Structural mass spectrometry for the analysis of complex biological samples: ion mobility-mass spectrometry for broad-scale systems and synthetic biology

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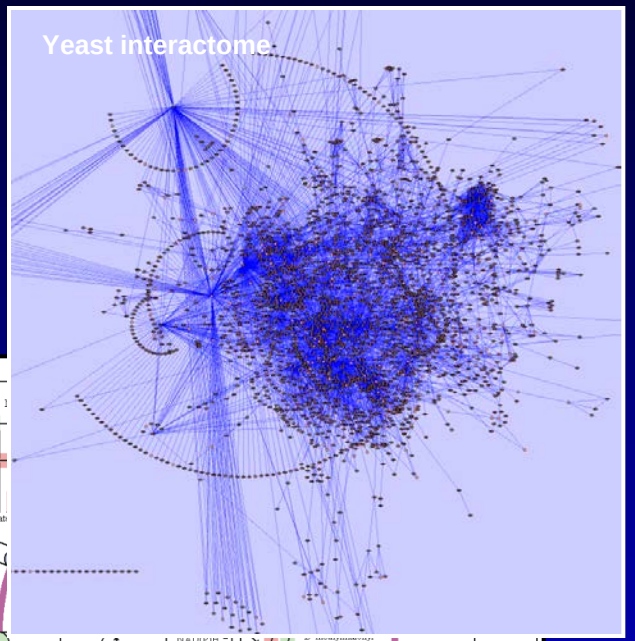
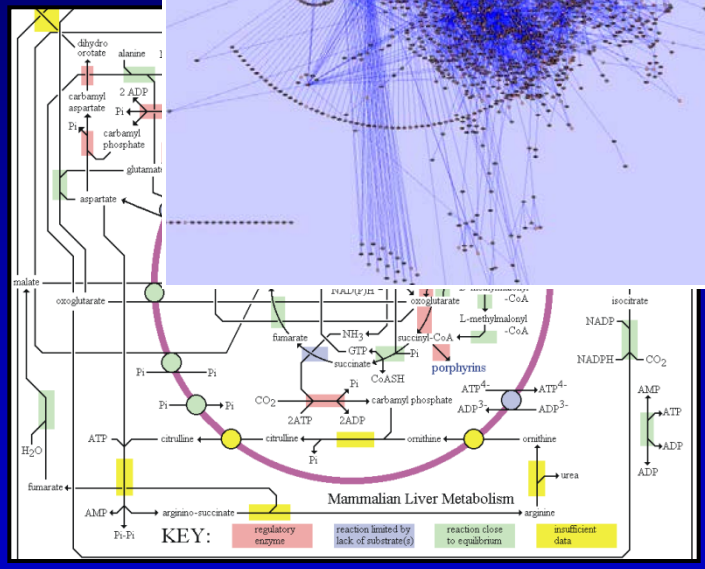
Nashville, TN 37235

GEN – Genetic Engineering and Biotechnology News
March 25th, 2014

Integrating omics for systems biology





Characterizing, quantifying, and cataloging the biomolecular inventory of a sample at specific dimensions of:

(i) Space (*e.g.* cellular, tissue, or organism level)

(ii) Time (*e.g.* point in the life cycle, healthy vs. diseased state).

One of the grand challenges in Systems Biology is the development of new technologies for characterizing the dynamic temporal change of the biomolecular inventory…

Paraphrasing Leroy Hood
Pittcon Heritage Award Address 2008

On the dimensions of cartography…

Suarez Miranda,Viajes de varones prudentes, Libro IV,Cap. XLV, Lerida, 1658:

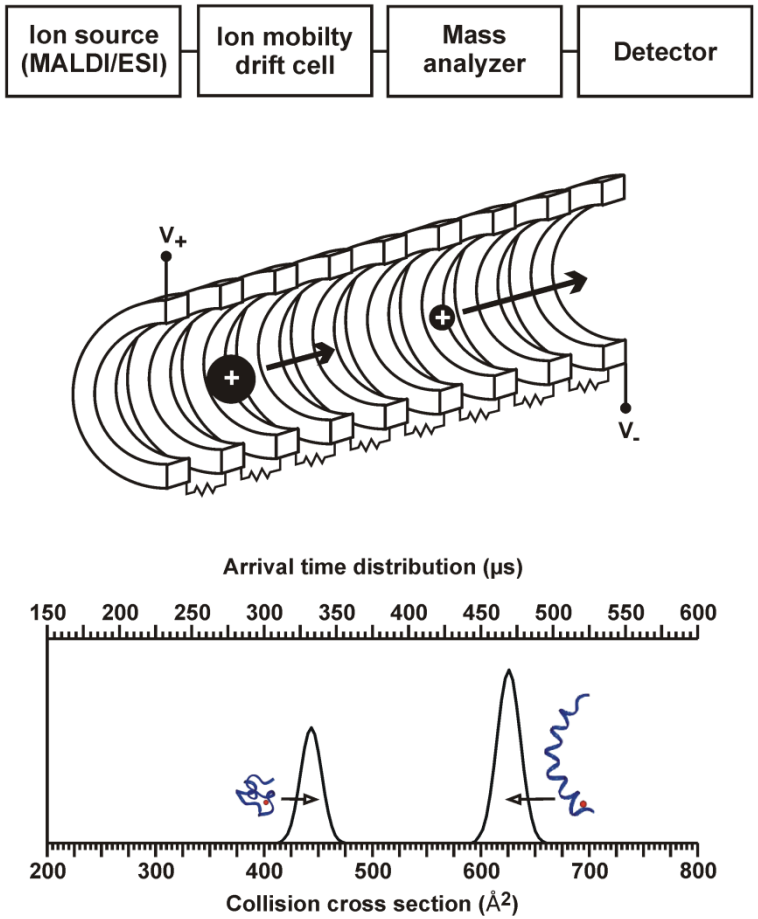
". . . In that Empire, the Art of Cartography attained such Perfection that the map of a single Province occupied the entirety of a City, and the map of the Empire, the entirety of a Province. In time, those Unconscionable Maps no longer satisfied, and ***the Cartographers Guilds struck a Map of the Empire whose size was that of the Empire, and which coincided point for point with it.*** The following Generations, who were not so fond of the Study of Cartography as their Forebears had been, saw that that vast Map was Useless, and not without some Pitilessness was it, that they delivered it up to the Inclemencies of Sun and Winters. In the Deserts of the West, still today, there are Tattered Ruins of that Map, inhabited by Animals and Beggars; in all the Land there is no other Relic of the Disciplines of Geography."

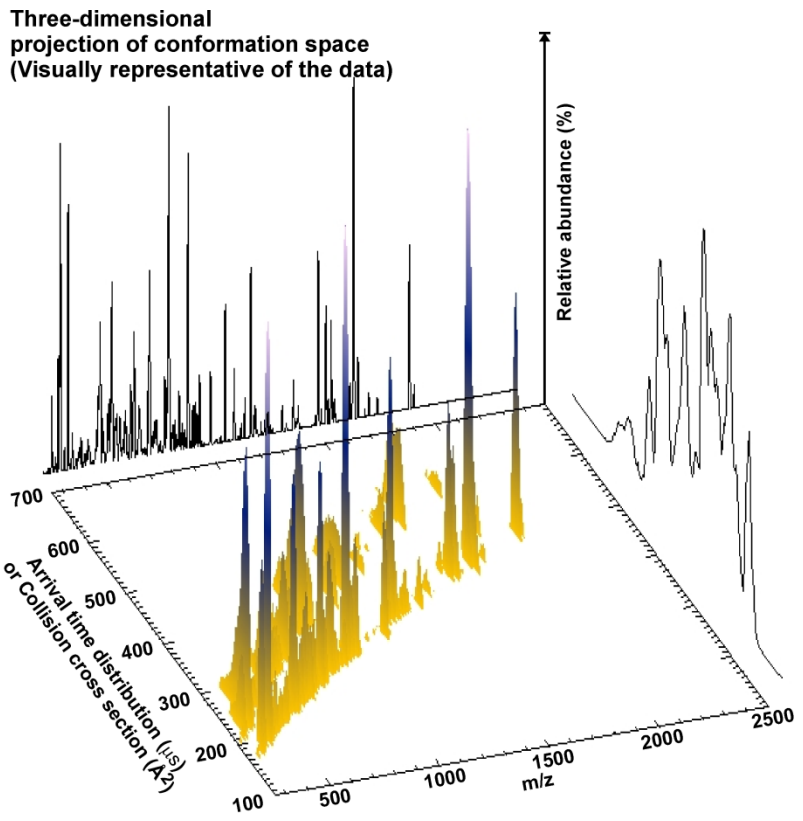
(From Jorge Luis Borges, Collected Fictions translated by Andrew Hurley

On the dimensions of dynamics in omics…

A broad timescale ranging from genomics to metabolomics

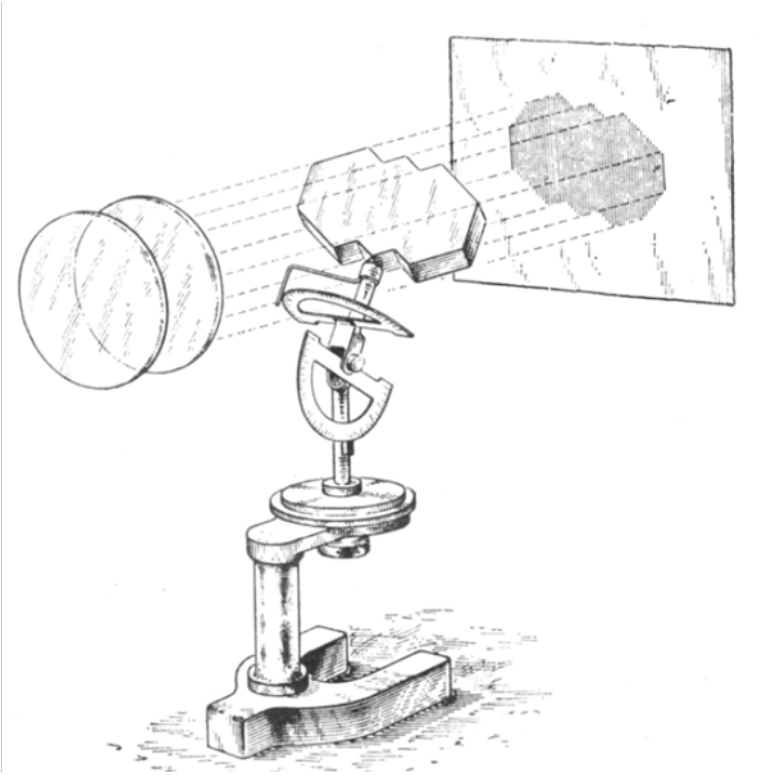
On the dimensions of ion mobility-mass spectrometry…





L. S. Fenn and J. A. McLean, *Analytical Bioanalytical Chemistry* 391, 905-9 (2008).

Molecular structure determines collision cross section



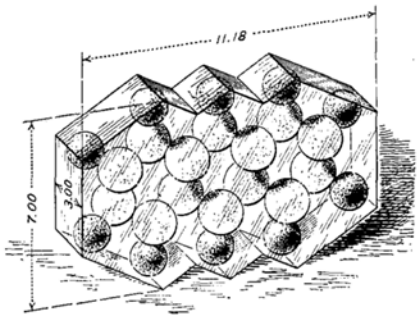


Fig. 7.—Anthracene.

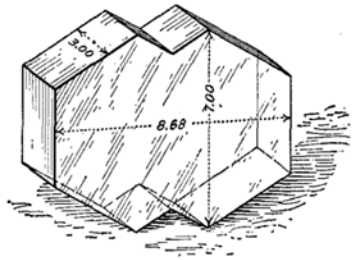
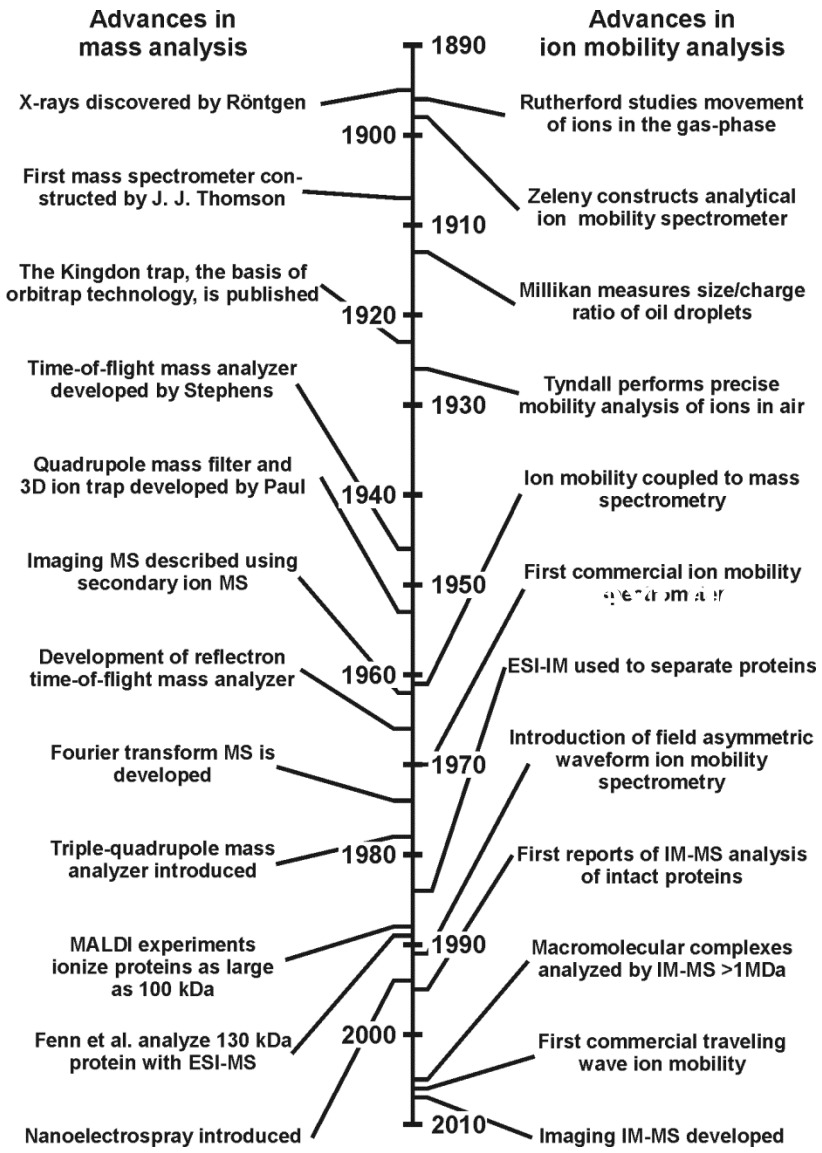


Fig. 8.—Naphthalene.

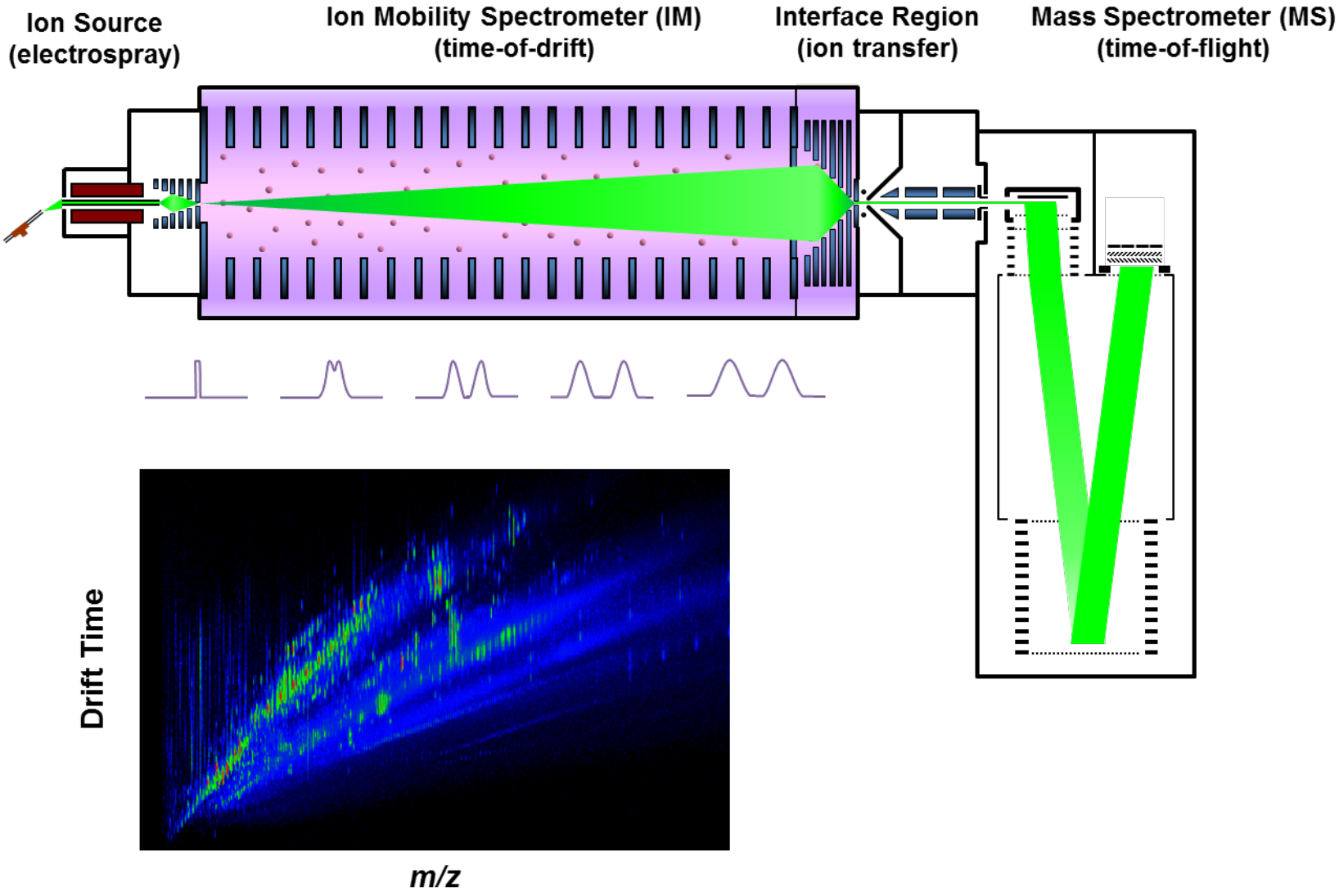
E. Mack Jr., *J. Am. Chem. Soc.* 47, 2468-82 (1925).
Ref. 1. Langmuir, *J. Am. Chem. Soc.* 39, 1848 (1917).
Ref. 3. Bragg, *Proc. Phys. Soc.* 34, 33 (1921).

Evolution of ion mobility with mass spectrometry



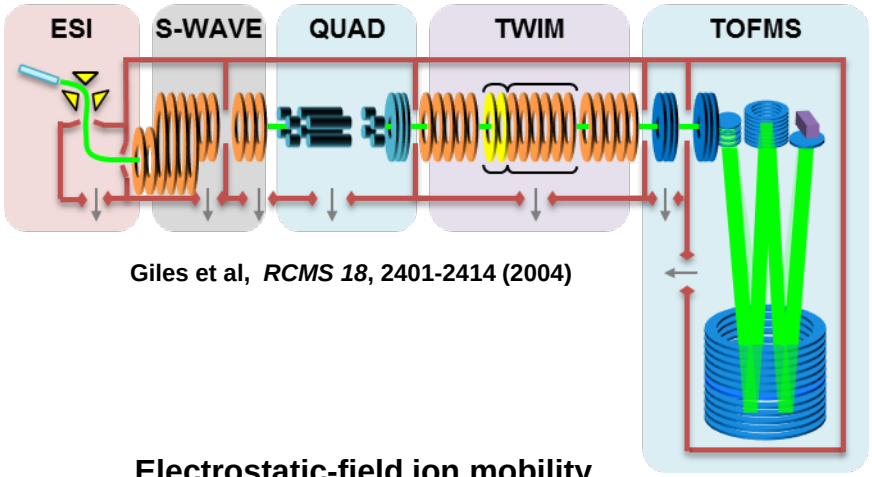
K. M. Hines, J. R. Enders, and J. A. McLean, *Encyclopedia of Analytical Chemistry*, R. Myers and D. C. Muddiman, Eds., John Wiley & Sons (2012).

Time-dispersive ion mobility-mass spectrometry
Charge-to-size and mass-to-charge separations



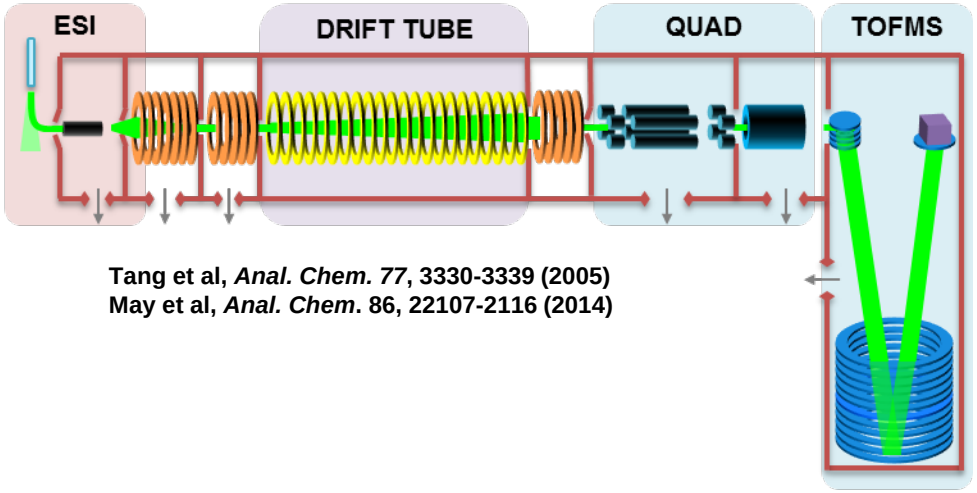
Three major types of time-dispersive ion mobility-mass spectrometry instrumentation

Electrodynamic-field ion mobility (relative collision cross section)



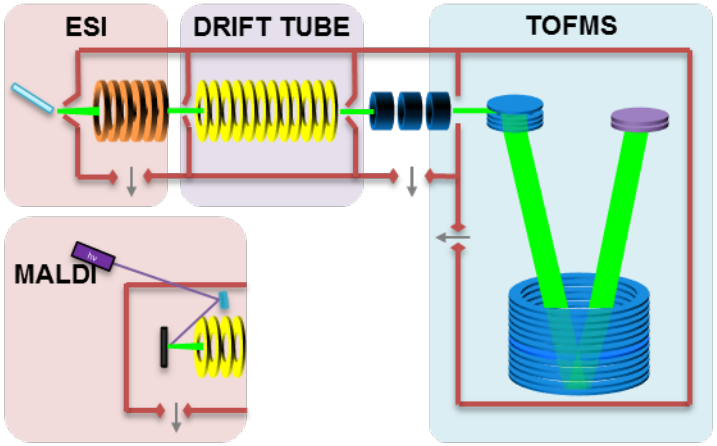
Giles et al, *RCMS 18*, 2401-2414 (2004)

Electrostatic-field ion mobility (absolute collision cross section)

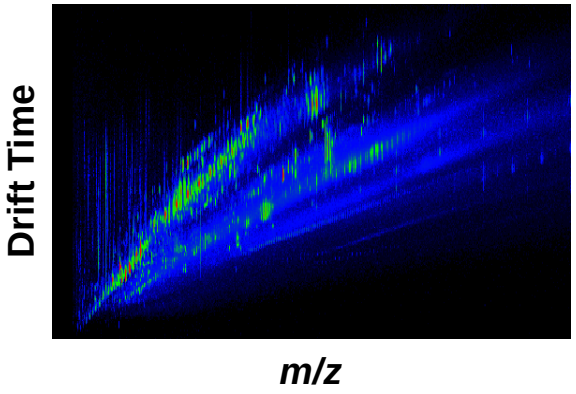


Tang et al, *Anal. Chem. 77*, 3330-3339 (2005)
May et al, *Anal. Chem*. 86, 22107-2116 (2014)

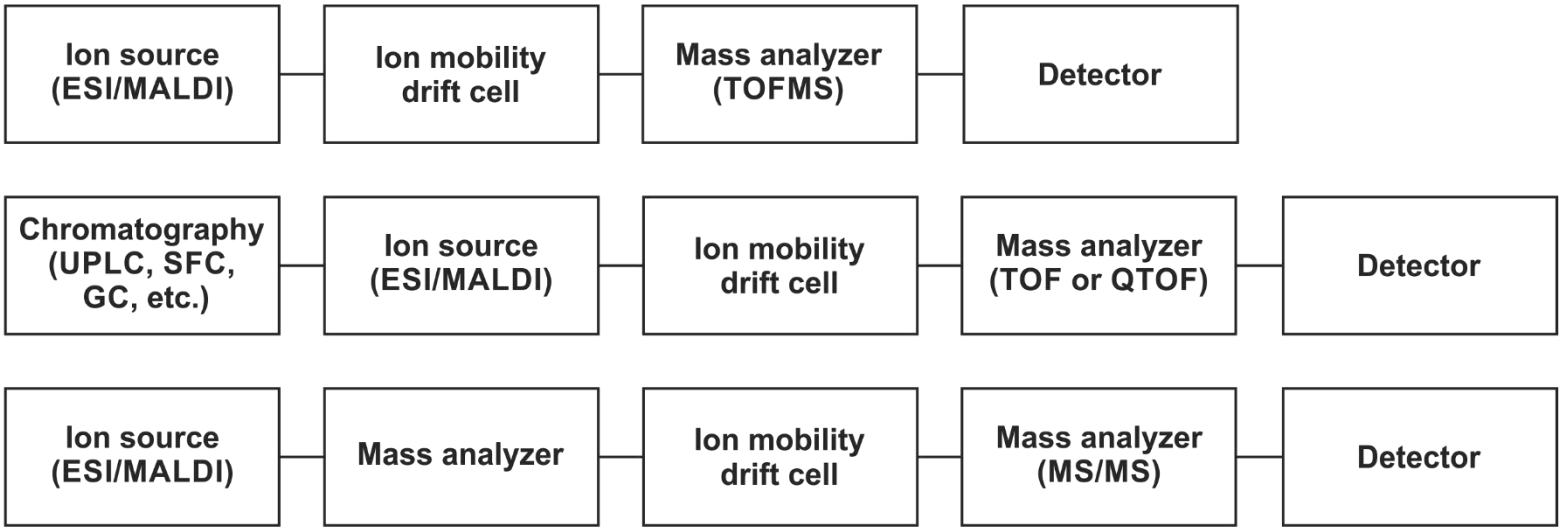
Electrostatic-field ion mobility (absolute collision cross section)

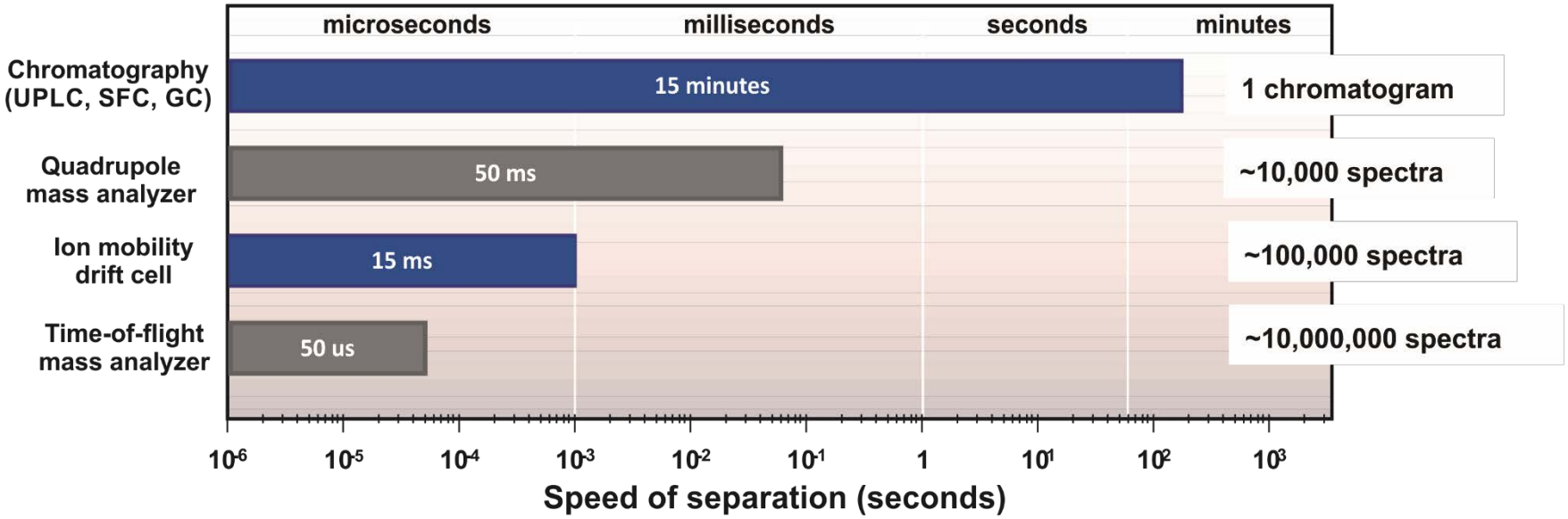


Sundarapandian et al, *Anal. Chem. 82*, 3247-3254 (2010)

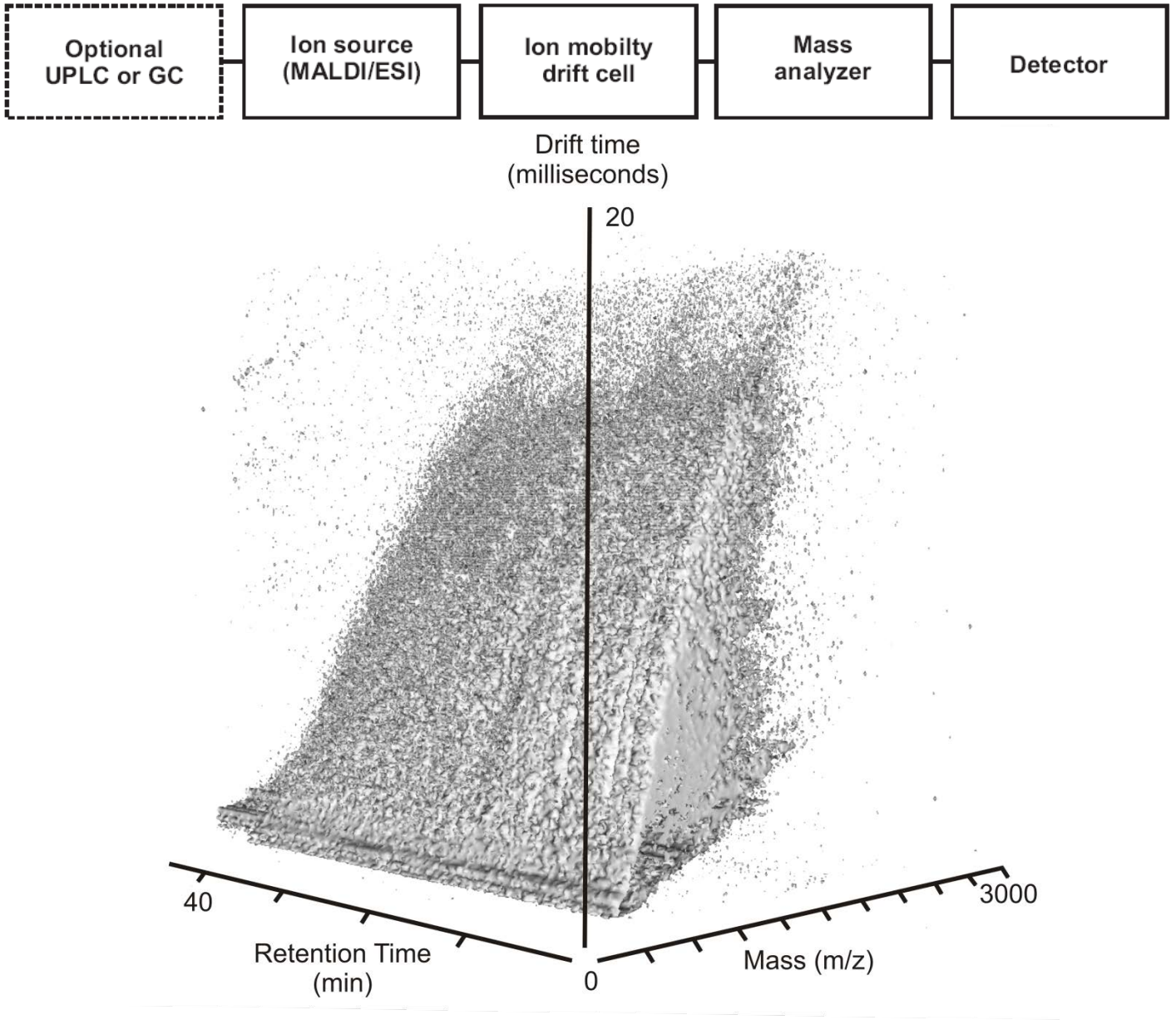


Nesting of analytical timescales and data scaling



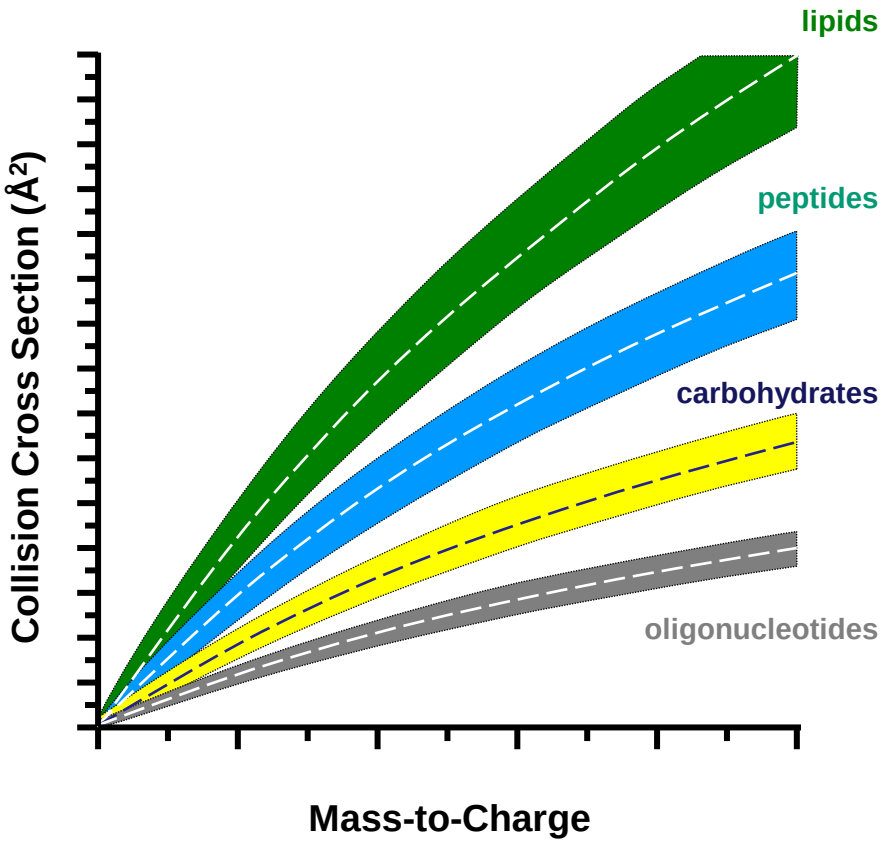


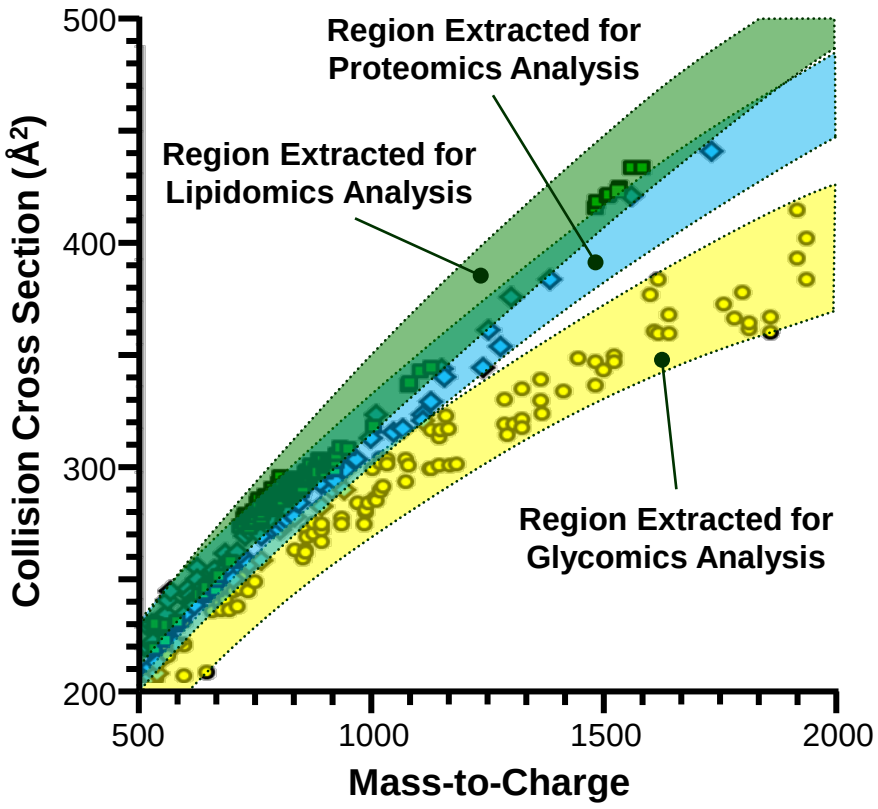
UPLC-IM-MS analysis of serum



Biomolecular class separations

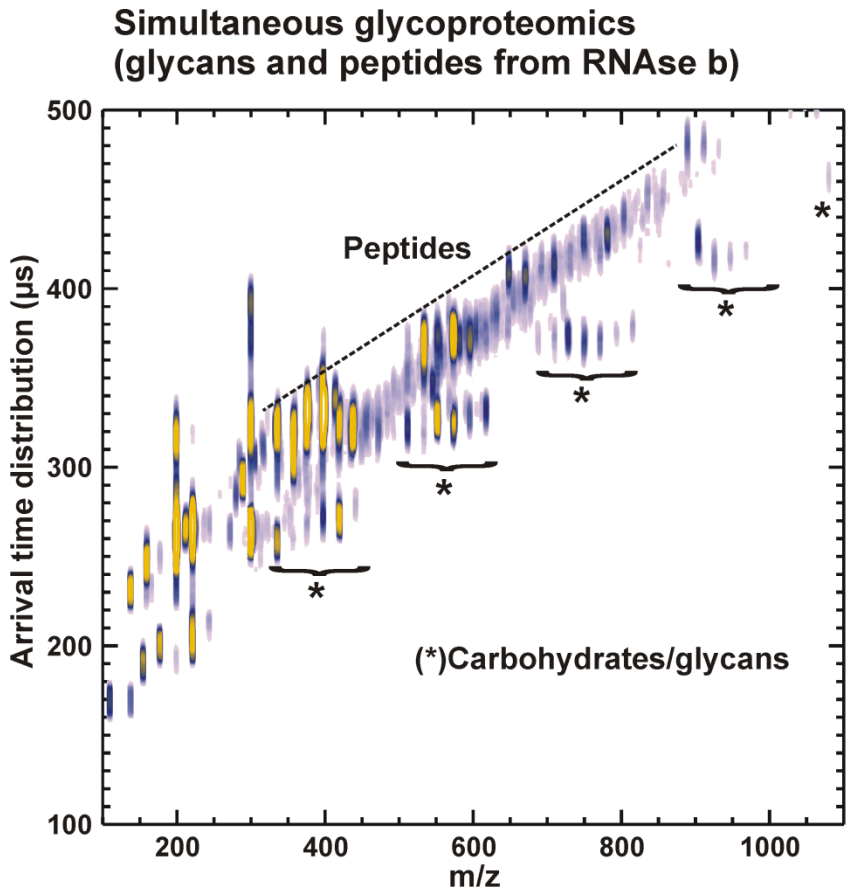
(Structural selectivity from prevailing structural characteristics of density)

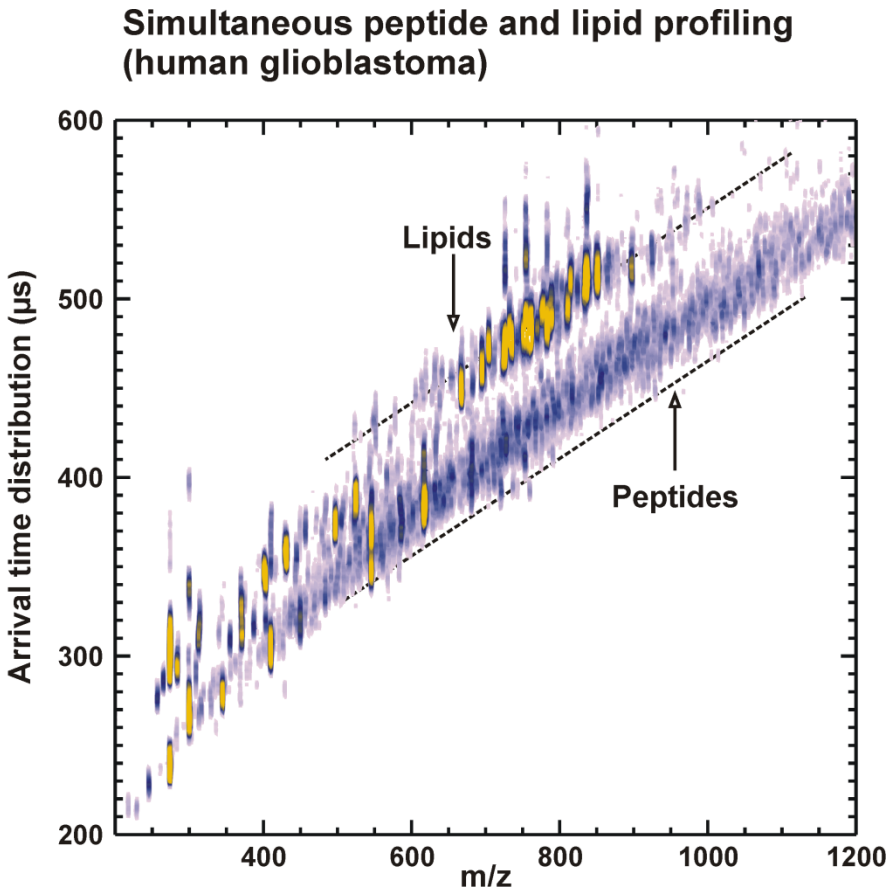




L. S. Fenn, M. Kliman, A. Mahsut, S. R. Zhao, and J. A. McLean, *Analytical Bioanalytical Chemistry* 394, 235-244 (2009).

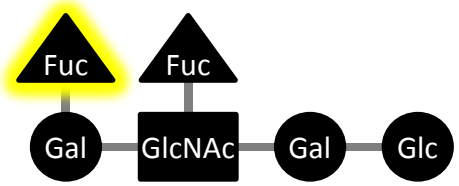
Integrated omics



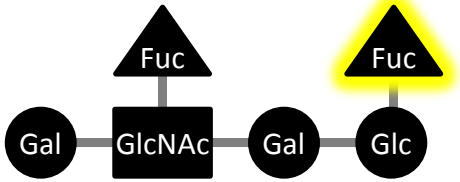


Carbohydrates

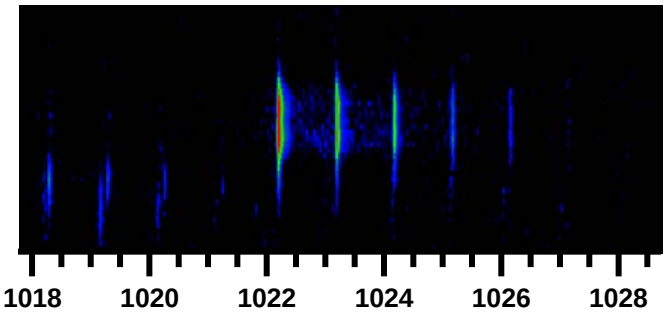
Lacto-N-difucohexaose I

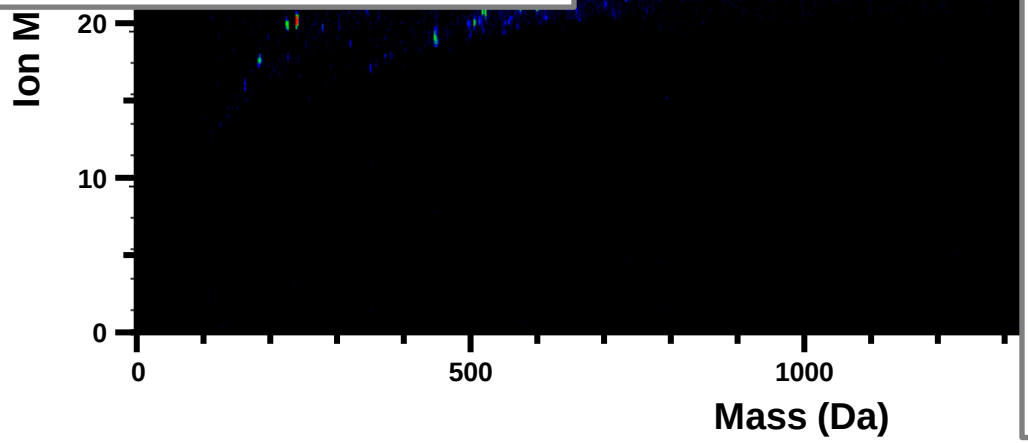


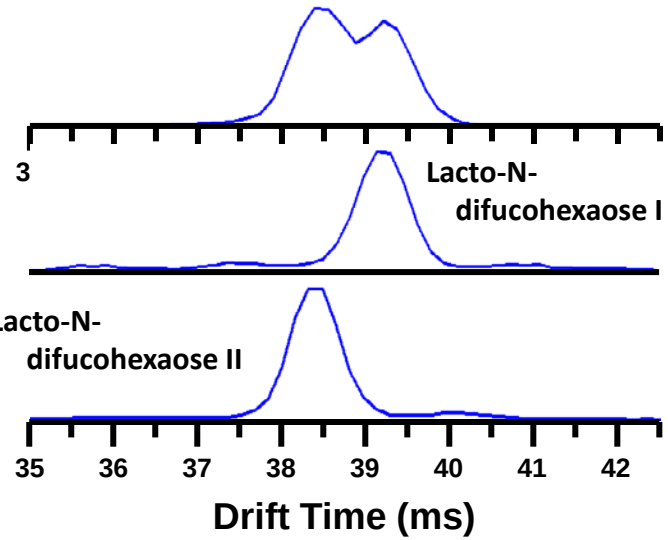
Lacto-N-difucohexaose II



Mixture of **Lacto-N-difucohexaose I & II**

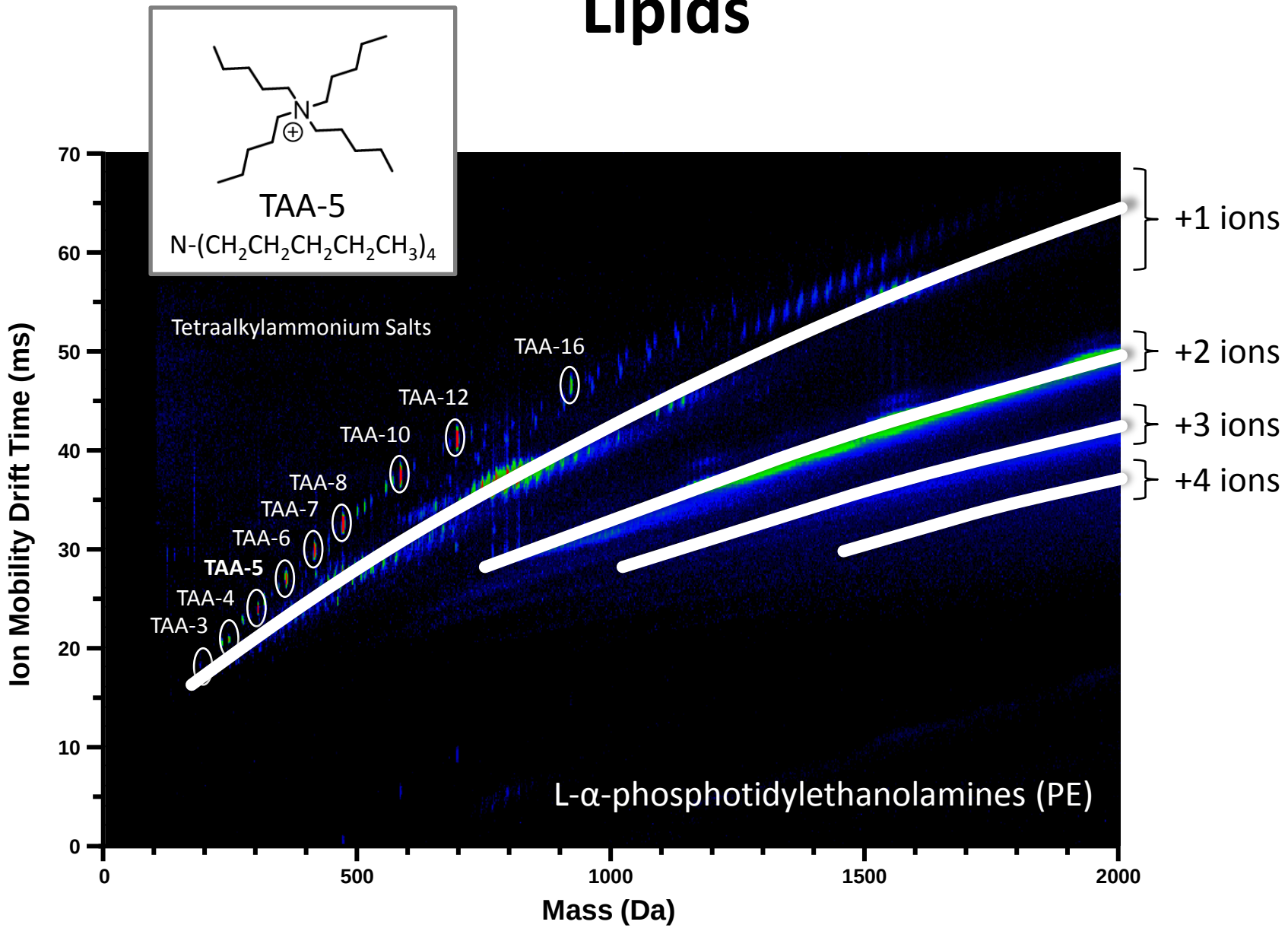






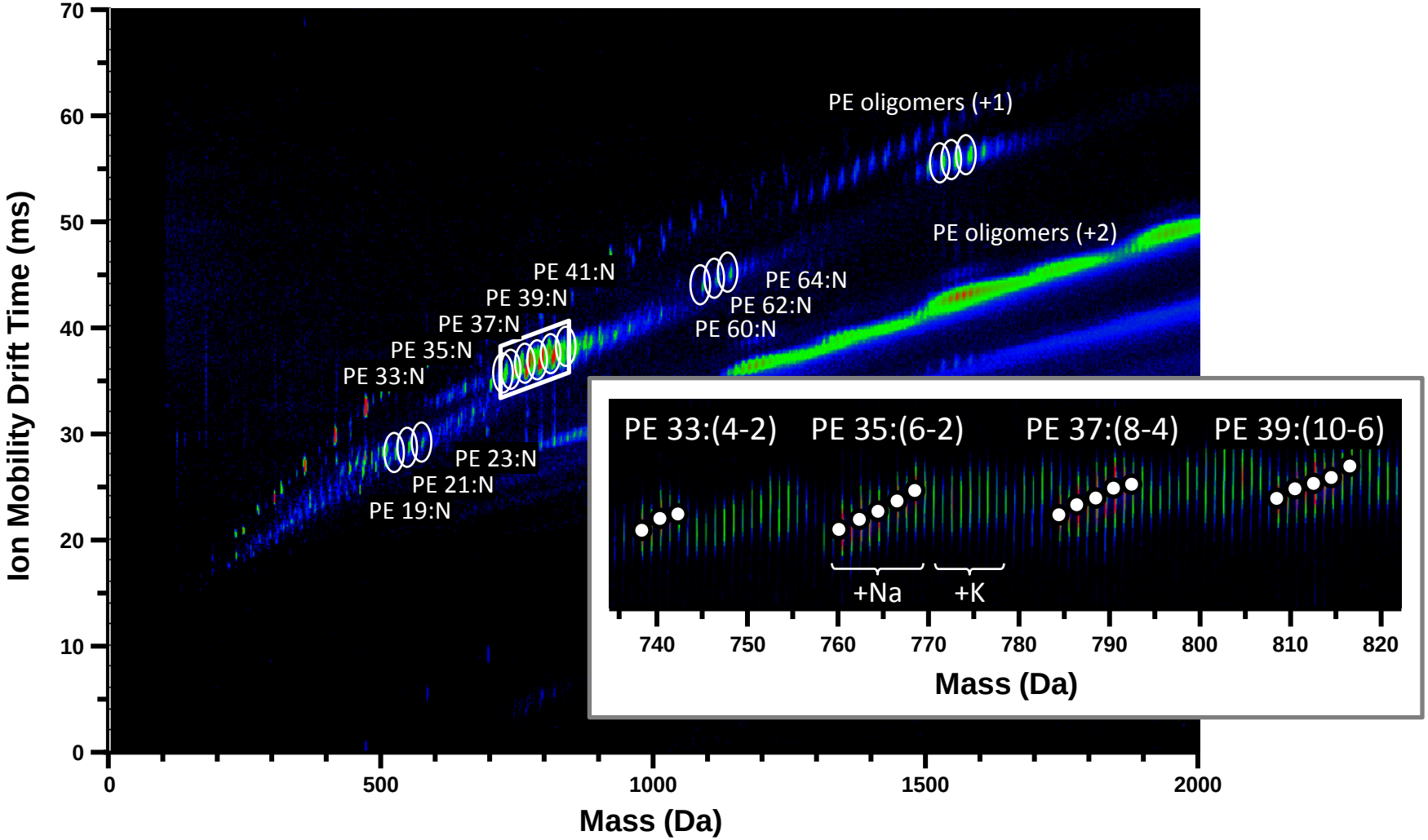
2D spectra is of a mixture of 14 carbohydrate standards. A mixture of TAA salts was added as internal IM and MS calibrants. Annotated are the sodiated (+Na) ions only.

Lipids



Distribution of PE lipids derived from chicken egg. An equimolar mixture of TAA salts was spiked in as an internal IM and MS calibrant. Structure shown is the tetrapentylammonium cation (TAA-5).

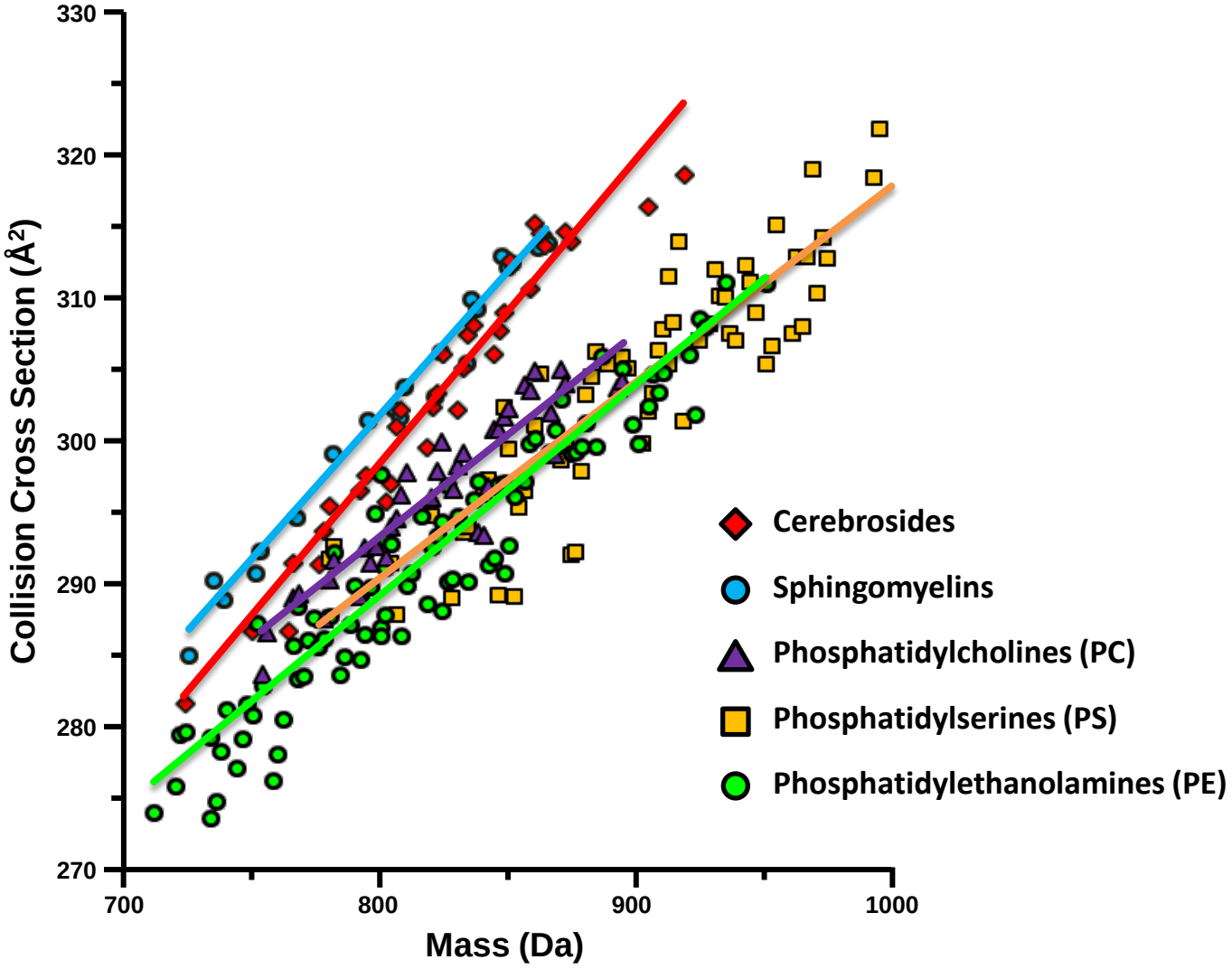
Lipids



Distribution of PE lipids derived from chicken egg. An equimolar mixture of TAA salts was spiked in as an internal IM and MS calibrant.

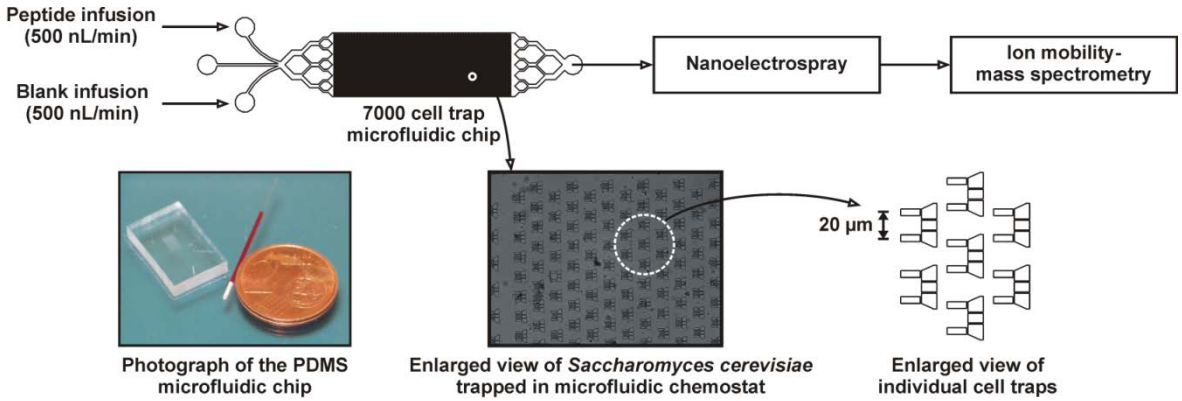
Conformational Space Mapping in High Resolution

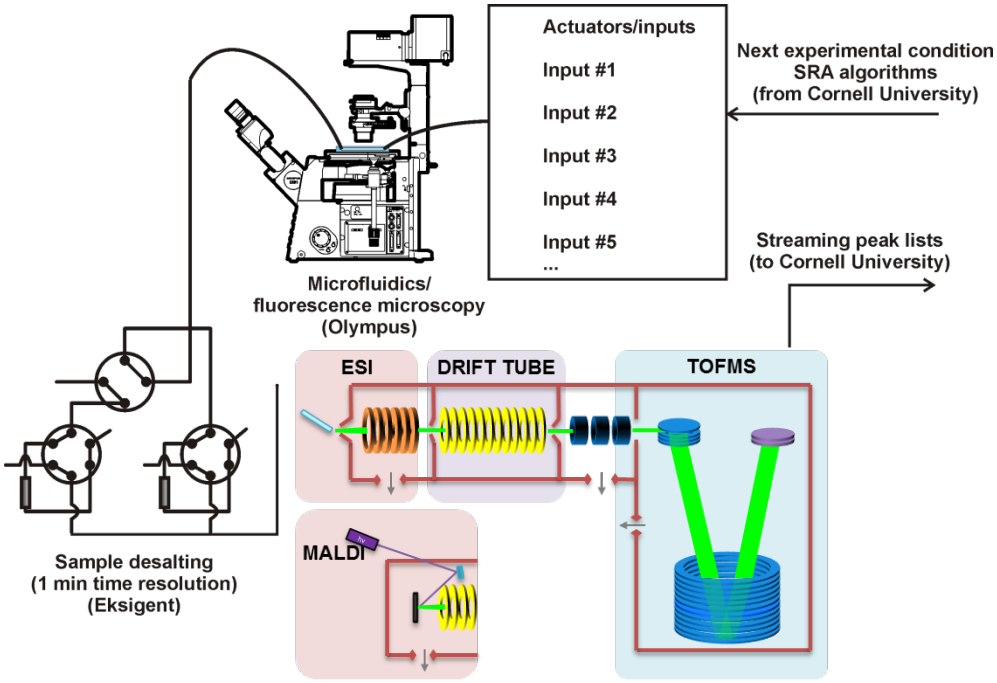
Sub-Class Trends in Lipid Data



J. May, C.R. Goodwin, N. Lareau, K. Leaptrot, C. Morris, R. Kurulugama, A. Mordehai, C. Klein, W. Barry, E. Darland, G. Overney, K. Imatani, G. Stafford, J. Fjeldsted, J.A. McLean, *Analytical Chemistry* 86, 22107-2116 (2014).

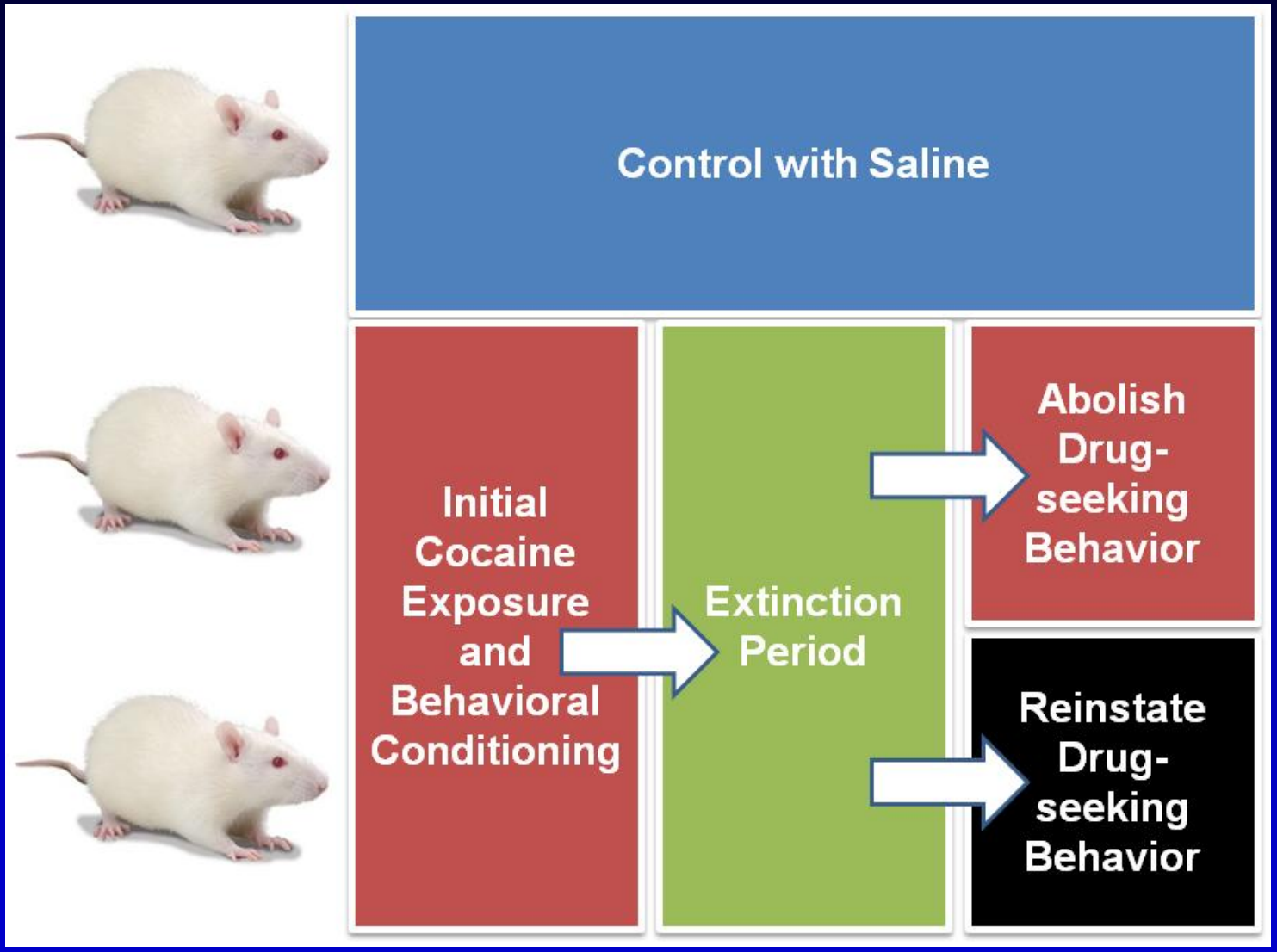
Dynamic systems biology
Automated robot scientist version 2.0





Collaboration with
Prof. John Wikswo (VU) and
Prof. Hod Lipson (Cornell)

Can leukocytes encode long-term metabolic changes to drug exposure? rat cocaine model



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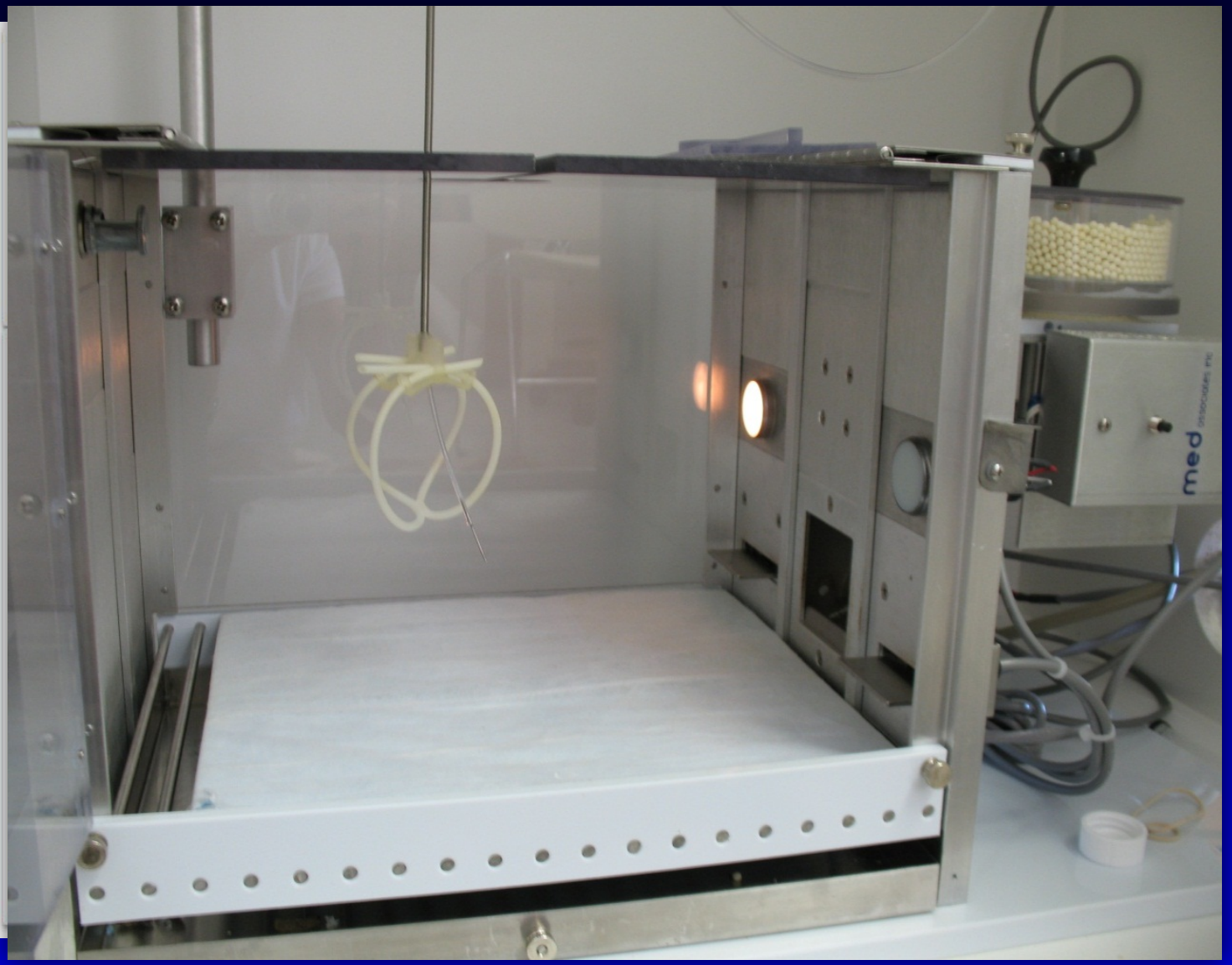
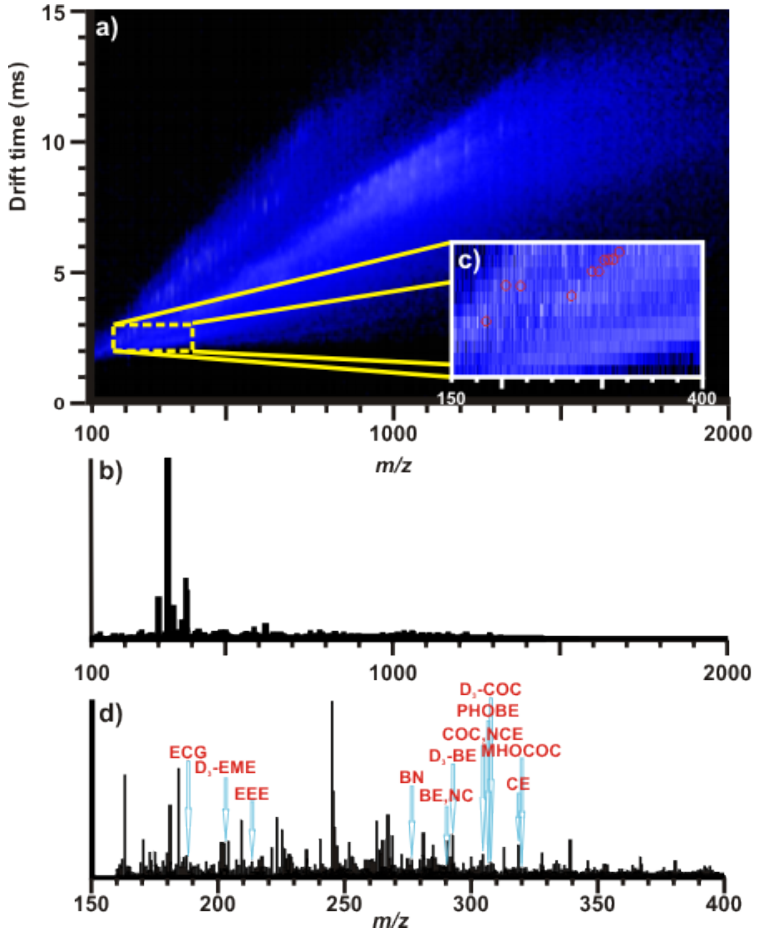
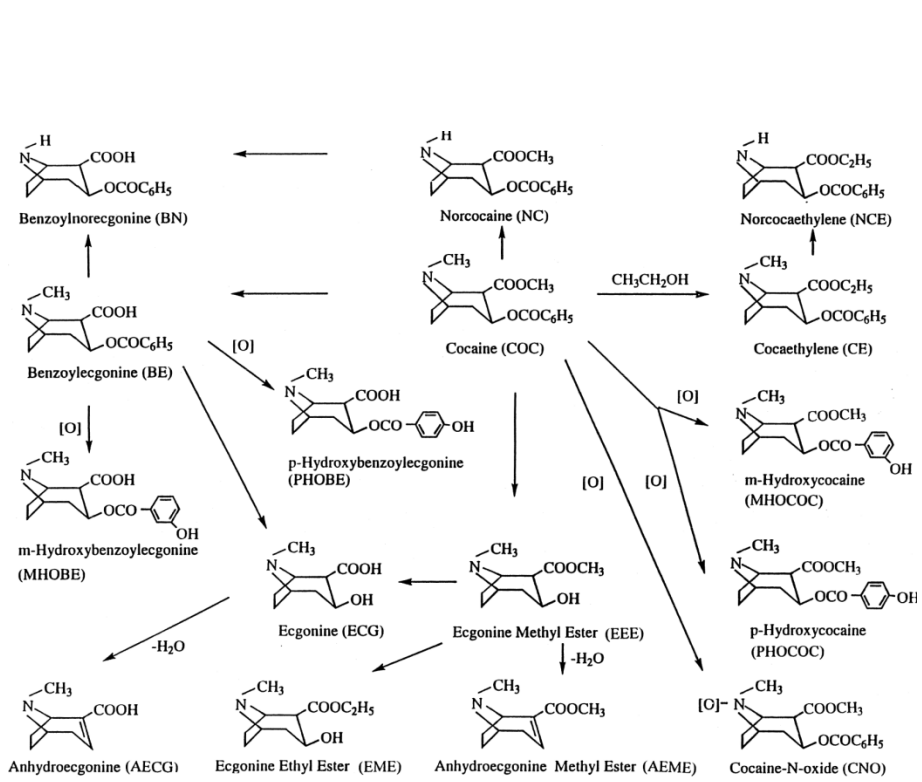


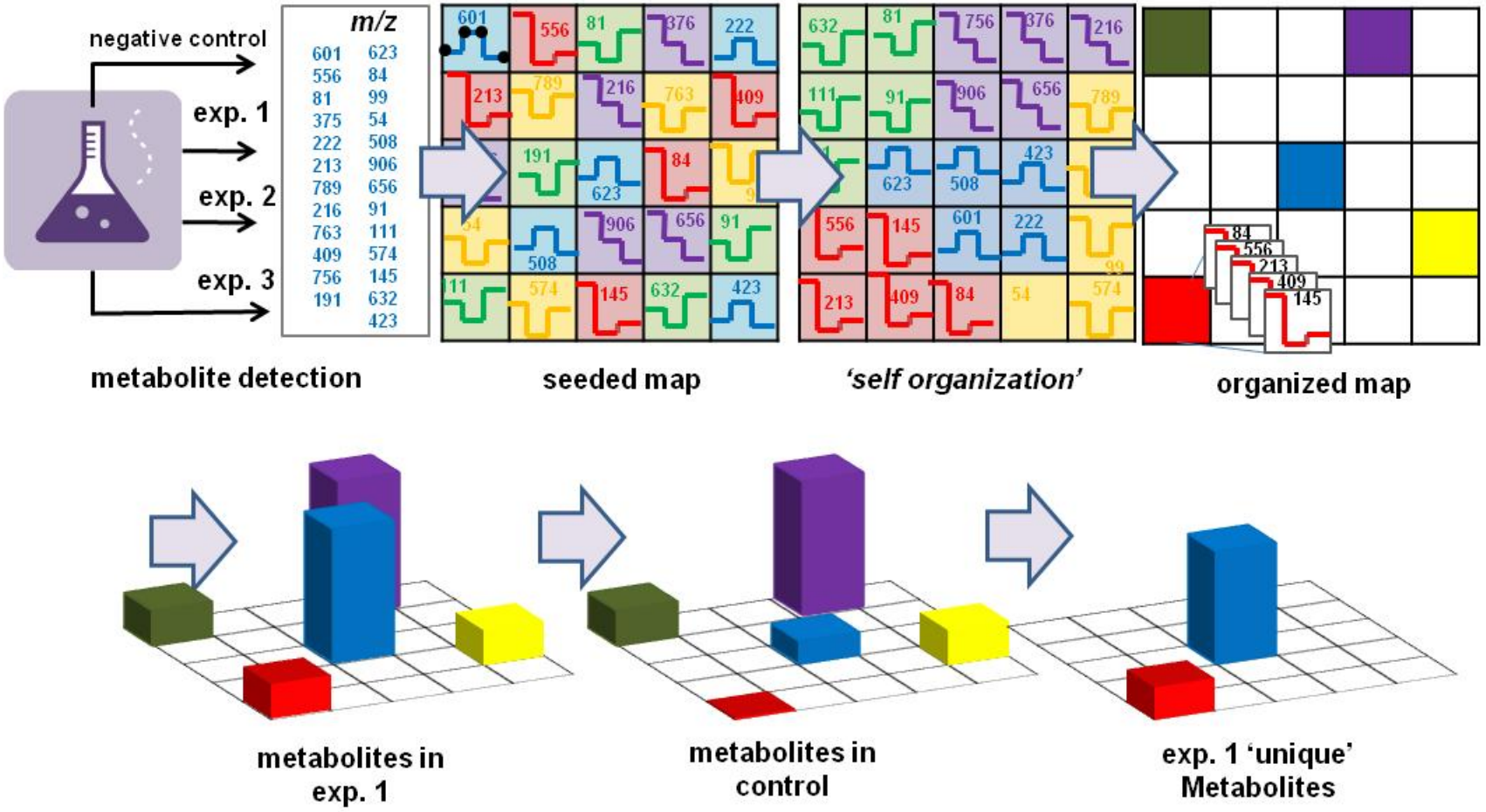
Cocaine metabolism in rat serum



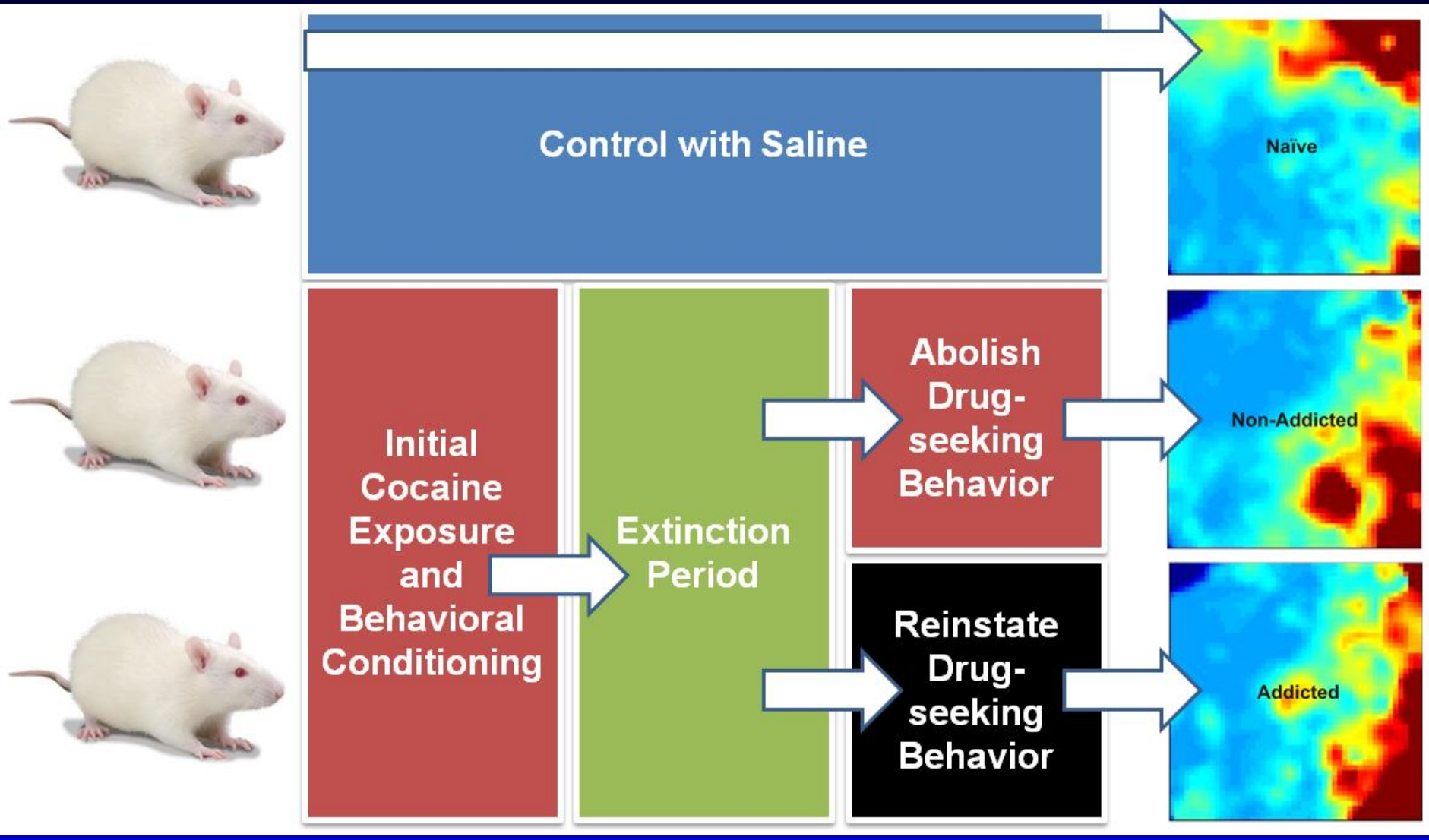


Collaboration with Prof. Shramm-Saypta (Duke University)

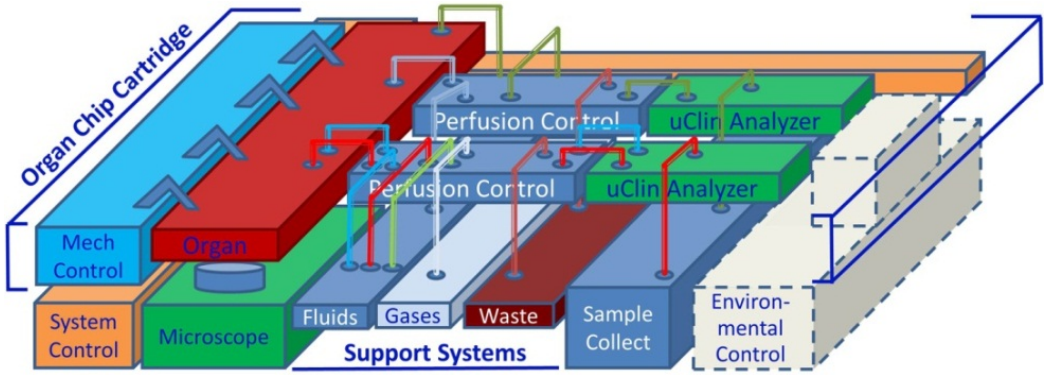
Metabolomic dynamics inspector (MEDI) self-organizing feature maps for target prioritization



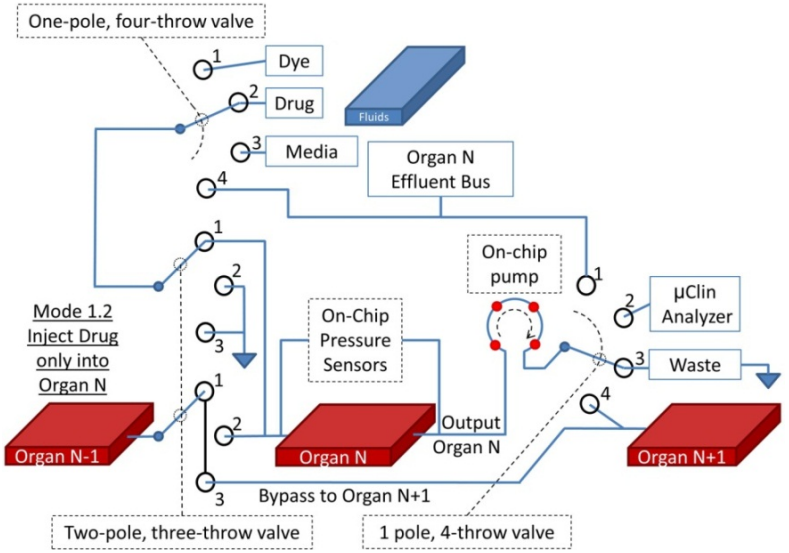
Can leukocytes encode long-term metabolic changes to drug exposure? rat cocaine model

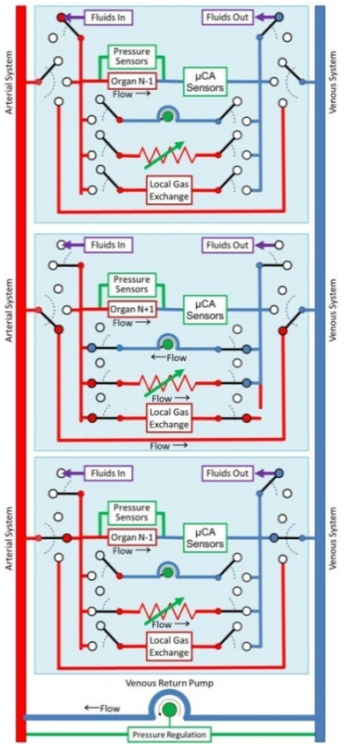


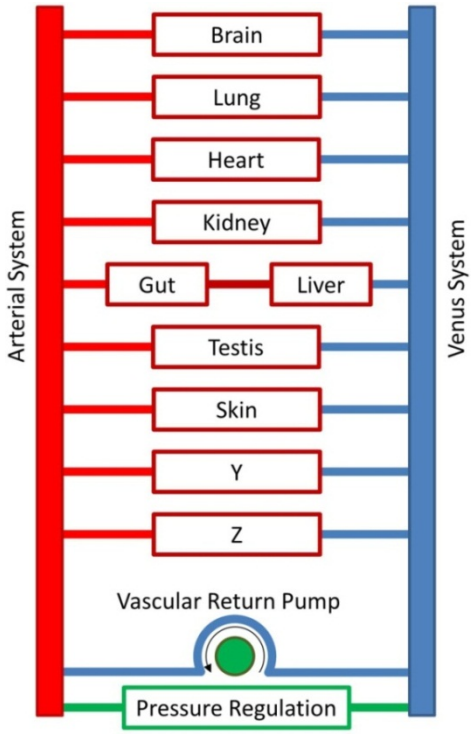
Generalized scheme of the μHuman



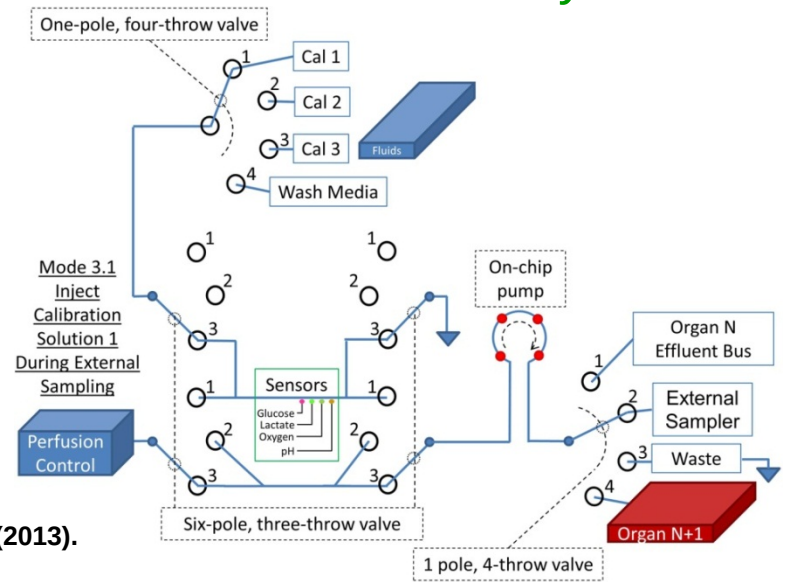
Perfusion Controller







MicroClinical Analyzer



J. P. Wikswo *et al.*, *IEEE Transactions on Biomedical Engineering* 60(3), 682-690 (2013).

The µHuman and mHuman in the press…

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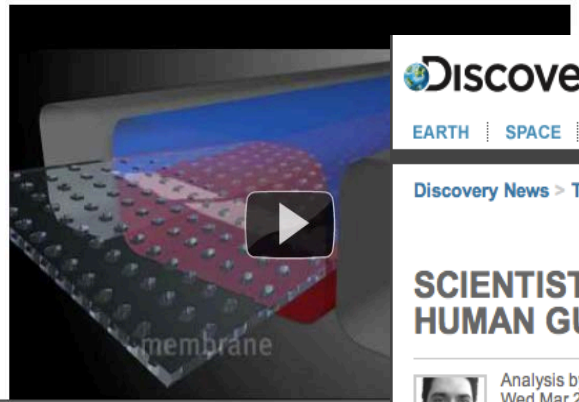

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Analysis by Jesse Emspak
Wed Mar 28, 2012 10:01 AM ET

Artificial jellyfish swims in a heartbeat

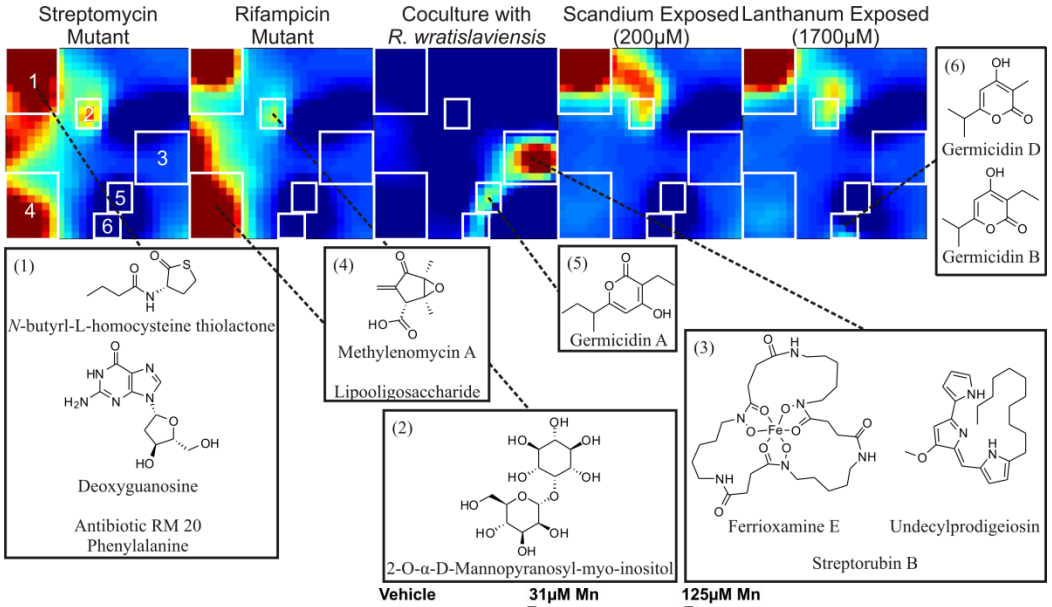
Date: Jul 22, 2012

Creation is an amalgam of silicone polymer and heart muscle cells

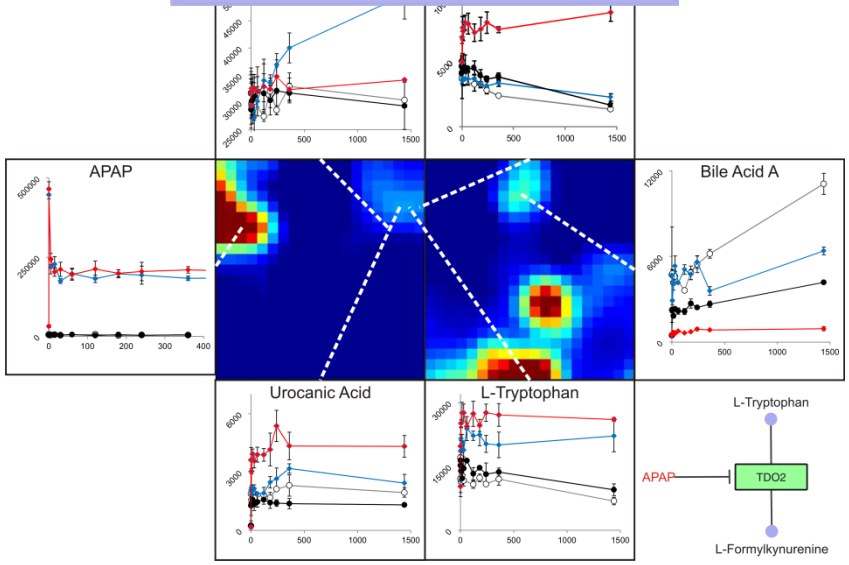
Integrating biology: Translating data to information
(Self-organizing maps for untargeted analyses to target identification)

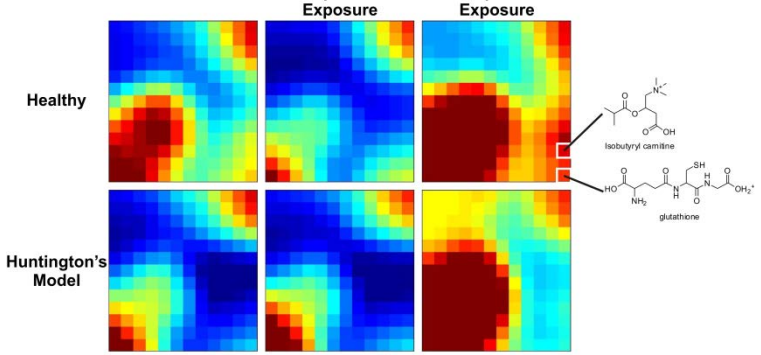
- Self-organizing maps to elucidate salient molecular features
- Heat map features direct target species for identification
- Initially untargeted analyses for panomic molecular coverage

Drug discovery using IM-MS



Synthetic biology: liver toxicity to acetaminophen (APAP) by IM-MS

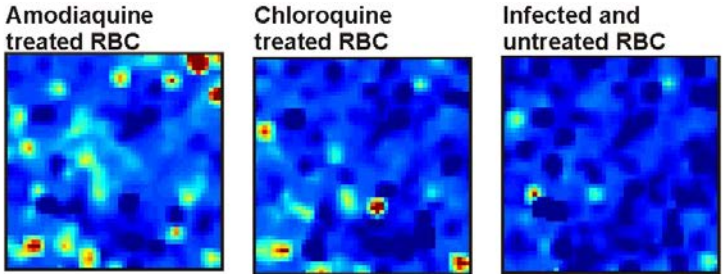




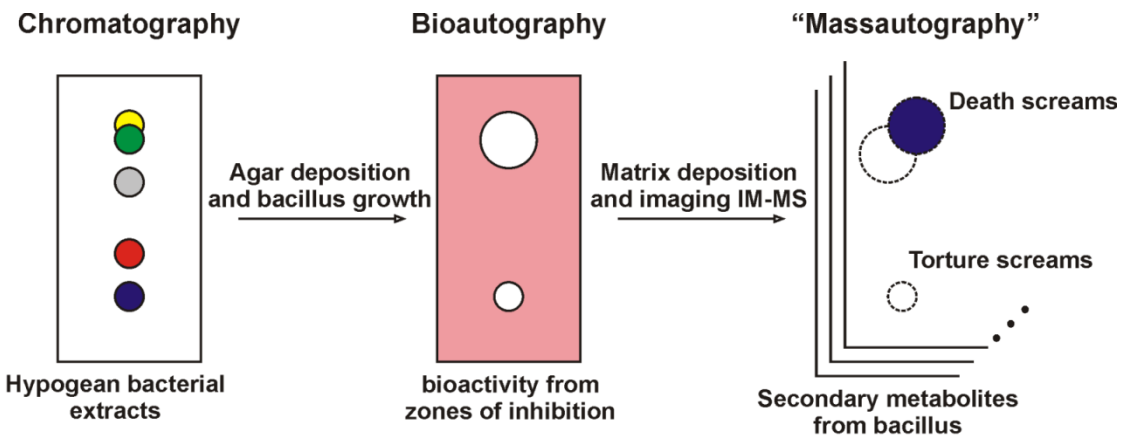
Disease diagnostics with IM-MS

Can we get to systems, synthetic, and chemical biology with integrated omics and informatics?

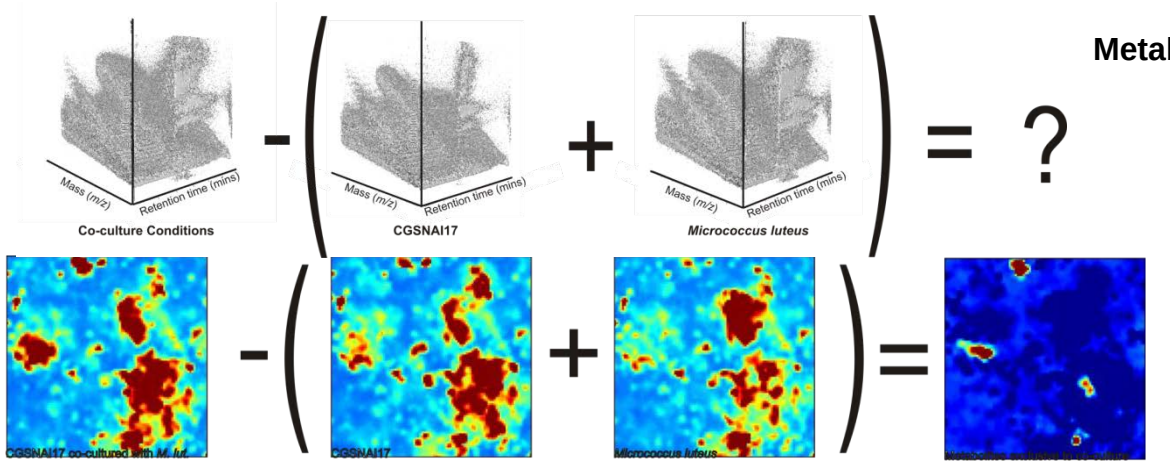
Integrating biology: feature identification



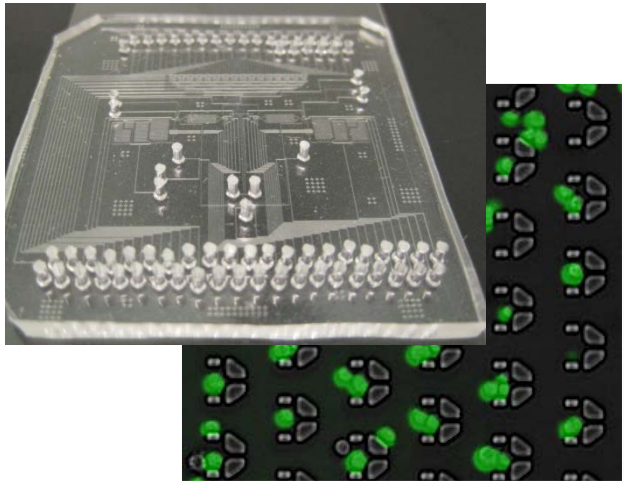
Massautography and imaging mass spectrometry



Drug discovery from complex biological



Metabolic dynamics of cellular perturbation



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