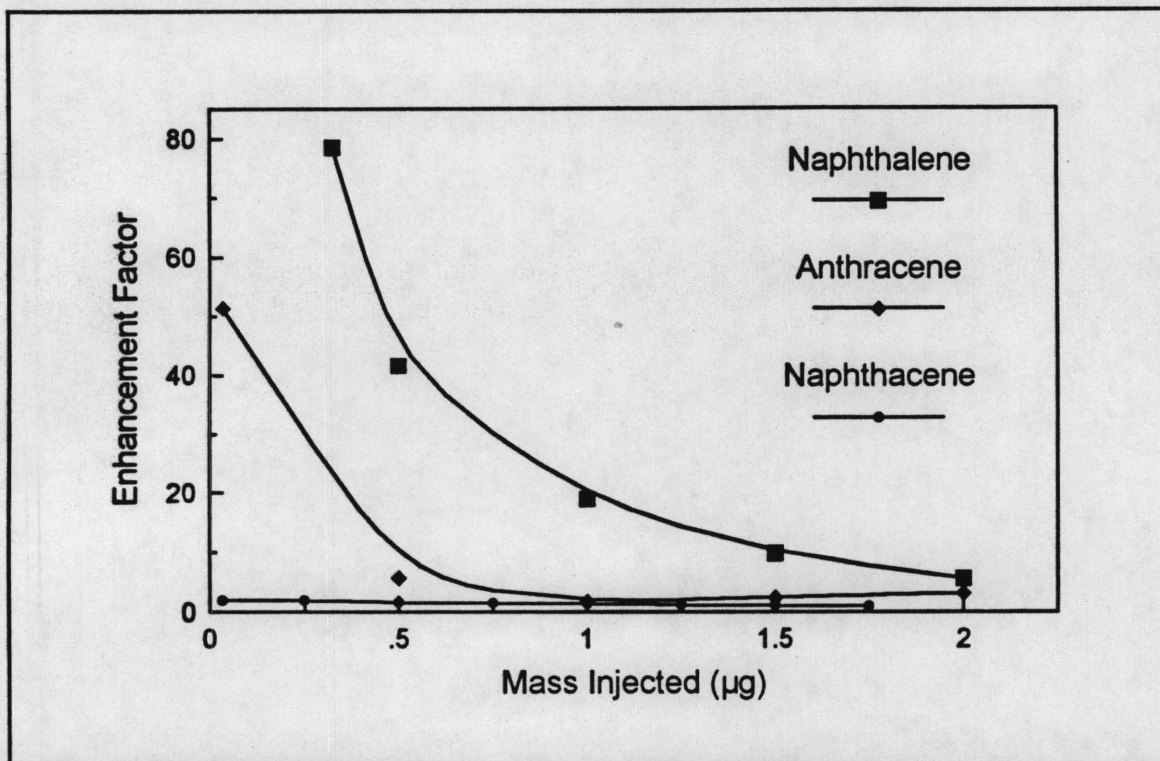


Figure 1.6 Enhancement Factor vs. Amount Injected (13.5 µg Carrier)

particle diameter). In fact, some examples in the literature in which an increase in dry particle mass is used to explain increases in signal, can also be explained on the basis of a decrease in SA/V ratios of slightly volatile analytes [9].

It must also be noted that a decrease in analyte volatility is only advantageous up to a point. Highly nonvolatile species are better transported through the interface; however, once inside the mass spectrometer, analyte vaporization must occur before mass analysis can be performed. Tinke *et al.* reported that of the particles that pass through the momentum separator, only about 10% are vaporized by collision with the inner walls of the hot ion source [10]. The remaining 90% strike the inner walls of the transport tube or the outer opening of the ion source. As a result of this gradient, some particles are flash vaporized, some vaporize much more slowly at lower temperatures, and some are not vaporized at all. This phenomenon results in decreased sensitivity, as well as considerable peak broadening. These researchers demonstrated that increased sensitivity and decreased peak broadening of some nonvolatile compounds could be initiated by derivatization to form more volatile compounds [11]. Therefore, both transport *and* vaporization must be considered when appraising PB performance. (It should be noted that most newer versions of PB-LC/MS instruments have undergone design improvements in which the momentum separator is positioned much closer to the ion source, with little or no transport tube. This greatly reduces peak broadening and increases sensitivity.)

Concerning quantitation and linearity in PB-LC/MS, the carrier effect will continue to cause unpredictable signal intensities. However, several researchers have demonstrated that accurate quantitation is possible with the use of isotopically labelled internal standards. Difficulties in quantitation are common to almost all LC/MS interfaces, including electrospray and thermospray.

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PUBLICATIONS UNDER PRESENT GRANT
DURING REPORT PERIOD

Reviewed Journals (Citing DOE Support)

1. "Chromatographic Evaluation of the Particle Beam LC/MS Interface," W.E. Harris, D.D. Perkins and R.F. Browner, *Journal of the American Society for Mass Spectrometry*, submitted for publication.
2. "Transport Characteristics of the Particle Beam LC/MS Interface," K. Edman and R.F. Browner, *Analytical Chemistry*, submitted for publication.
3. "Aerosol Properties of the Particle Beam LC/MS Interface," W. Eric Harris and R.F. Browner, *Analytical Chemistry*, submitted for publication.

Conference Presentations (Citing DOE Support)

1. "The Next Logical Step: LC/MS in Environmental Analysis," 6th Waldbronner Themen, Enklosterle, West Germany, March 1990 (invited talk).
2. "Particle Beam LC/MS for Environmental Monitoring," Environmental Teleconference on Newest Analytical Methods and Techniques, San Jose, CA, April 1990 (invited talk).
3. "An Overview of Particle Beam LC/MS," Richard F. Browner, J. Daniel Kirk and W. Eric Harris, 7th (Montreux) Symposium on Liquid Chromatography Mass Spectrometry, Montreux, Switzerland, Nov. 1990 (invited talk).
4. "Aerosol Characterization for ICPAES and ICP/MS," Richard F. Browner, 201st ACS Meeting, Atlanta, GA, April 1991, Peter Keliher Memorial Symposium (invited talk).
5. "Strategies for Increasing the Molecular Weight and Polarity Range of Particle Beam LC/MS," Richard F. Browner, Ohio Valley Chromatography Symposium., Heuston Woods, OH, June 1991 (invited talk).
6. "Particle Beam LC/MS in Environmental Analysis: Considerations for Vaporization and Ionization of Thermally Labile Species," Richard F. Browner and W. Eric Harris, 8th Montreux LC/MS Meeting at Cornell, Cornell, NY, July 1991 (invited talk).
7. "Particle Size Effects In Aerosol Generation, Transport and Vaporization for Particle Beam LC/MS," Richard F. Browner, W. Eric Harris and Katherine Edman, 202nd ACS Meeting, New York, NY, August 1991 (invited talk).
8. "LC/MS Interfacing: Fundamental Studies of Aerosol Formation and Transport," Matthew A. Tarr, Kevin L. Goodner, Brian A. Williams, Guangxuan Zhu and Richard F. Browner, 1992 Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, New Orleans, LA, March 1992
9. "Influence of Aerosol and Source Properties on EI, CI and FAB Spectra from Particle Beam LC/MS," Richard F. Browner, W. Eric Harris, J. Daniel Kirk and Jerry C. Richardson, 1992 Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, New Orleans, LA, March 1992 (invited talk).
10. "Optimization of Transport Characteristics for the Particle Beam LC/MS Interface," J. Chris Richardson, Katherine R. Edman, W. Eric Harris, and Richard F. Browner, 1992 Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, New Orleans, LA, March 1992.

11. **"Influence of Aerosol Drop Size on Response Factors and Linearity in Particle Beam Liquid Chromatography/Mass Spectrometry Interfacing," W. Eric Harris, Katherine Edmans, J. Chris Richardson and Richard F. Browner, American Society for Mass Spectrometry Meeting, Washington, D.C. 1992.**
12. **"Particle Beam LC/MS Interfacing for Trace Organic Compound Detection," Richard F. Browner, Society for Applied Spectroscopy, Cincinnati Section, April 1992 (invited talk; SAS Tour Speaker).**
13. **"Strategies for Increasing the Molecular Weight and Polarity Range of Particle Beam LC/MS," Richard F. Browner, Ohio Valley Chromatography Symposium., Heuston Woods, OH, June 1991, (invited talk).**