

# Failure is an Option if you Keep Trying

Perspectives from Academia to Industry to Business

September 11, 2019 | APA Conference | Boston, MA

Mike S. Lee  
Milestone Development Services







# Can You See the Future? – Keep Trying (Failure is an Option)!



- Jeremiah Tipton – CPSA Metabolomics 2019 (Atlanta, GA)



# Drug Discovery is a Story – Tell It and Find It (or Discovery Finds You)!

- What's your story?
- You are here!
  - Establish a framework (a strategy) for your story
  - Education and experience are good places to start
  - Benchmarking – a balance between time and content
- Find your story
  - Movement to find opportunities, fulfillment and success
- Go looking but never forget where you are
  - Relationships may be the key to sustained success as well as contentment and happiness
  - Discovery may find you if failure is an option and you keep trying
- **Sharing Stories Enables Success!**



# What's Mike Lee's Story?

- Biotechnology Entrepreneur
  - Integration of new technologies into clinical and industrial settings
- Over 30 years pharmaceutical industry experience
  - Bristol-Myers Squibb, 1987-1998 (Buspar®, Serzone®, TAXOL®)
  - Milestone Development Services, 1998-present
  - Mozaic Solutions, 2012-present
- Education and Training
  - American Chemical Society
  - American Society for Mass Spectrometry
  - Eastern Analytical Symposium
  - Pittsburgh Conference
  - Symposium on Clinical and Pharmaceutical Solutions through Analysis
    - Annual meetings in USA, China, Brazil and Europe
    - CPSA Charitable Foundation
    - CPSA Institute
- **Thinking Big to Change the World!**



# Framework of Your Career – Education, Experience and Mentors

- Education
  - B.S. Chemistry, 1982 - University of Maryland, College Park, MD
  - M.S. Chemistry, 1985 - University of Florida, Gainesville, FL
  - Ph.D. Chemistry, 1987 - University of Florida, Gainesville, FL
- Industry Experience
  - Bristol-Myers Squibb, 1987-1998
  - Milestone Development Services, 1998-present
- Mentors
  - Rick Yost and Ira Rosenberg





# Find Your Story – Digital LC and Precision Medicine (Mozaic Solutions)

- Revolutionize analytics in the pharmaceutical, biotechnology and diagnostic industries
  - Movement away from platforms that require expert training to expert systems that feature pre-set applications dedicated to a specific solution
- Lead the movement toward personalized healthcare
  - Analysts, technicians and patients will not need to know how the technology works; only the information provided and what to do with it

- **Digital LC Enables Personalized Healthcare**

# The Market Story – Global Pharmaceutical Industry Perspectives

- Research & Development Cost
  - No guarantee of success
- Market and Geographical Shift
  - Aging population
  - Prevention and diagnosis
  - Asia
  - Personalized medicine
- Diagnostics
  - Accurate and efficient
- Biotechnology
  - Genetic differences
  - Precise treatment
- **On the Brink of a Healthcare Revolution**

# The Opportunity – Considerations in a Post-Genomic Society

- Clinical knowledge management
- Patient information
- Virtual patient
- **Personalized medicine**
- Disease at the atomic scale
  - DNA
  - Genetic vaccines
  - Biomimetic engineering
- Stem cells
- **The Desire for Longevity is a Key Driver**
  - Brain
  - Aging



# But Wait! – What Does Drug Discovery Success Look Like?

- Clinical **knowledge** management
  - Patient **information**
  - Virtual **patient**
  - **Personalized** medicine
  - **Disease** at the atomic scale
    - DNA
    - Genetic vaccines
    - Biomimetic engineering
  - Stem cells
- 
- The Desire for Longevity (**success**) is a Key Driver
    - Opportunity redefined

# But Wait! – What Does Drug Discovery Success Look Like?



John Martin led biotech firm Gilead Sciences for two decades as CEO through March 2016.

Martin, who has a PhD in organic chemistry, worked at Bristol-Myers Squibb and Syntex before joining Gilead in 1990 as chief scientist.

Gilead made its mark with several antiviral drugs to treat HIV.

# But Wait! – What Does Drug Discovery Success Look Like?



John Martin, 61, is a University of Chicago chemist with a Golden State University MBA specializing in marketing.

He started his professional career at Syntex in 1978, and then moved to Bristol-Myers Squibb (\$BMY) in 1984.

At BMS, he served as director of antiviral chemistry. He jumped ship in 1990 to be Gilead's (\$GILD) vice president for R&D. By 1996, he had become CEO and president.



# John Martin – Drug Discovery Success!

John C. Martin (businessman)  
From Wikipedia, the free encyclopedia

## **Syntex Corporation**

Martin worked at [Syntex Corporation](#) from 1978 to 1984.

## **Bristol-Myers Squibb**

Martin was director of antiviral chemistry at [Bristol-Myers Squibb](#) from 1984 to 1990.

## **Gilead Sciences Inc**

Martin joined the American [biotechnology](#) company [Gilead Sciences](#) in 1990 as its vice president for research and development. He was Gilead's [CEO](#) from 1996 to 2016. He became chairman in May 2008, and executive chairman in 2016.

# John Martin – Drug Discovery Success!

John C. Martin (businessman)  
From Wikipedia, the free encyclopedia

At Gilead, Martin helped to develop [Atripla](#), a single pill combining Gilead's drug Truvada (a combination of tenofovir and emtricitabine) with Bristol-Myers Squibb's Sustiva (efavirenz).

Truvada and Sustiva were already "the most widely prescribed antiretroviral treatment regimen in the U.S." for the treatment of HIV and AIDS.

One of the benefits of a combined pill was that patients would be more likely to consistently comply with treatment by taking a full dose of the prescribed drugs, which in turn would lessen the chance that drug-resistant HIV strains would develop.

The two companies announced that they would collaborate on the drug in 2004. An initial formulation of once-a-day single-dose Atripla was approved by the [FDA](#) on July 12, 2006.

Purchase of Atripla was included in the [President's Emergency Plan for AIDS Relief](#) (PEPFAR) program.

*Milestone Development Services*

# John Martin – Drug Discovery Success!

John C. Martin (businessman)  
From Wikipedia, the free encyclopedia

In 2014, Martin led the commercialization of Sovaldi ([sofosbuvir](#)) — "a treatment for the liver virus hepatitis C that can cure 90% of patients and generated \$12 billion in revenue in its first year on the market."

Martin is credited with taking Sovaldi from "zero-to-blockbuster in a couple of months" with profits topping \$10 billion for 2014.

However, in April 2014, U.S. House Democrats [Henry Waxman](#), [Frank Pallone, Jr.](#), and [Diana DeGette](#) wrote Martin questioning the \$84,000 price for Sovaldi.

[Sofosbuvir](#) is cited as an example of how [specialty drugs](#) present both benefits and challenges.



# John Martin – Drug Discovery Success!

John C. Martin (businessman)  
From Wikipedia, the free encyclopedia

## **Syntex Corporation = Frog egg**

Martin worked at [Syntex Corporation](#) from 1978 to 1984.

## **Bristol-Myers Squibb = Tadpole**

Martin was director of antiviral chemistry at [Bristol-Myers Squibb](#) from 1984 to 1990.

## **Gilead Sciences Inc = Bullfrog**

Martin joined the American [biotechnology](#) company [Gilead Sciences](#) in 1990 as its vice president for research and development. He was Gilead's [CEO](#) from 1996 to 2016. He became chairman in May 2008, and executive chairman in 2016.

**Footnote:** Everyone Looks Here (At Gilead)! You are the Audience!

Look Where You Are – And Dream Big and Fail!

# But Wait! – What Does Drug Discovery Success Look Like?



Scott Biller, Ph.D. Chief Scientific Officer

Dr. Biller joined Agios as chief scientific officer in September 2010, with more than 25 years of drug discovery and development experience.

Most recently, from 2003 to September 2010, he was vice president and head of global discovery chemistry at the Novartis Institutes for Biomedical Research (NIBR).

Prior to that, Dr. Biller held the positions of vice president, pharmaceutical candidate optimization at the Bristol Myers Squibb (BMS) Pharmaceutical Research Institute and executive director of drug discovery chemistry for the BMS research site in Lawrenceville, NJ.

*Milestone Development Services*

# But Wait! – What Does Drug Discovery Success Look Like?



Scott Biller, Ph.D. Chief Scientific Officer, Agios

He contributed to robust pipelines at both BMS and Novartis, culminating in two medicines launched worldwide (Onglyza™ for the treatment of Type 2 diabetes and Juxtapid™ for familial hypercholesterolemia) and three additional drugs reaching Phase 3 clinical development.

Dr. Biller earned a B.S. in chemistry at MIT, a Ph.D. in organic chemistry at Caltech and was an NIH Postdoctoral Fellow at Columbia University in natural product synthesis.

# But Wait! – What Does Drug Discovery Success Look Like?



Roy J. Vaz received his Ph.D. from the University of Florida, Gainesville in Chemistry with Profs. G. B. Butler and M. Zerner.

He obtained an undergraduate degree from the Indian Institute of Technology, Bombay.

After his Ph.D., he obtained an MBA from the University of Illinois, UC and most recently an MS in Molecular Biology from Lehigh University.

He has authored or co-authored over 50 publications in peer-reviewed journals, contributed towards many book chapter and several patents and edited 2 books related to Antitargets.

# But Wait! – What Does Drug Discovery Success Look Like?



He was responsible for managing the CADD, SB and Cheminformatics efforts at Sanofi, Bridgewater, NJ prior to relocating and supporting small molecule discovery at Sanofi-Genzyme, Waltham, MA.

He was previously Director of the Investigative Product Optimization department at Aventis in Bridgewater.

He has worked with Bristol-Myers Squibb, Hopewell as Principal Scientist as well as Tripos, Inc, St. Louis as a Research Scientist.



# But Wait! – What Does Drug Discovery Success Look Like?



# What Does Opportunity Look Like? – There is a Pattern (Like a Map)

- Foundation of **Education**
    - Experience and Perspective
  - Make, Sustain and Value **Relationships**
    - Seek, Commit, Travel, Adventure
  - Understand the role of **Technology**
    - Combine with key criteria to make good decisions
  - Share **Solutions**
    - Integrate with key leaders and market relevance and need
- 
- Keep Trying – **Failure** is an Option (and story for success)!

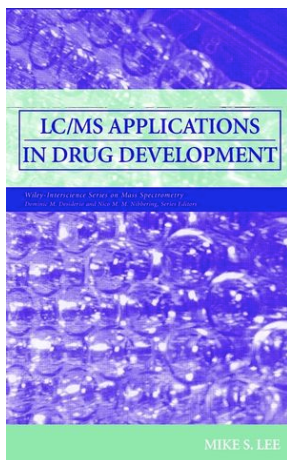
# Personalized Healthcare



# Reverse Engineer Success – Solutions for Healthcare

- Early detection of disease
    - Leads to earlier treatment
  - Response-guided medication
    - Leads to better treatment
  - Clinical trials to mirror patient therapy
    - Companion diagnostics
  - Treatments tailored to specific sub-groups
    - Personalized medicine
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- **Future Treatments will be Tailored to Specific Subgroups**

# Mass Spectrometry Applications in Drug Discovery & Development



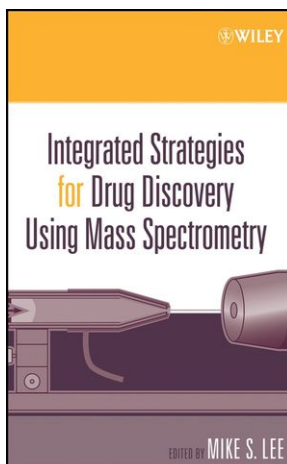
## LC/MS Applications In Drug Development

[Mike S. Lee](#)

ISBN: 978-0-471-40520-7

March 2002

John Wiley & Sons,  
New York, NY



## Integrated Strategies for Drug Discovery Using Mass Spectrometry

[Mike S. Lee](#)

ISBN: 978-0-471-46127-2

June 2005

John Wiley & Sons,  
New York, NY

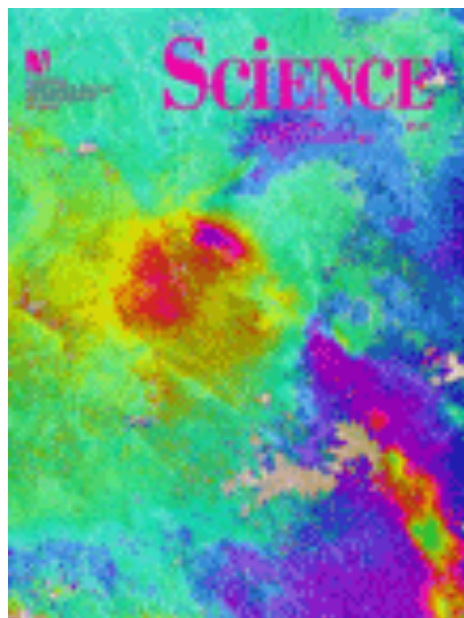


# Method Development Strategies

- Standard Methods
  - Template Structure Identification
  - Databases
  - Screening
  - **Integration**
  - **Miniaturization**
  - Parallel Processing
  - **Visualization**
  - Automation
- 
- **Transformation of the Mass Spectrometer into a Clinical Analyzer**

M.S. Lee, *LC/MS Applications in Drug Development*,  
John Wiley & Sons; New York **2002**

*Milestone Development Services*



# Attomole Protein Characterization by Capillary Electrophoresis–Mass Spectrometry

Gary A. Valaskovic, Neil L. Kelleher, Fred W. McLafferty\*

Electrospray ionization with an ultralow flow rate ( $\leq 4$  nanoliters per minute) was used to directly couple capillary electrophoresis with tandem mass spectrometry for the analysis and identification of biomolecules in mixtures. A Fourier transform mass spectrometer provided full spectra ( $>30$  kilodaltons) at a resolving power of  $\approx 60,000$  for injections of  $0.7 \times 10^{-18}$  to  $3 \times 10^{-18}$  mole of 8- to 29-kilodalton proteins with errors of  $<1$  dalton in molecular mass. Using a crude isolate from human blood, a value of 28,780.6 daltons (calculated, 28,780.4 daltons) was measured for carbonic anhydrase, representing 1 percent by weight of the protein in a single red blood cell. Dissociation of molecular ions from  $9 \times 10^{-18}$  mole of carbonic anhydrase gave nine sequence-specific fragment ions, more data than required for unique retrieval of this enzyme from the protein database.

The molecular elucidation of biochemical events at the cellular and subcellular level is increasingly dependent on innovative methodologies for molecular characterization and imaging (1). These techniques have been especially successful for pre-

lected specific (“targeted”) compounds, but their ability to reveal and characterize unknown biomolecules at the single-cell level is limited. Molecular complexity is a primary problem. Microcolumn mixture separation, especially capillary electrophoresis (CE) (2), can efficiently and rapidly separate  $<10^{-10}$ -liter samples to detect attomole ( $10^{-18}$  mol) components, a level suitable for minor component analysis in a

Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, NY 14853, USA.

\*To whom correspondence should be addressed.





# Attomole Protein Characterization by Capillary Electrophoresis–Mass Spectrometry

Gary A. Valaskovic, Neil L. Kelleher III

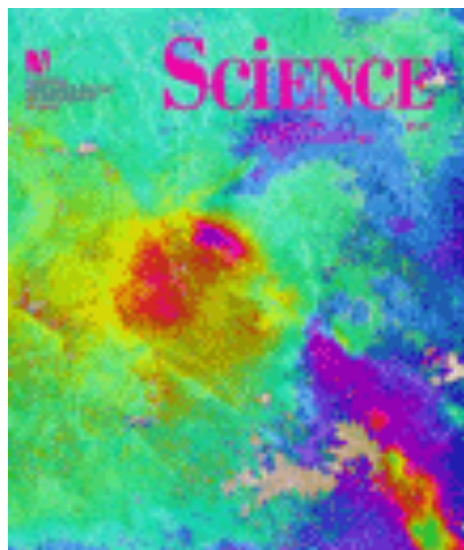
Electrospray ionization with an ultralow flow rate directly couple capillary electrophoresis with tandem mass spectrometry for the separation and identification of biomolecules in mixtures. This method provides full spectra (> 20 kDa daltons) at a rate of 1000 spectra per minute.



1,780.6 daltons representing 1 molecular ion, fragment ions, protein database.

compounds, but characterize un- single-cell level complexity is a primary mixture separation by electrophoresis and rapidly able to detect components, a level of analysis in a





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# Attomol

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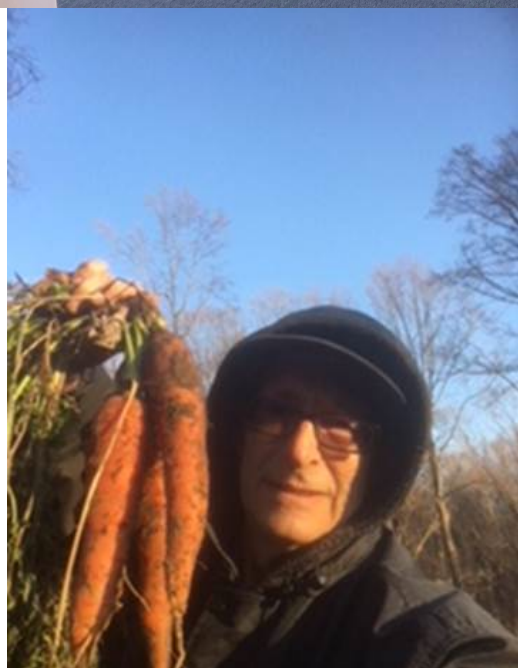
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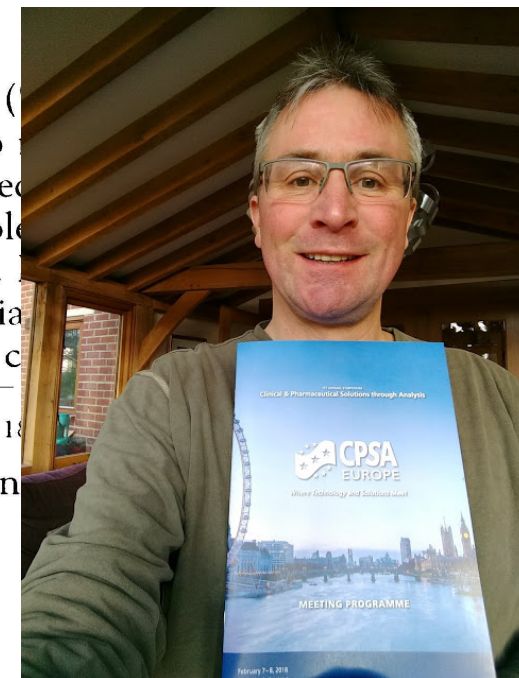




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 a single red blood cell. Dissociation of molecular ions  
 hydrazide gave nine sequence-specific fragment ions,  
 the retrieval of this enzyme from the protein database.



The molecular elucidation of biochemical events at the cellular and subcellular level is increasingly dependent on innovative lected specific ( their ability to known biomolec







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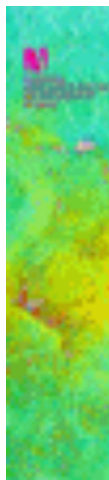
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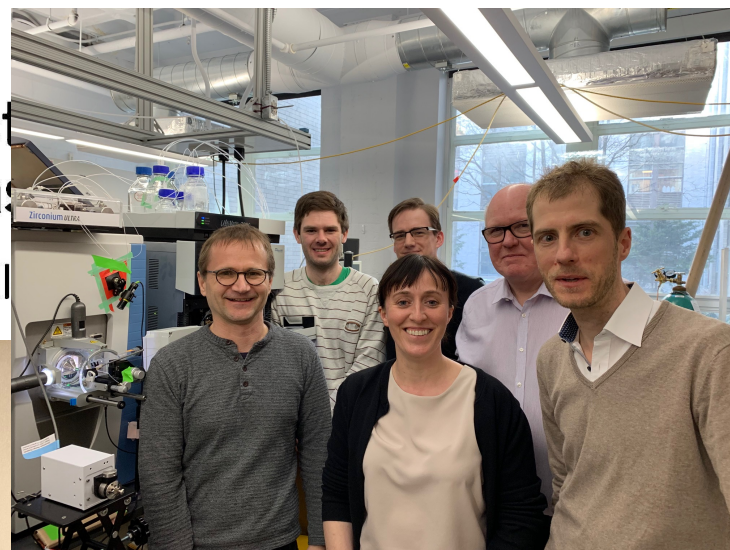






# Attomole Protein Characterization by Electrophoresis–Mass Spectrometry

by A. Valaskovic, Neil L. Kelleher III, and David A. Valaskovic



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28,780.6 daltons  
... representing 1  
... of molecular ions  
... fragment ions



... Chemistry, Baker Laboratory, Cornell University, Ithaca, NY 14853, USA.

... correspondence should be addressed.



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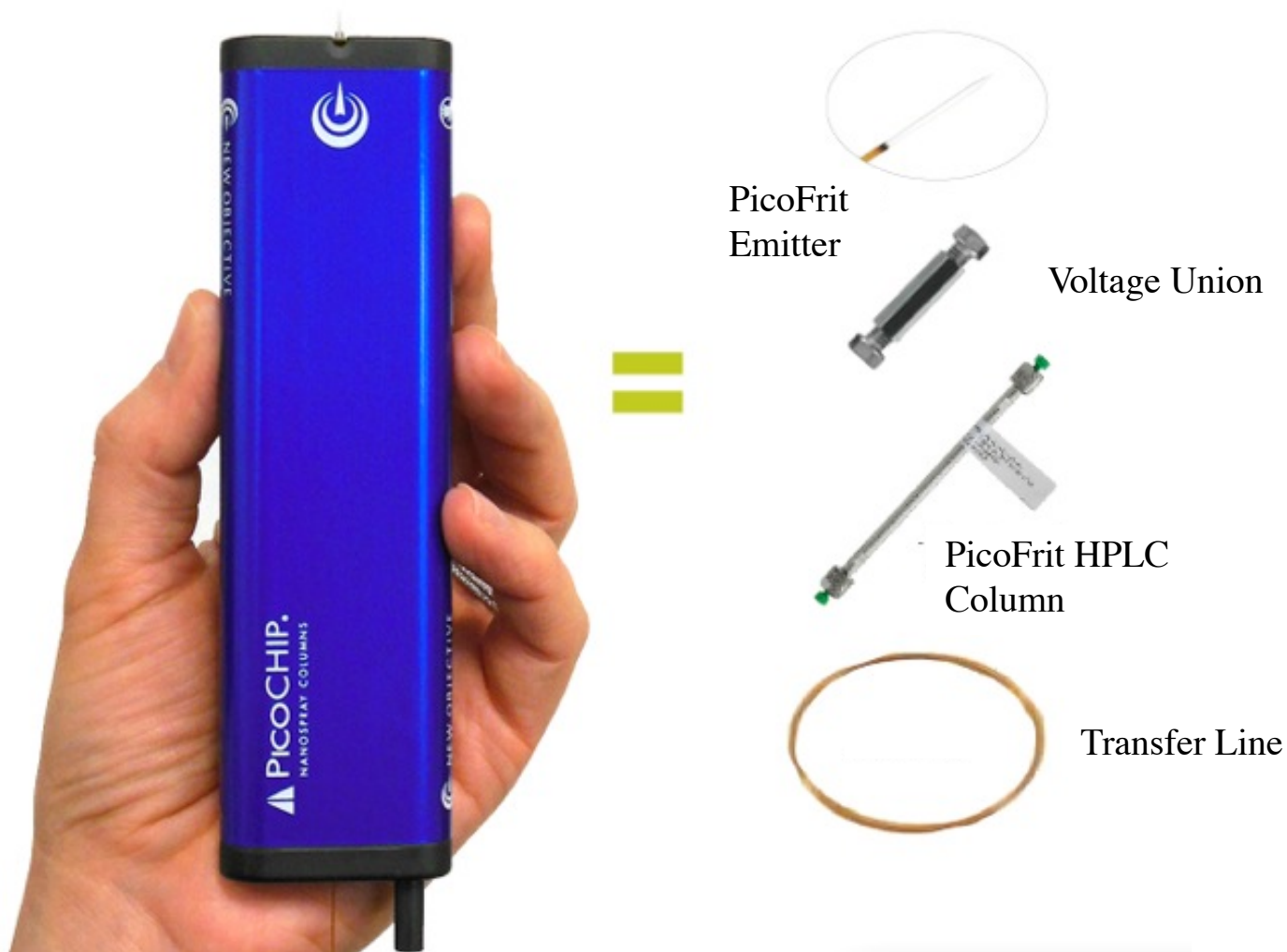
# Integration and Miniaturization – The Future of High Performance LC/MS



Nathan Yates | University of Pittsburgh



# Integrated and Miniaturized High Performance LC/MS – iPhone Analytics



- Integration and Miniaturization Improves Performance

“Chromatography is analog, we need to digitize chromatography.”

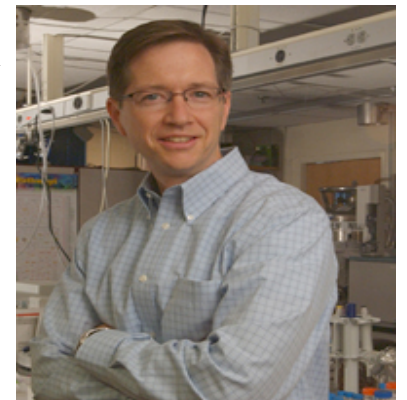


Mike S. Lee  
Milestone Development  
(Circa 1998)



Mozaic Solutions  
Annual Meeting  
May 7, 2015

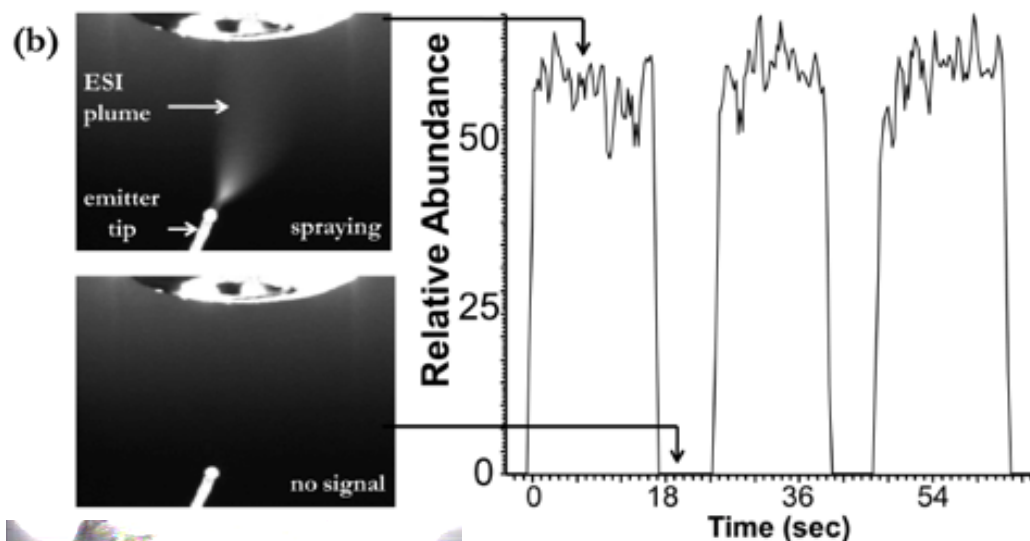
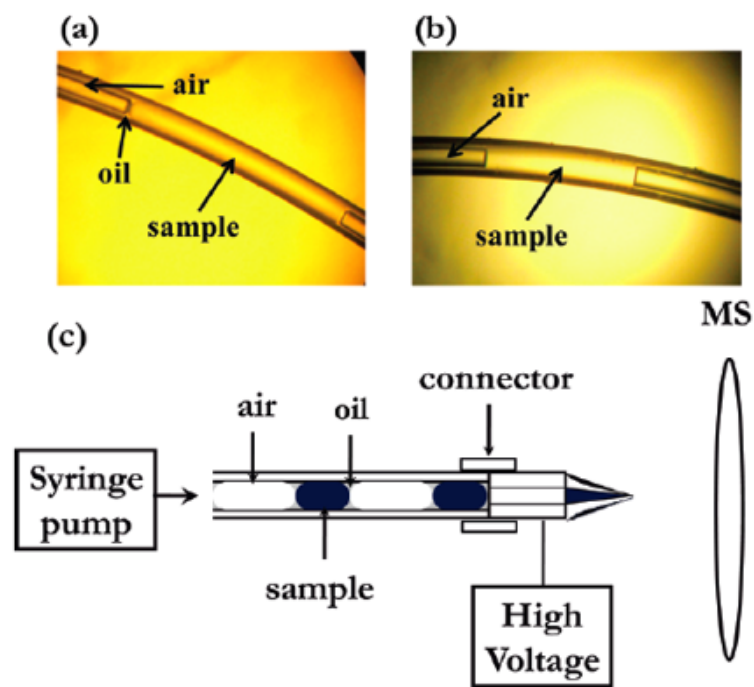
Bob Kennedy  
University Michigan



# Analysis of Samples Stored as Individual Plugs in a Capillary by Electrospray Ionization Mass Spectrometry

Jian Pei,<sup>†</sup> Qiang Li,<sup>†</sup> Mike S. Lee,<sup>‡</sup> Gary A. Valaskovic,<sup>§</sup> and Robert T. Kennedy<sup>\*,†,||</sup>

Departments of Chemistry and Pharmacology, University of Michigan, Ann Arbor, Michigan 48109-1055, Milestone Development Services, Milestone Development Services Inc., Newtown, Pennsylvania 18940, and New Objective, Inc., 2 Constitution Way, Woburn, Massachusetts 02139



Partnership for Performance

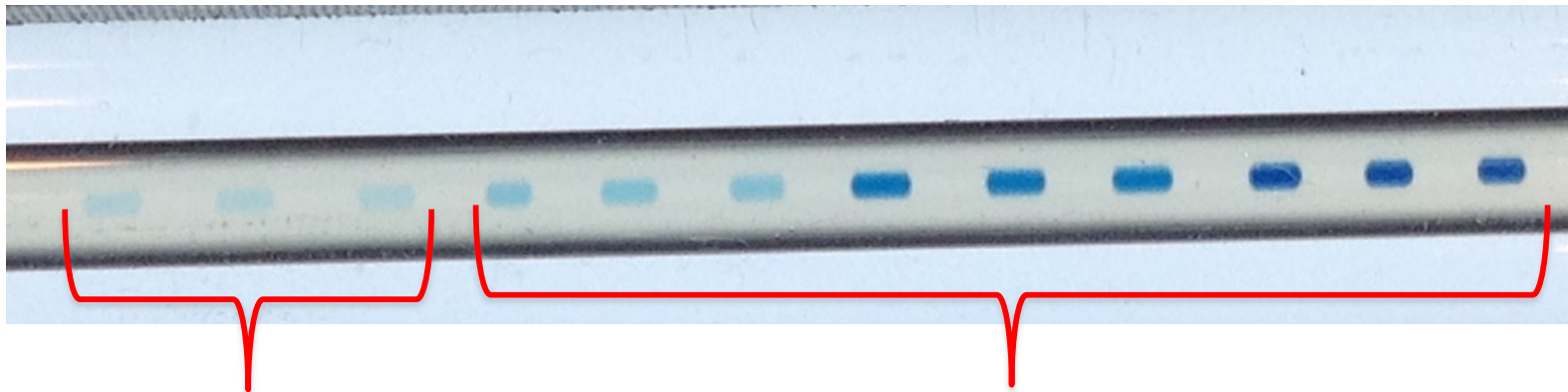


# What can you do with “Infinite” Speed?



Lucinda Cohen | Merck

Collect an Individual QA Curve for *Each* Sample



Samples for Analysis (triplicate)

QA “Curve” (triplicate)

# Mass Spectrometry and Chromatography for Healthcare

- Early detection
  - Mass Spectrometer Transformed into a Clinical Analyzer
  - A Molecular Microscope
- Response-guided medication
  - Chromatography-Mass Spectrometry Platforms Evolve into a Clinical Analyzer
  - A Molecular Plate Reader
- **Mass Spectrometry and Chromatography Uniquely Positioned to Enable Personalized Healthcare**
  - Integration, Miniaturization and Visualization are Critical for Success

# Mass Spectrometry and Chromatography for Healthcare

- Early detection
  - Mass Spectrometer Transformed into a Clinical Analyzer
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  - Chromatography-Mass Spectrometry Platforms Evolve into a Clinical Analyzer
  - A Molecular Plate Reader
- **Mass Spectrometry and Chromatography Uniquely Positioned to Enable Personalized Healthcare**
  - Hope, care and compassion to make a difference
  - Execution of plan (signature)

# Perspectives on Success – Your Story

- Time and Content – Begin Early (but never too late)!
  - Transform – from market to industry to self
  - Simplify – easier to do (realistic) when based on time
  - Solutions – reverse engineer your solution (be realistic)
- Response – Opportunity
  - Set goals and pursue
  - Be realistic and continually measure and feel
  - Find it! – or sometimes success finds you (when not looking)
- Stay Connected – Treasure Relationships
  - Passion – identify and position into a community and preferred culture allowing for acceptance and growth
  - Lead – courage to share and own your story
  - Trust – always know where you are
- **Remember to Share Your Story!**
  - Looking back on both success and failure can point you in the right direction

# Perspectives on Success – Your Story is What Success Looks Like!



Chicago to Ithaca to Cambridge

New Objective - Bringing Electrospray Into Focus

The Future of Proteomics

The Future of Healthcare







