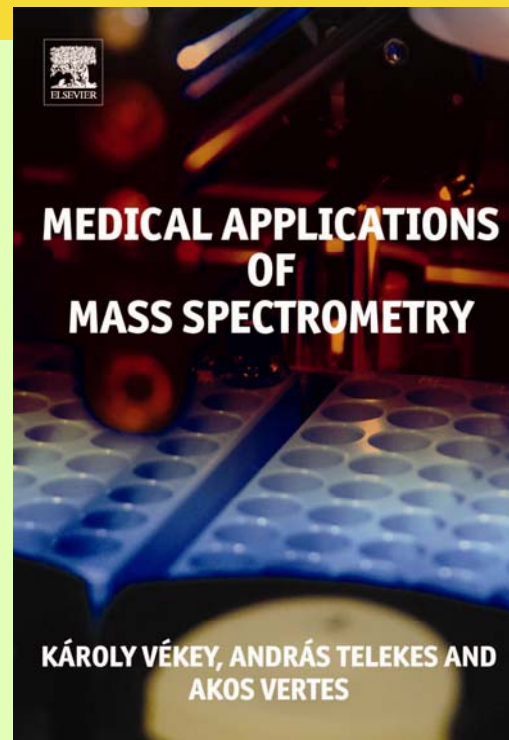
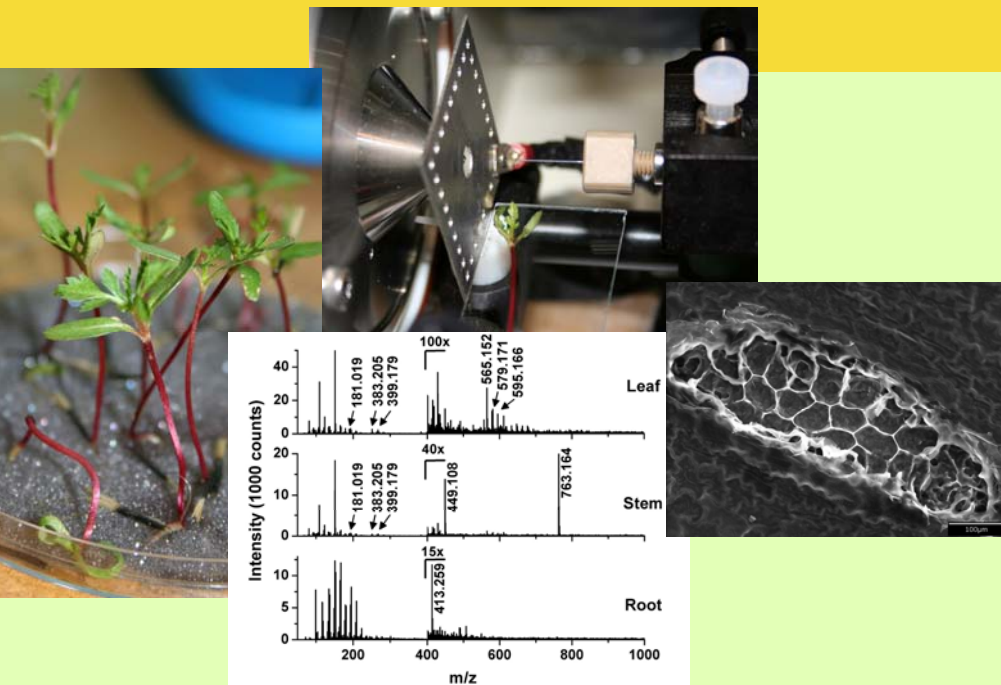
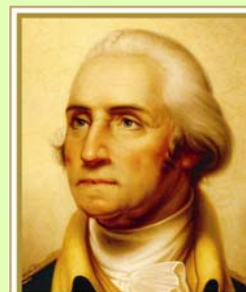


Ambient Ion Sources for Biology, Medicine, Safety and Security



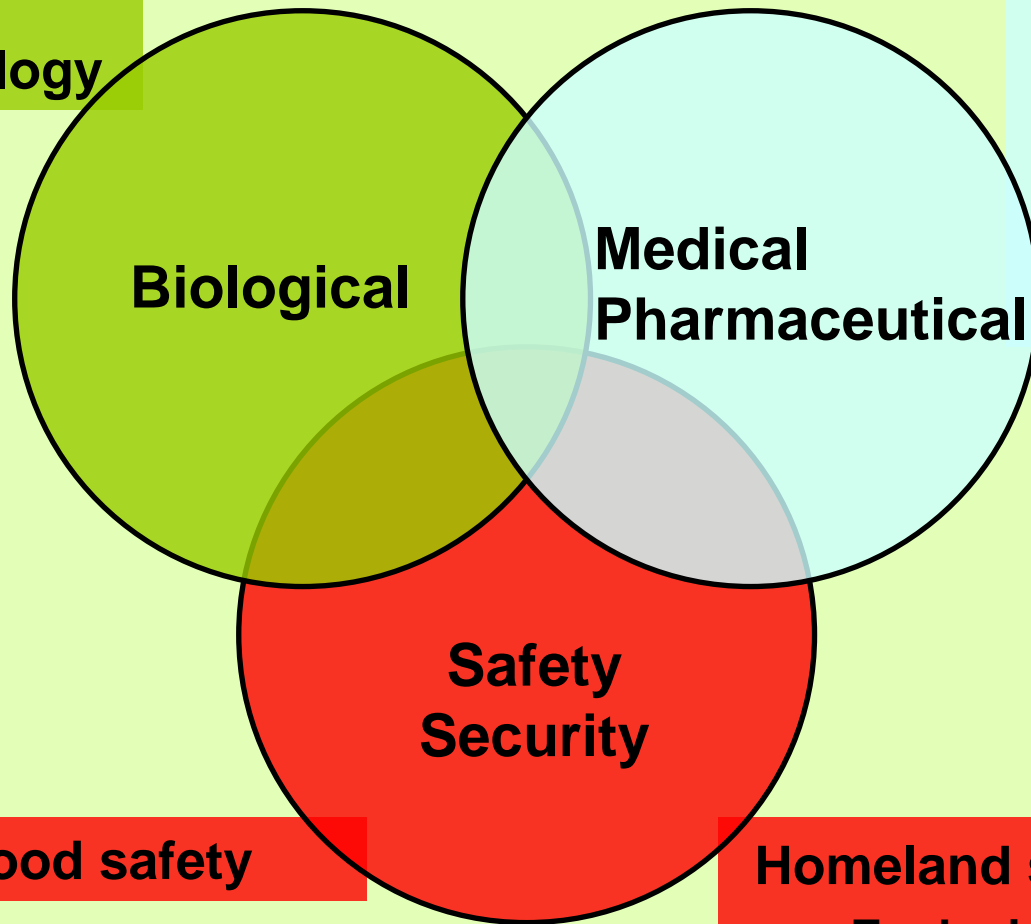
Akos Vertes and Peter Nemes
W. M. Keck Institute for Proteomics
Technology and Applications
Department of Chemistry



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UNIVERSITY
WASHINGTON D.C.

Current analytical challenges

Metabolomics
Proteomics
Chemical ecology



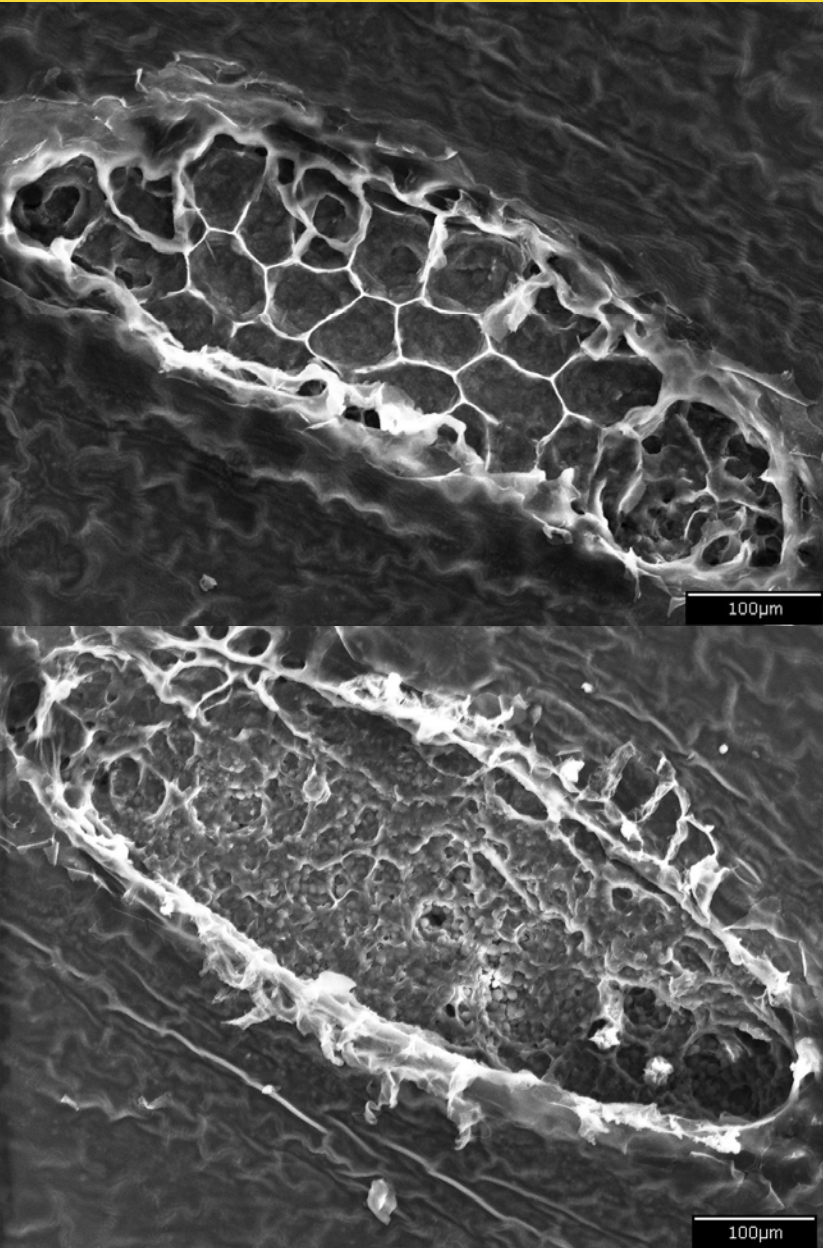
Diagnosis
Biomarkers of disease
Drug testing
Treatment
Prognosis
Drug development

Food safety

Homeland security
Explosive detection

New approach: in vivo imaging mass spectrometry

Technical challenges for imaging MS



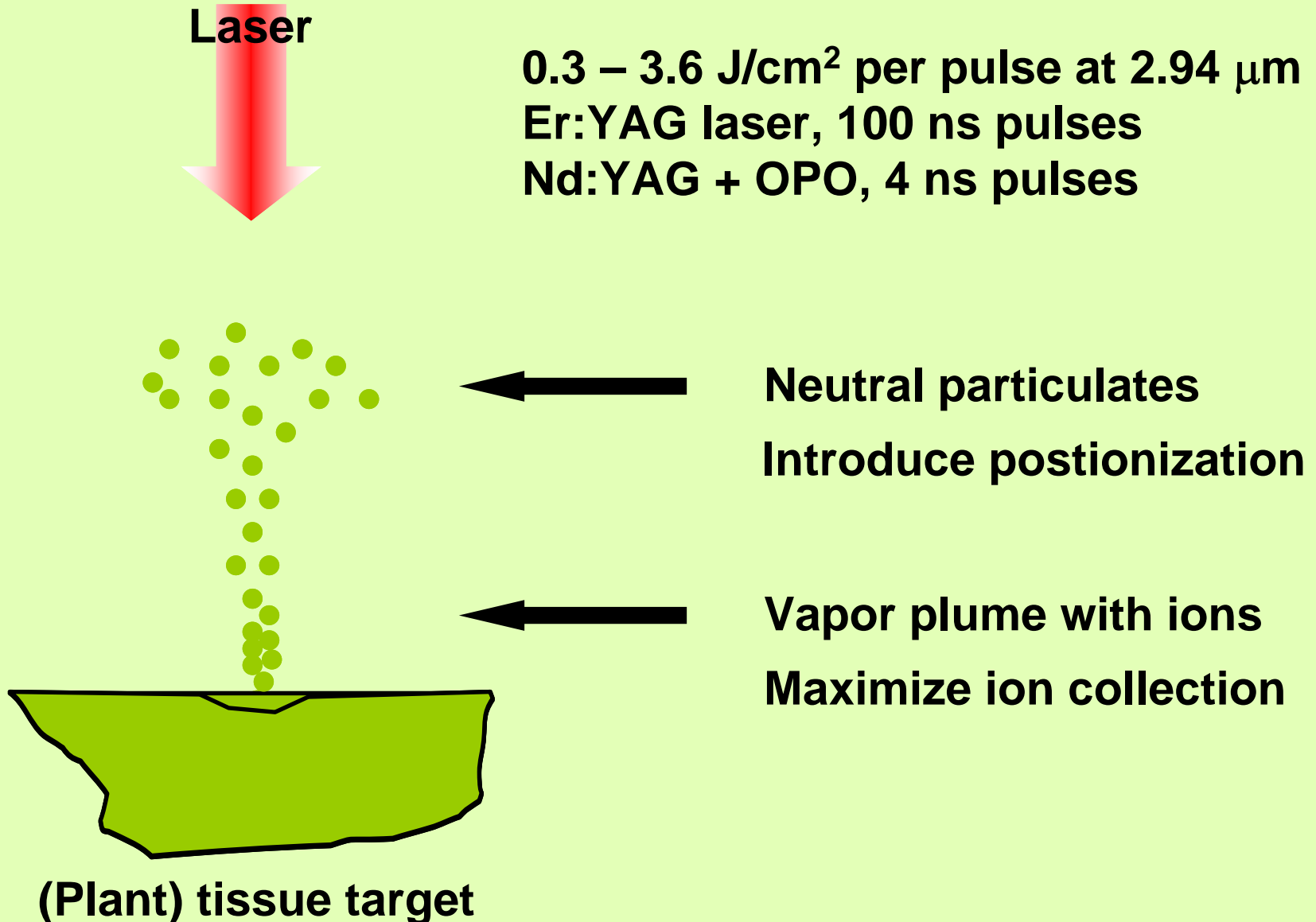
Obstacles for (*in vivo*) observations:

- vacuum conditions
- denaturing matrixes in MALDI
- diffraction limited resolution

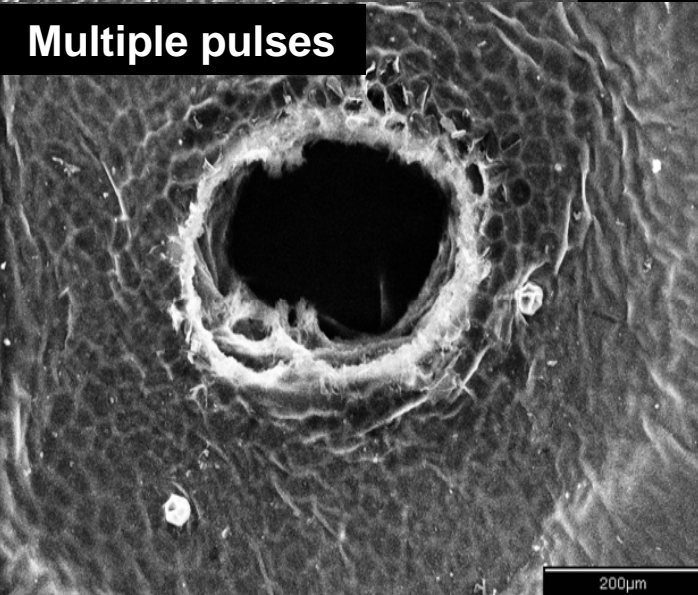
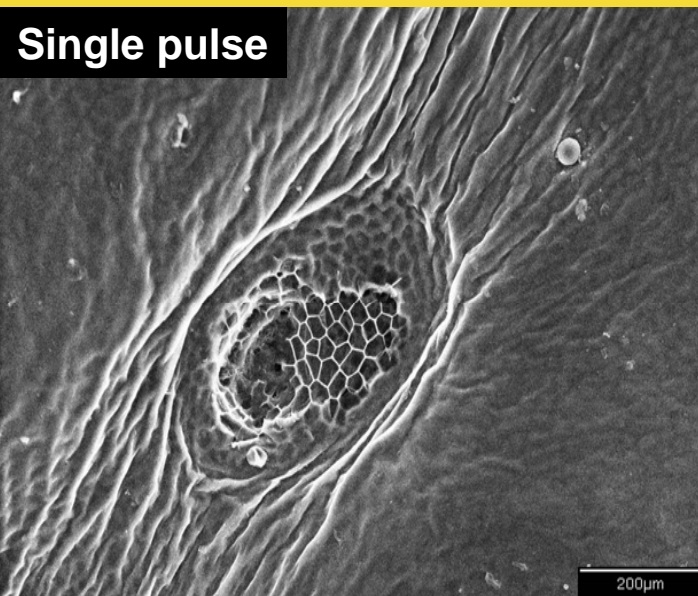
Objective:

High resolution MS imaging at atmospheric pressure with no matrix

Mid-IR laser ablation of water-rich targets



Mid-IR laser ablation of tissue



2 J/cm² per pulse

Single shot ablation of leaf

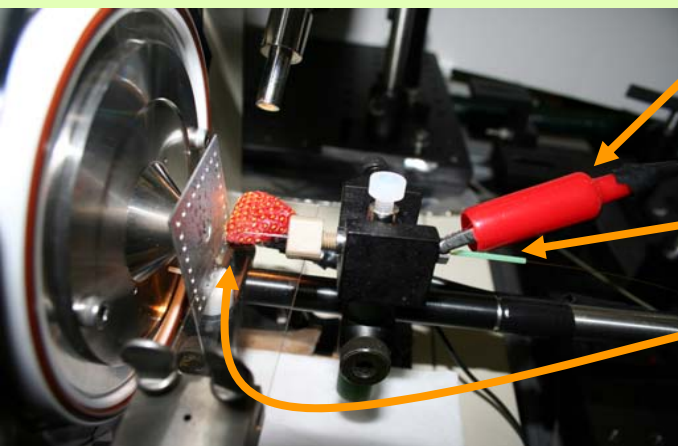
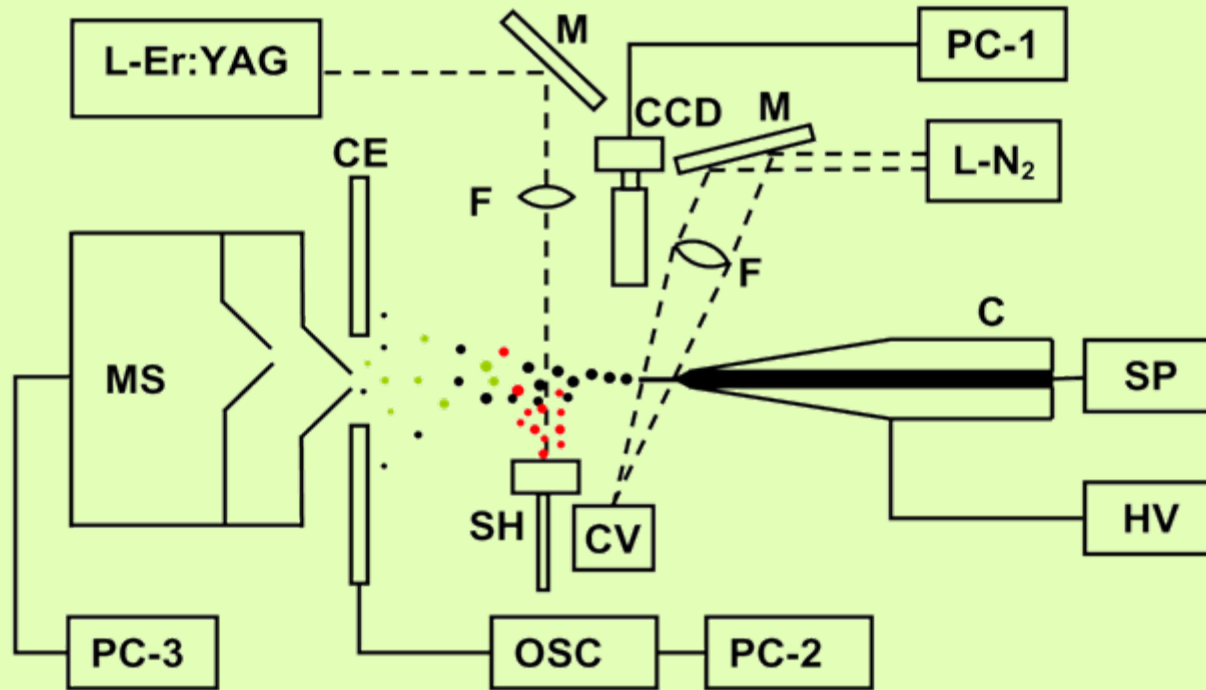
- cuticle
- upper epidermal cells



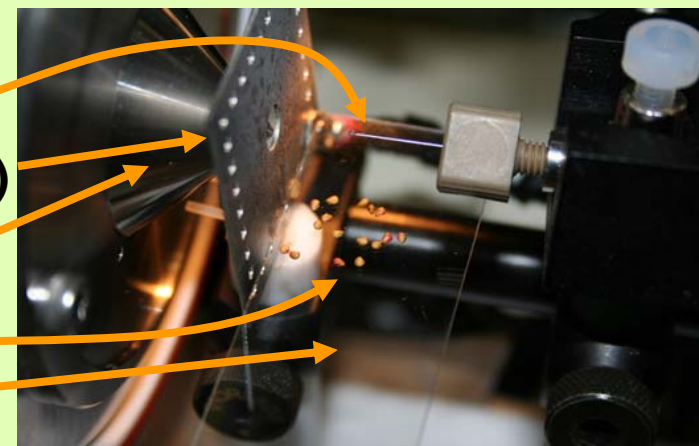
Ablation of leaf with multiple shots

- cuticle
- upper epidermal cells
- palisade and spongy mesophyll
- subaxial epidermal cells
- cuticle

Laser ablation electrospray ionization (LAESI)



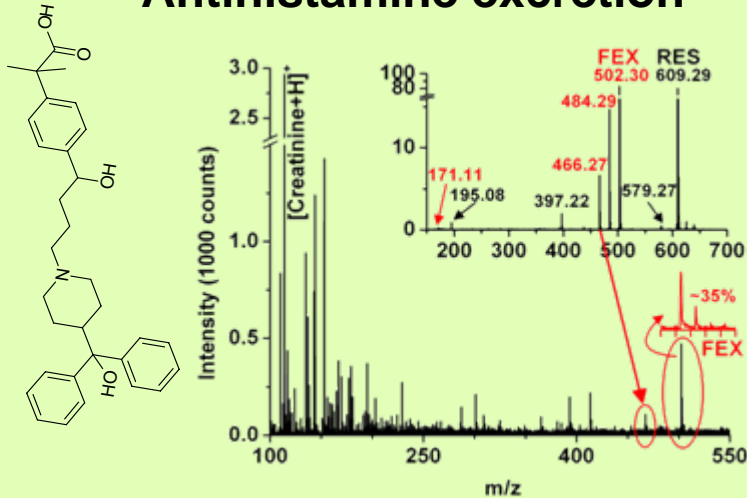
High voltage (HV)
Capillary (C)
Counter electrode (CE)
Syringe pump (SP)
Mass spec (MS)
Sample
Sample holder (SH)



LAESI MS figures of merit

From small drug molecules to large biomolecules:

Antihistamine excretion

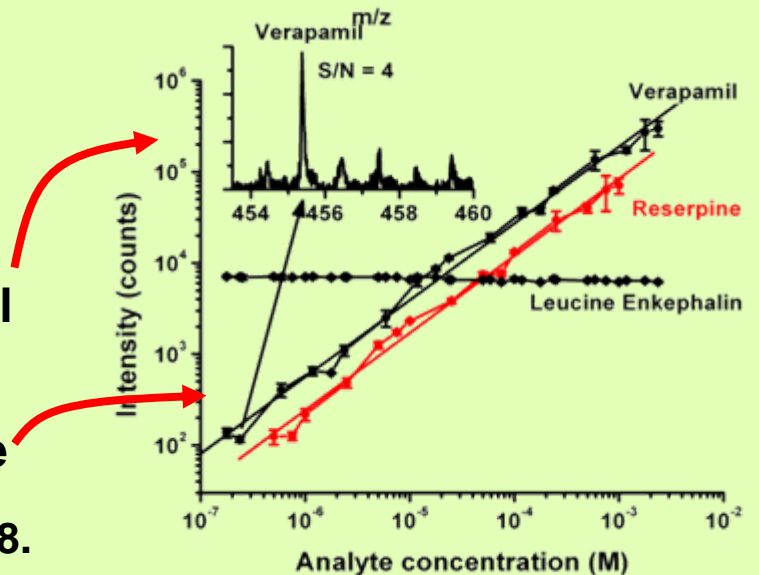
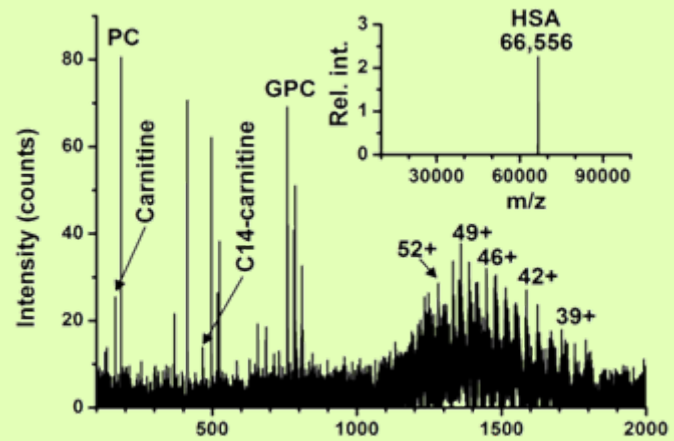


Fexofenadine (FEX), the active component of Allegra, detected directly from urine 2 hours after administration caplet.

Limit of detection: 8 fmol for verapamil

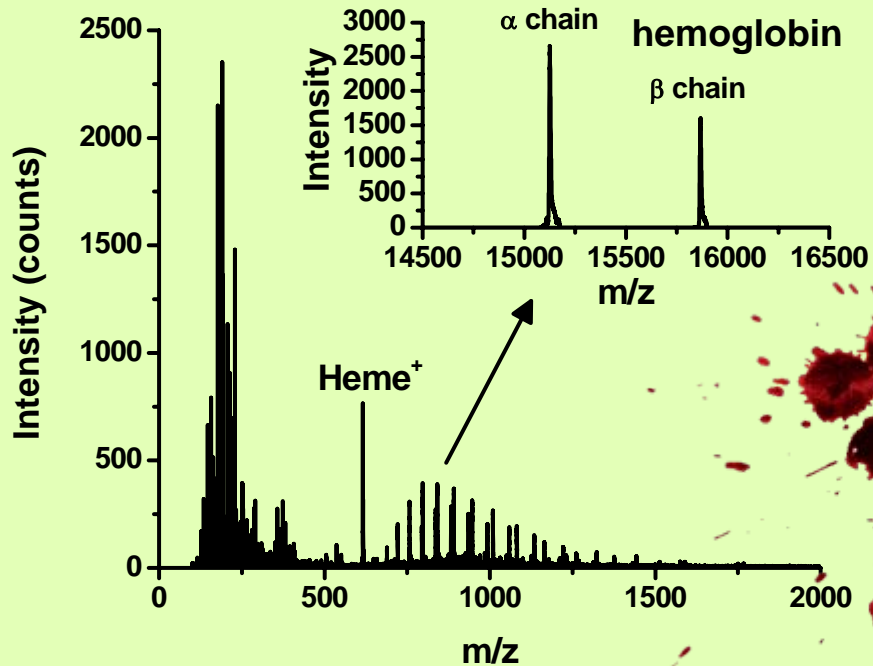
Quantitation: 4-decade dynamic range

Human serum albumin in serum



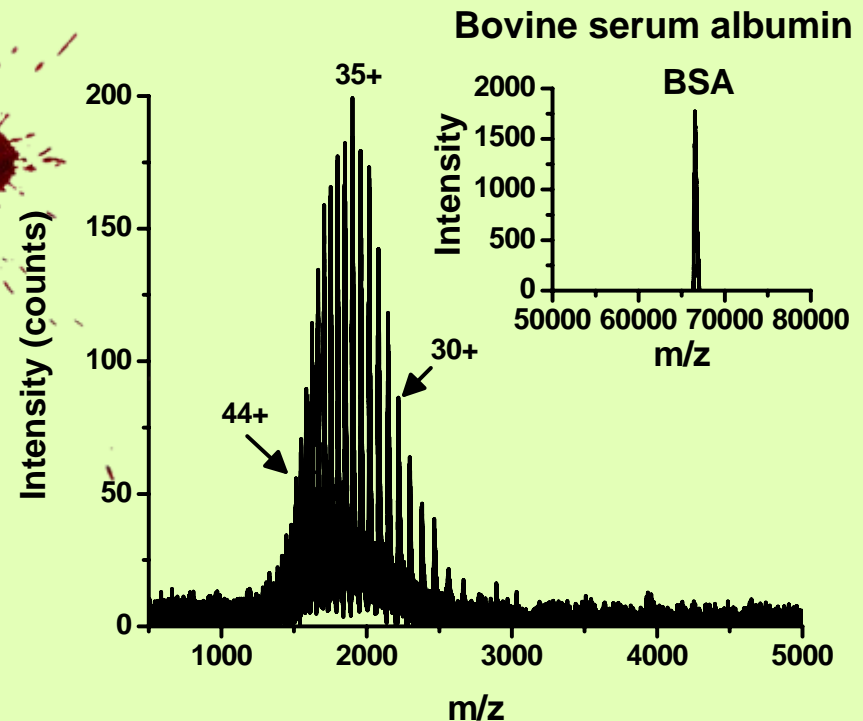
Protein identification - LAESI

Laser ablation electrospray ionization (LAESI) mass spectrometry



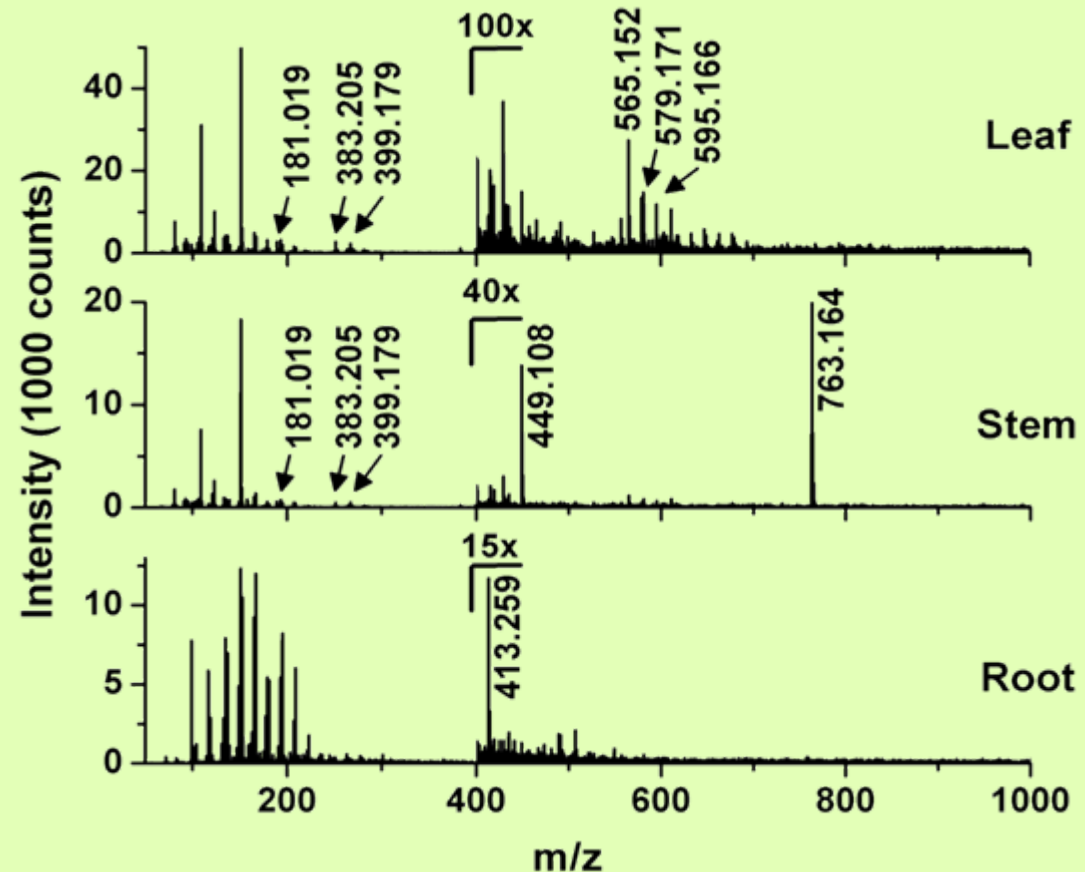
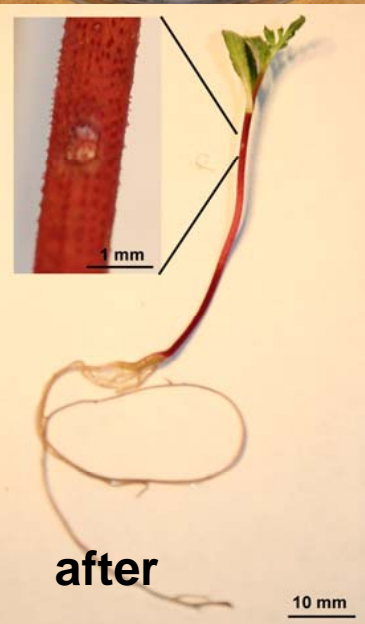
Direct analysis of
proteins in human blood

High mass discrimination
resolved:
Molecular mass 66,547 Da



LAESI for in vivo spatial profiling

LAESI profiling of 1-week old French marigold (*Tagetes Patula*) seedlings



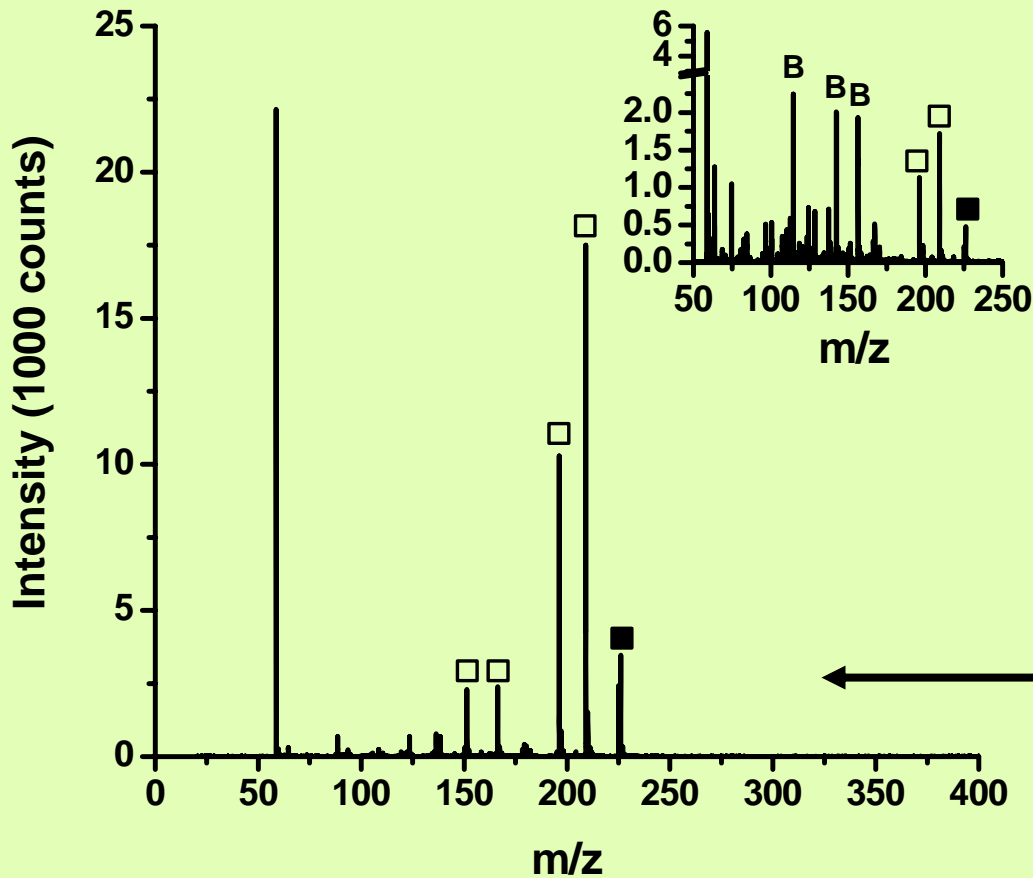
Organ-specific chemicals detected *in vivo*, e.g.:

- kaempferol dirhamnoside (m/z 579.1) in leaf
- cyanidin glucoside m/z 449.1) in stem
- methylsalicylate (m/z 154.0) in root

Explosive detection

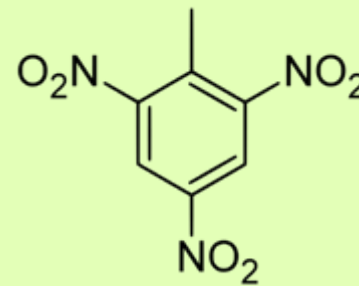


LAESI – MS in negative ion mode



← from dollar bill

Trinitrotoluol
TNT



← from glass surface

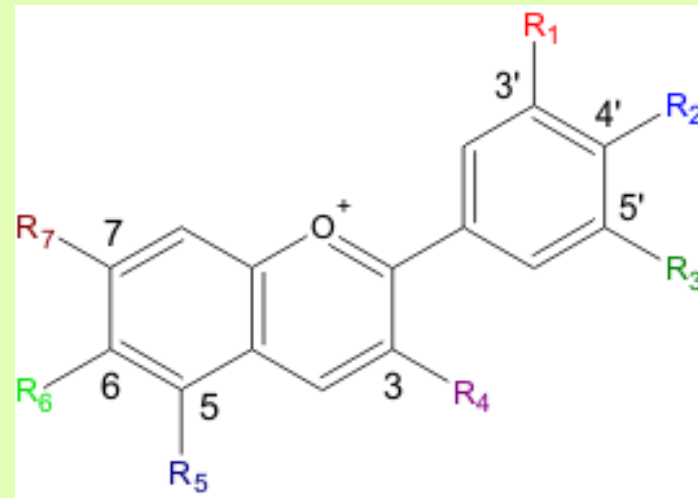
Conclusions - LAESI

- Introduced novel ambient ionization technique
- LAESI figures of merit
 - High mass capabilities up to 66 kDa
 - Quantitation: four-decade dynamic range
 - 8 fmol LOD
- LAESI molecular imaging of plant tissue
 - 300-400 μm spatial resolution
 - MS/MS for structure identification
 - Secondary metabolites in variegated plants
- Depth profiling and 3D molecular imaging
- LAESI promises cell by cell analysis

Metabolic response to genetic changes



Variegated *tdy1* maize mutant shows accumulation of soluble sugars and starch in yellow sectors.

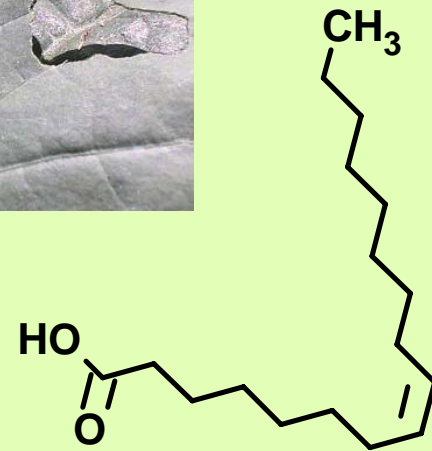


Anthocyanins accumulate in yellow sectors

Problems in Chemical Ecology

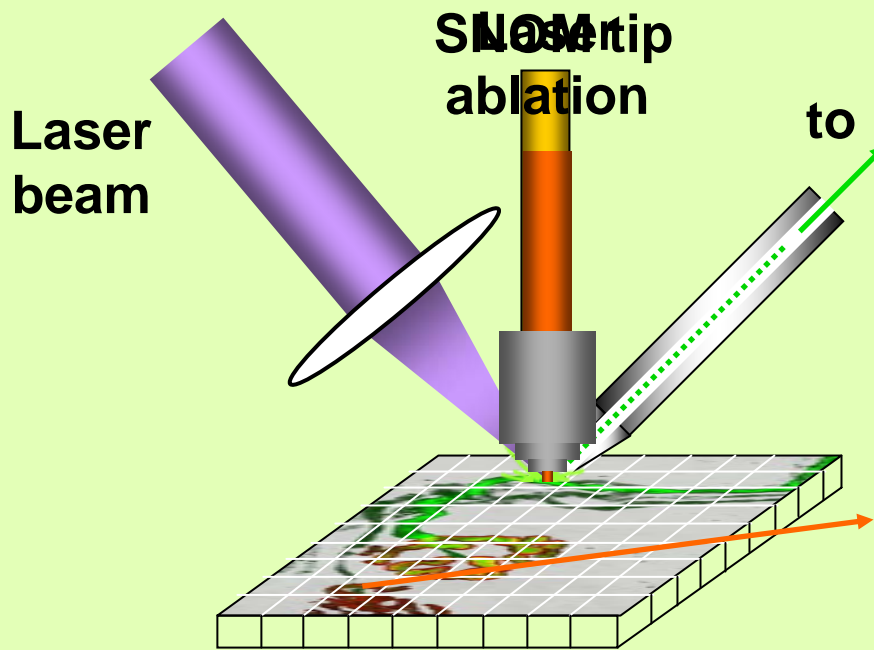


Cotesia glomerata wasp –
a parasite of imported cabbageworm
uses fatty acids
in host searching

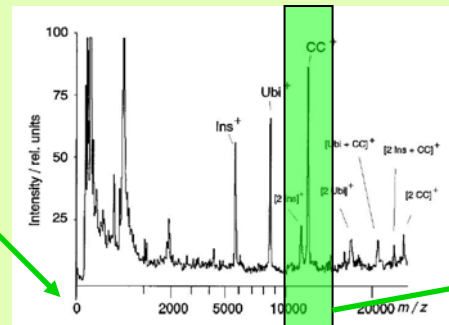


Oleic acid

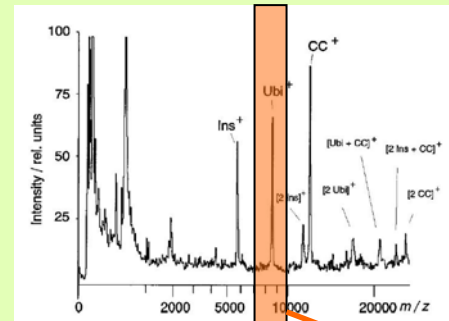
Challenges - Depth profiling



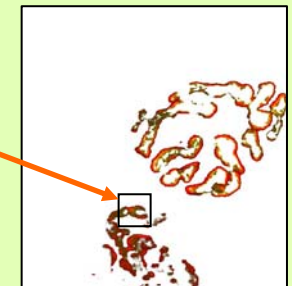
to MS



composite images



spectra



Combination with surgery

Acknowledgements

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