

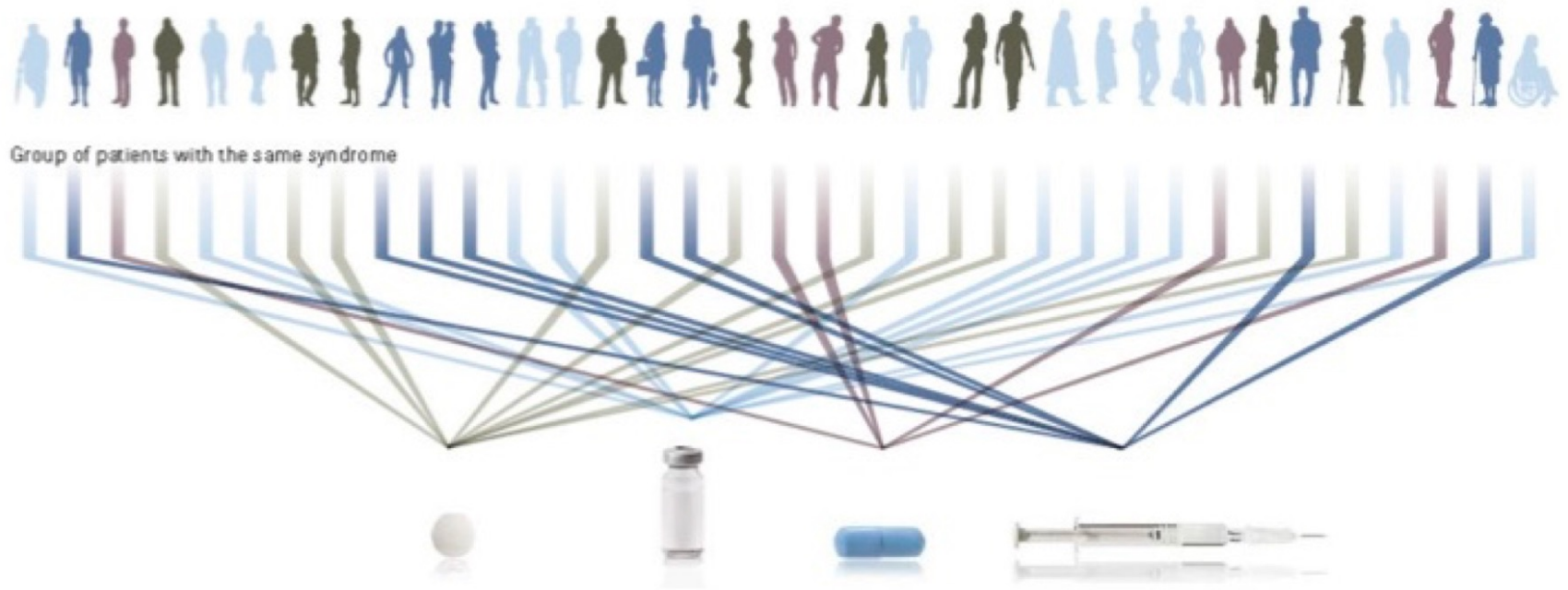
Mozaic Solutions

May 21, 2021

Gary A. Valaskovic

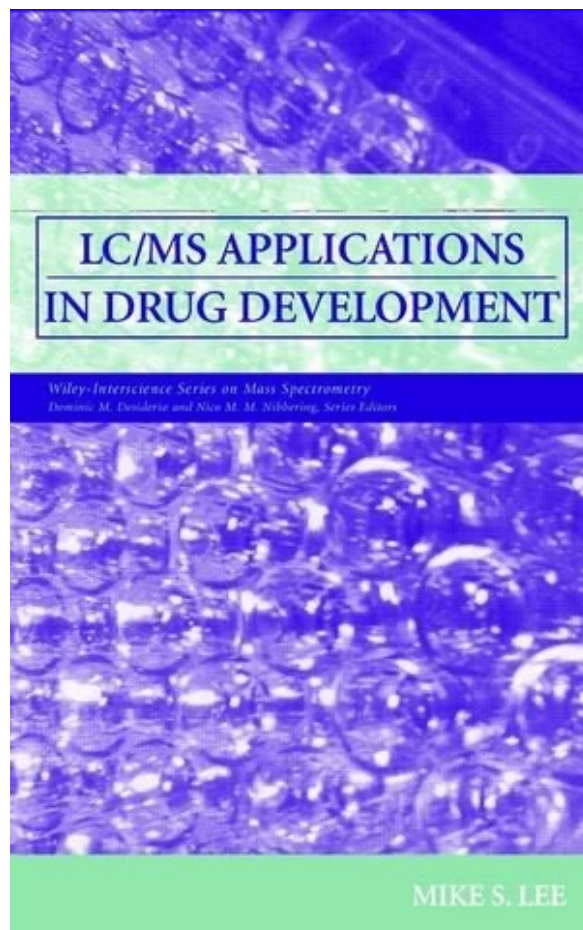
Mike S. Lee

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
-
- **Future Treatments will be Tailored to Specific Subgroups**



Analysis Strategy	Drug Development Application	Development Stage	Selected References
Standard methods	Open-access	DD	Taylor et al., 1995; Pullen et al., 1995
	Pharmacokinetics	DD	Olah et al., 1997
	Metabolite identification	PD	Kerns et al., 1997
Template structure identification	CYP450 metabolism	CD	Ayrton et al., 1998
	Natural products	DD	Lee et al., 1996
	Degradants	PD	Volk et al., 1997
	Degradants	CD	Qin et al., 1994; Volk et al., 1996
	Impurities	CD	Nicolas and Scholz, 1998; Williamson et al., 1998
	Metabolites	CD	Dear et al., 1998
Databases	QC/proteins	M	Chang et al., 1997
	Library searching	DD	Henzel et al., 1993; Eng et al., 1994; Arnott et al., 1995; McCormack et al., 1997; Kleintop et al., 1998
Screening	Natural products dereplication	DD	Gilbert and Lewer, 1998; Janota and Carter, 1998
	Impurity identification	PD	Kerns et al., 1994
	Substructure nomenclature	PD	Kerns et al., 1995
	Glycoprotein mapping	DD	Carr et al., 1993
	Phosphorylated peptides	DD	Ding et al., 1994
	Target screening	DD	Hsieh et al., 1997
	Drug-protein binding	DD	Tiller et al., 1995
	Pharmacokinetics	DD	Olah et al., 1997; Bryant et al., 1997; Hop et al., 1998; Beaudry et al., 1998; Allen et al., 1998
	Caco-2 models	DD	Caldwell et al., 1998
	Metabolic stability	DD	Ackerman et al., 1998; Davis and Lee, 1998
Integration	In vitro metabolites	DD	Roon et al., 1996
	Bioaffinity screening	DD	Davis et al., 1999
	Predictive models	DD	Rourick et al., 1996; 1998; Jurva et al., 2000
	Toxicology	PD	Stevens et al., 1997
	Toxicology	CD	Maurer et al., 1997
	Sulfates/glucuronides	CD	Bean and Henion, 1997
	Peptide mapping	DD	Heath and Giordani, 1993
	Multidimensional chromatography	DD	Apffel et al., 1995; 1996; Link et al., 1998; Washburn et al., 2001
	Metabolism	DD	Li et al., 1995
Miniaturization	Metabolic stability	PD	Herron et al., 1995; Wood et al., 1996; Heath et al., 1997; Manini et al., 1998
	Pharmacokinetics	CD	Covey et al., 1986; Fouda et al., 1991; Wang-Iverson et al., 1992; Kaye et al., 1992; Hoke et al., 2001
	In vivo microdialysis	CD	Scott and Heath, 1998; Wong et al., 1999
	Biotransformation	CD	Chen et al., 1991
	Direct analysis of plasma	CD	Ayrton et al., 1997; Needham et al., 1998
	On-line immunoaffinity extraction	CD	Cai and Henion, 1997
	Chiral analysis	CD	Kanazawa et al., 1998; Joyce et al., 1998
	Impurities	CD	Evans et al., 2001
	Organic extractables	M	Wu et al., 1997
	Peptide mapping	DD	Liu et al., 1998
Parallel processing	Protein identification	DD	Wolters et al., 2001
	Glycoprotein mapping	DD	Liu et al., 1996
	Cellular uptake	DD	Kerns et al., 1998
	In vitro hydrolysis	DD	van Breemen et al., 1991
	Biotransformation	DD	Tiller et al., 1998
	In vitro biotransformation	PD	Beattie and Blake, 1989
	Impurities	PD	Liu et al., 1997
	Biotransformation	CD	Ackerman et al., 1996b
	Chiral separations	CD	Zavitsanos and Alebic-Kolbah, 1998
	96-well SPE	CD	Kaye et al., 1996
Visualization	Protein analysis	DD	Houthaave et al., 1995
	Predictive models/degradants	PD	Rourick et al., 1996
	Off-Line SPE	CD	Allanson et al., 1996; Simpson et al., 1998
Automation	Natural products	DD	Ackerman et al., 1996a
	Combinatorial chemistry	DD	Tong et al., 1998; Richmond et al., 1999; Yates et al., 2001
	Peptide mapping	DD	Arnott et al., 1995
	Protein Analysis	DD	Houthaave et al., 1997
	Protein purification	DD	Feng et al., 2001
	Peptide sequencing	DD	Taylor and Johnson, 2001
	Combinatorial library purity assessment	DD	Zeng and Kassel, 1998
	Metabolite identification	DD	Lopez et al., 1998
	Impurities	PD	Josephs, 1996
	SPE extraction	CD	Allanson et al., 1996; Janiszewski et al., 1997; Simpson et al., 1998
Automation	Impurities	M	Eckers et al., 1997
	Toxic leachables	M	Tiller et al., 1997

Note: DD = drug discovery; PD = preclinical development; CD = clinical development; M = manufacturing.

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**

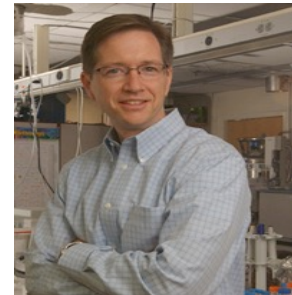
M.S. Lee, *LC/MS Applications in Drug Development*,
John Wiley & Sons; New York **2002**

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



Mike S. Lee
Milestone Development Services
(Circa 1998)

Bob Kennedy
University Michigan

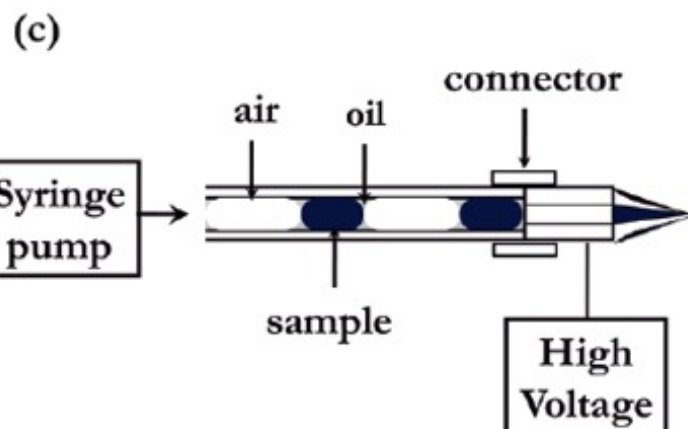
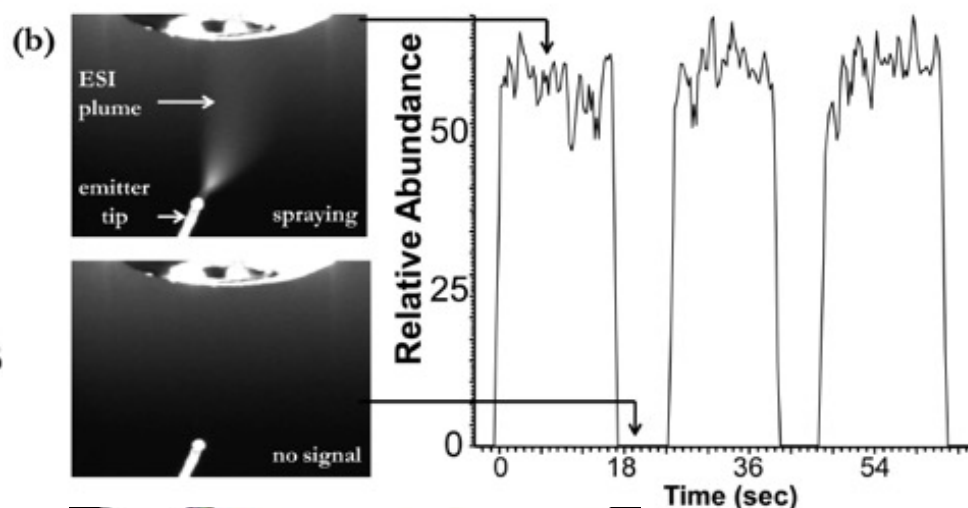
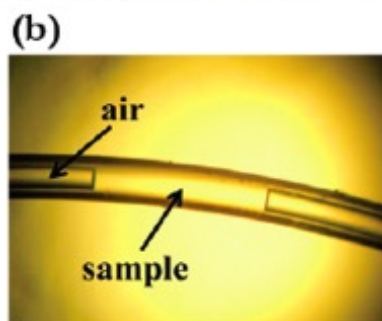
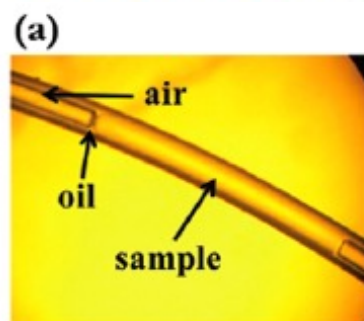


Analysis of Samples Stored as Individual Plugs in a Capillary by Electrospray Ionization Mass Spectrometry



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US Patent: 8,431,888

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US Patent 8,431,888

Figure 1 (a)

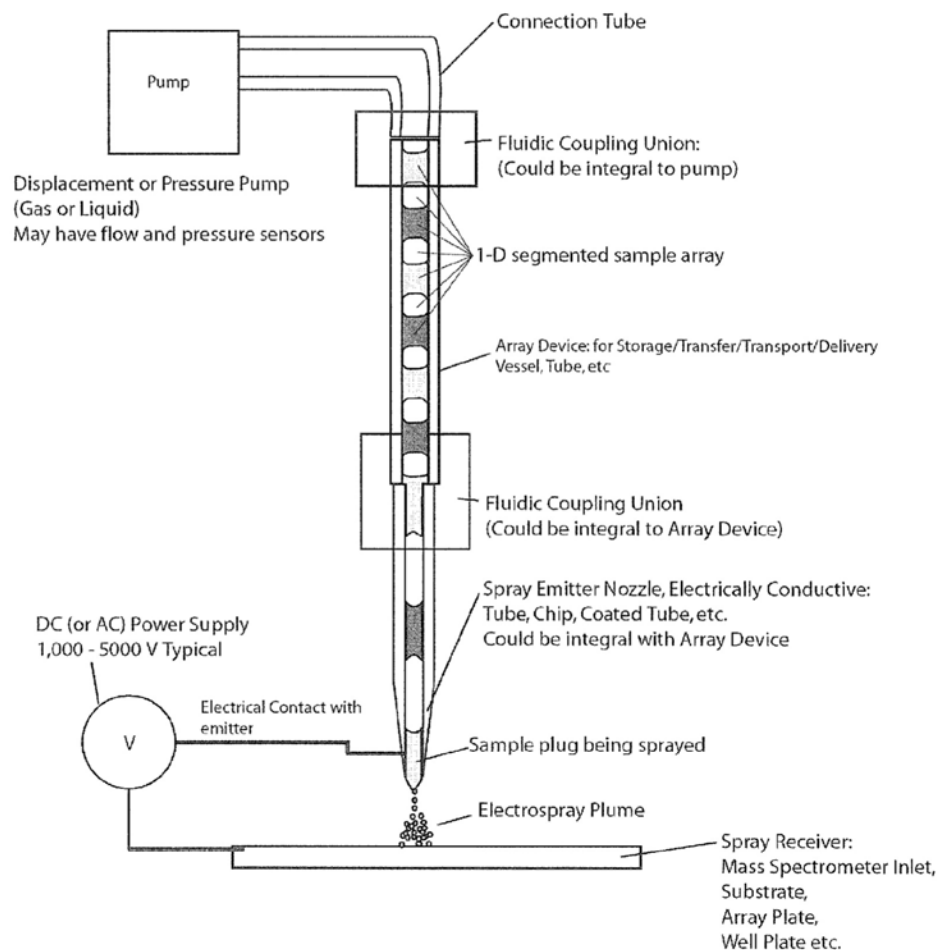
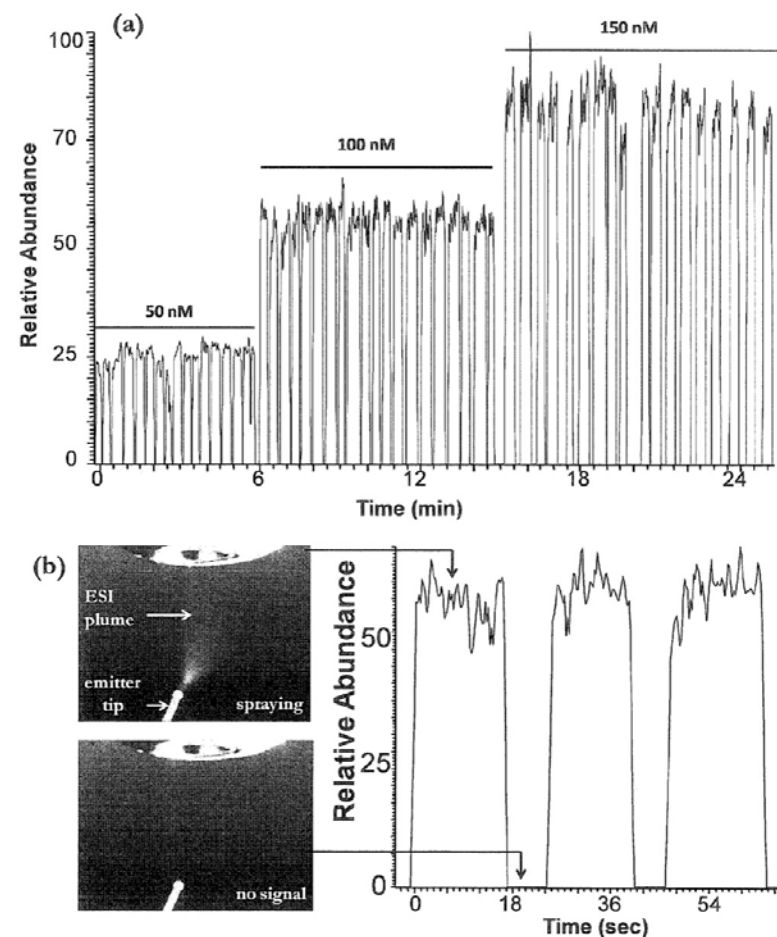


Figure 8



Droplets are the new vials/tubes/plates

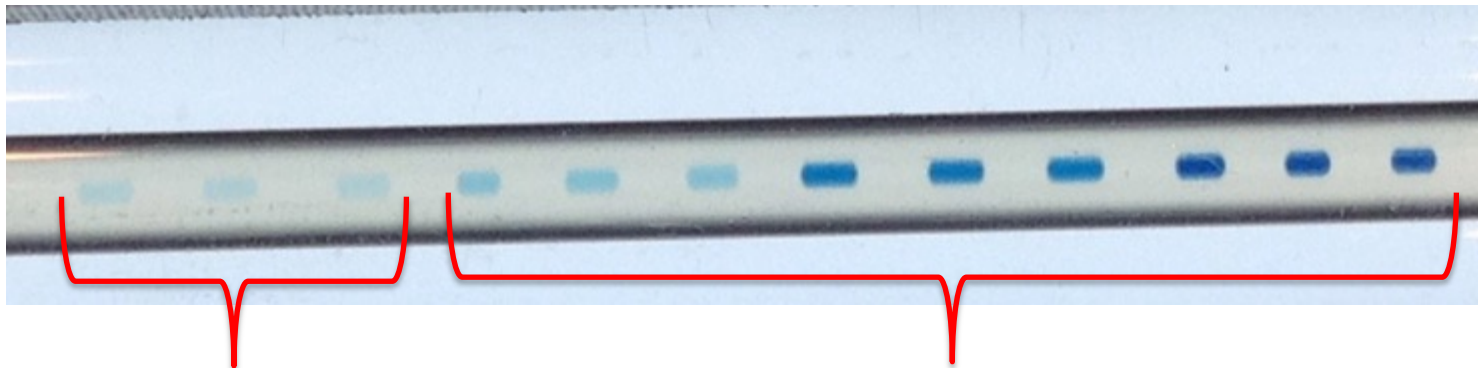


“What would you do with Infinite Speed?”



Lucinda Cohen | Merck Research Laboratories

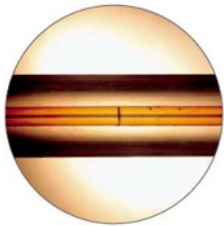
Collect an Individual QA Curve for *Each* Sample



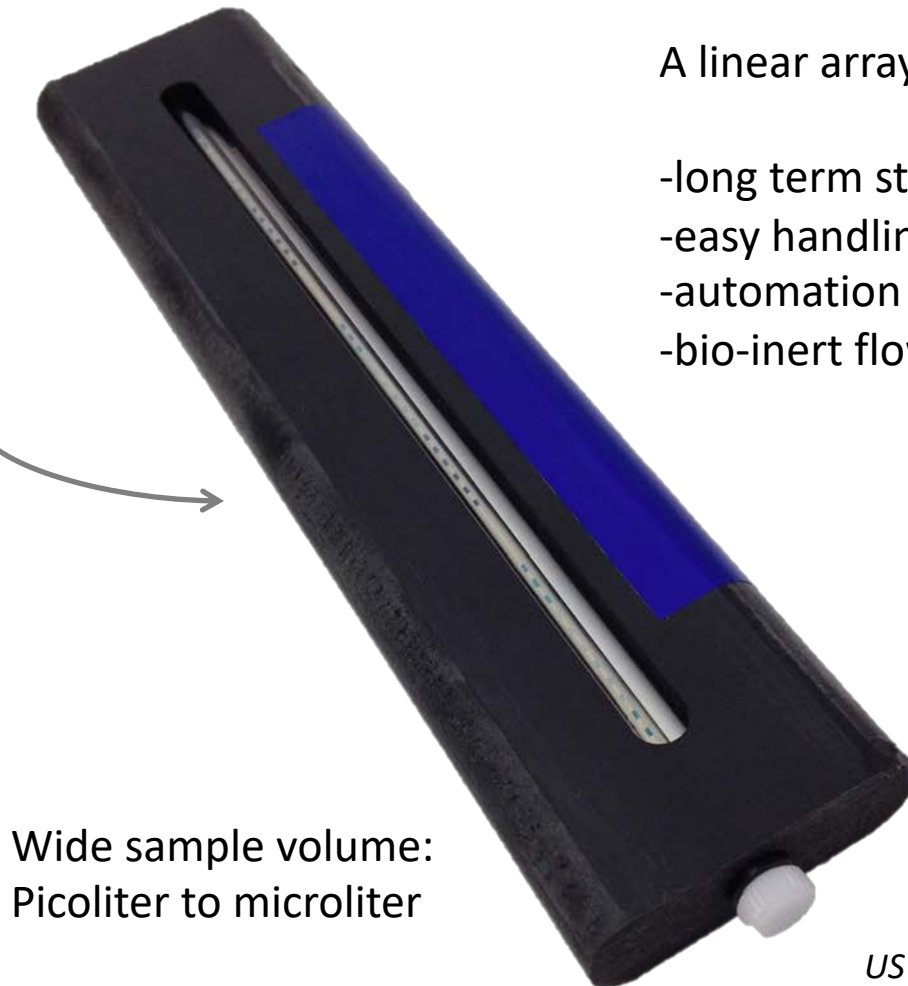
Samples for Analysis (triplicate)

QA “Curve” (triplicate)

Segmented array sample storage



 **PICOCLEAR™**
CONNECTORS



A linear array capable of:

- long term storage
- easy handling
- automation compatible
- bio-inert flow path

Wide sample volume:
Picoliter to microliter

US Patent: 8,431,888

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Can we further exploit droplets for sample preparation?

- (1) Concentrate (amplify)
- (2) Separate (purify)
- (3) Combine with analysis (integrate)

Mozaic Solutions for Healthcare

- Early detection of disease
 - Segmented Flow Technology Transforms the Mass Spectrometer into a Clinical Analyzer
 - A Molecular Microscope!
- Response-guided medication
 - Segmented Flow Technology Transforms the Mass Spectrometer into a Clinical Analyzer
 - A Molecular Plate Reader!
- **Digital LC and Fluidics is Uniquely Positioned to Enable Personalized Healthcare**