Emerging analysis techniques in Biochemistry

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EDTAS Human Biotechnologies
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THE UNIVERSITY OF MELBOURNE

bio21 institute

The Bio21 Institute: Fulfilling a Vision

Bio21 Molecular Science and Biotechnology Institute

The Bio21 Institute Vision: ***"To improve human health and the environment through innovation in biotechnology and molecular sciences, driven by multidisciplinary research and dynamic interactions with industry".***

Key Elements:

- ***Leadership*** **in world-class multidisciplinary research and research training (Research Excellence)**
- ***Core Platform Technology Facilities*** **(shared resources, industry engagement)**
- ***Nurture Australia's biotechnology sector*** **(industry engagement; innovation)**
- ***Science Education*** **for secondary schools (partnership with the Elizabeth Blackburn Science School)**

Bio21 Institute Atrium – the Institute was officially opened in 2005

~650 members (40 research groups; ~ 66% future generation scientists; ~ 100 Industry)

7/20/2018

Melbourne Biomedical Precinct

Bio21 platform technologies in molecular life sciences

Bioresources Research Facility
Peptide Technologies
Specialist Stores

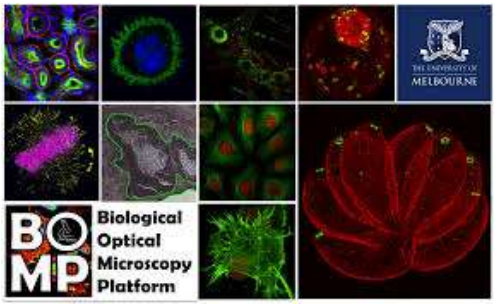
Electron Microscopy

Mass Spectrometry, Metabolomics Australia

Magnetic Resonance

Research Systems Infrastructure

Protein Characterisation



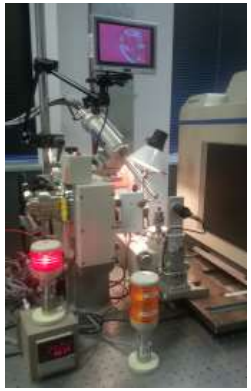
Molecular imaging in the life sciences – high speed, increased sensitivity and closer interconnectivity

Proteomics, lipidomics and metabolites

Cryo electron microscopy and tomography

Nuclear magnetic resonance (fragment screening)

Computational biology (virtual screening)



X-ray crystallography

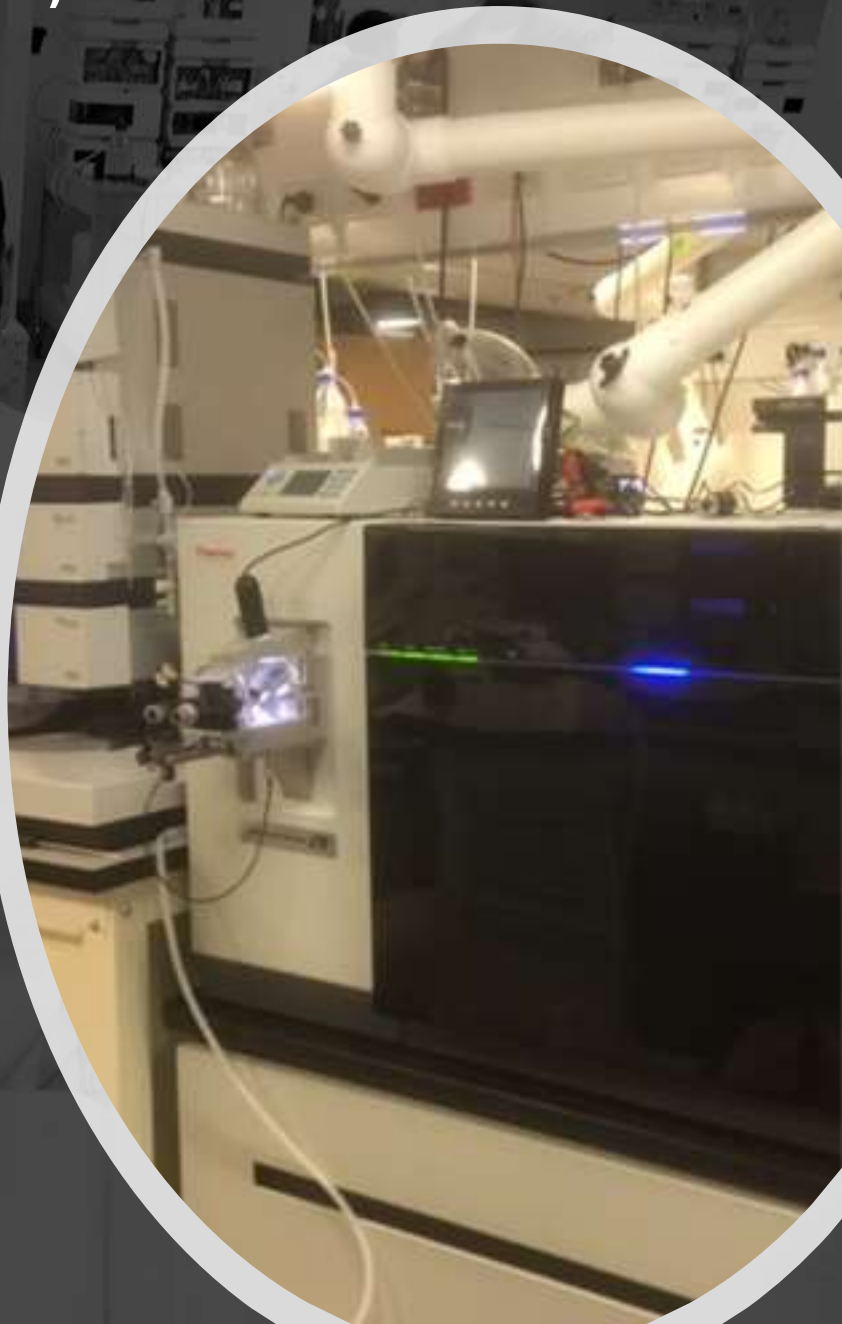
Protein drug binding

Bio21 Mass spectrometry (MMSPF) and Metabolomics Australia

Mass Spectrometry has emerged as a core analytical chemistry platform for proteomics and metabolomics. Proteomics determines the structure and regulation of individual proteins. Metabolomics defines the chemical state of cells and changes in cell metabolism that occur in response to genetic changes, diet and drugs.

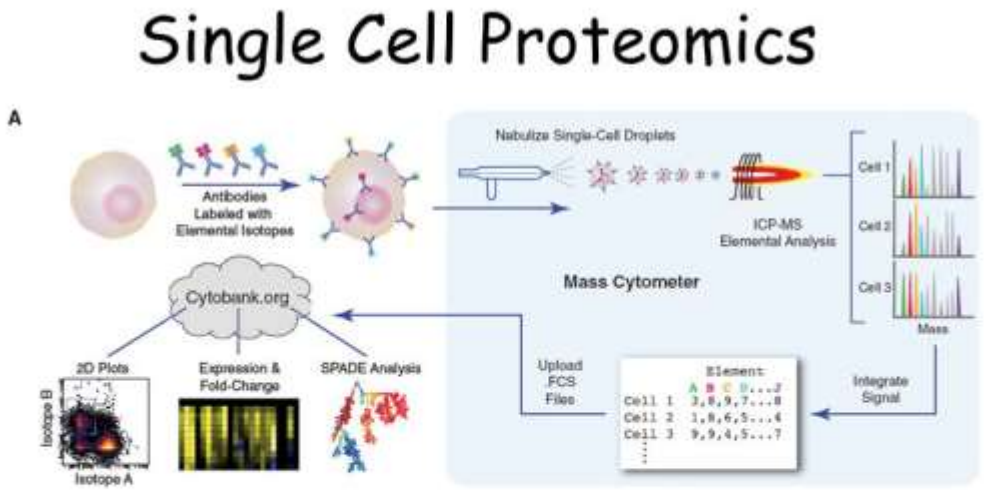
The Institute's mass spectrometry capability includes **22 instruments** which cover a range of applications including:

- High accuracy determination of molecular mass of naturally occurring proteins, nucleic acids, metabolites, and synthetic compounds
- Protein identification and modification by fragmentation analysis
- Identification of biomolecules (protein, metabolites) in tissue samples and biofluids to understand disease processes and identify new diagnostics
- Validation of chemical synthesis and definition of chemically diverse metabolites requiring a variety of ionization techniques

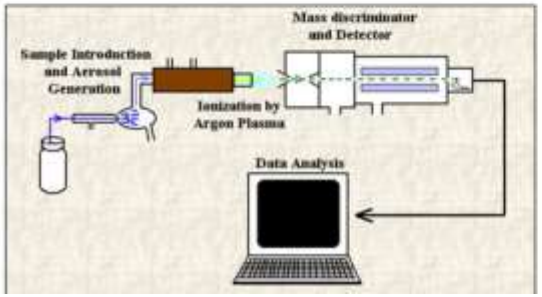


Proteomics towards 2040 – challenges and opportunities

Challenge: Mass spec will continue to get faster and more powerful but is 100% coverage attainable? We now get 70% coverage easily but lower abundance is difficult.



Opportunities: Aiming towards 'single cell proteomics'.



ICPMS

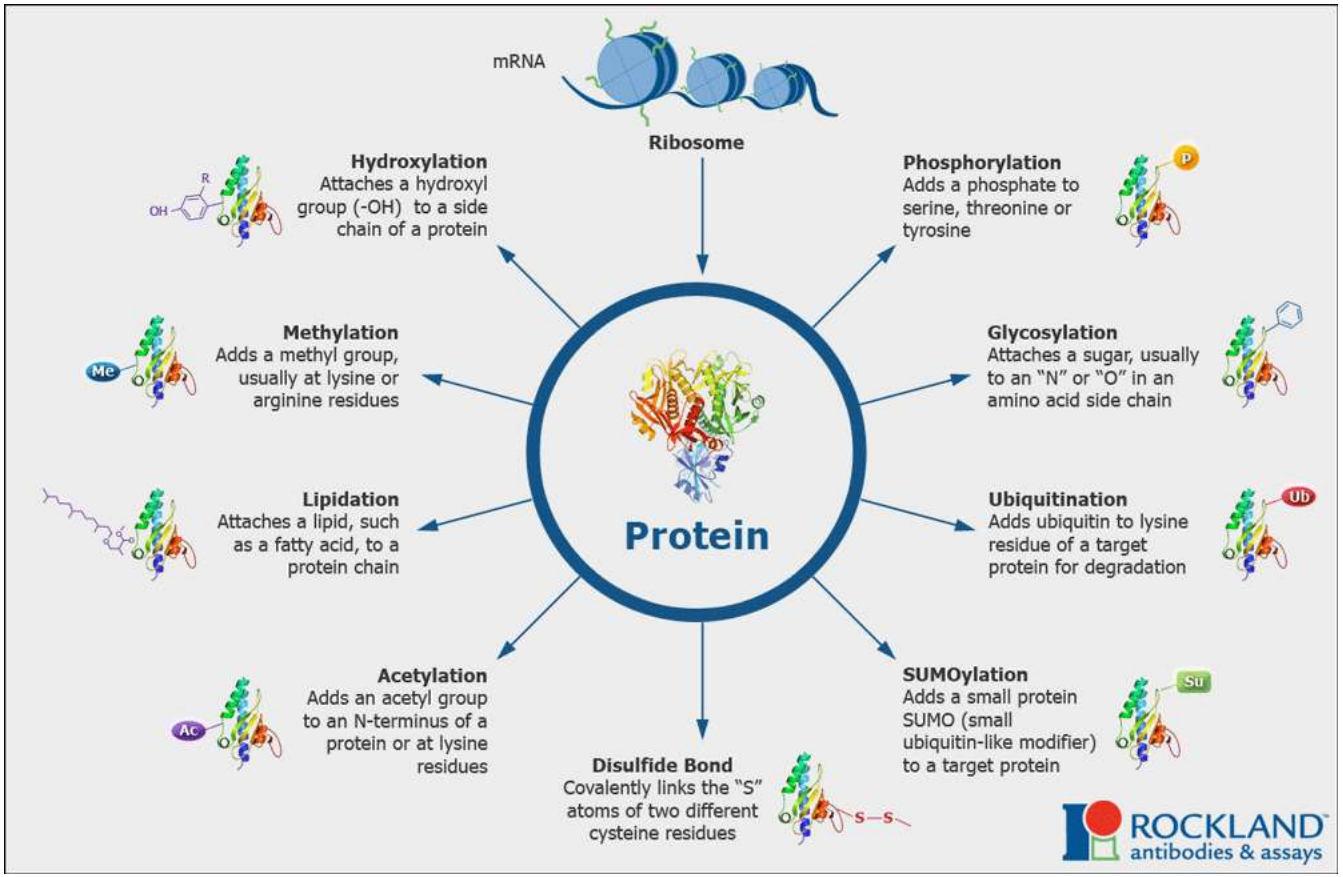
Inductively coupled plasma MS

Bendall et al (2011) Science

Vision: Will mass spec methods be replaced by nanopore technology?

Proteomics towards 2040 – challenges and opportunities

Challenge: How do we how make sense of what all this omic data means. How do you join it all together? Urgent need for systems biology software to catch up.

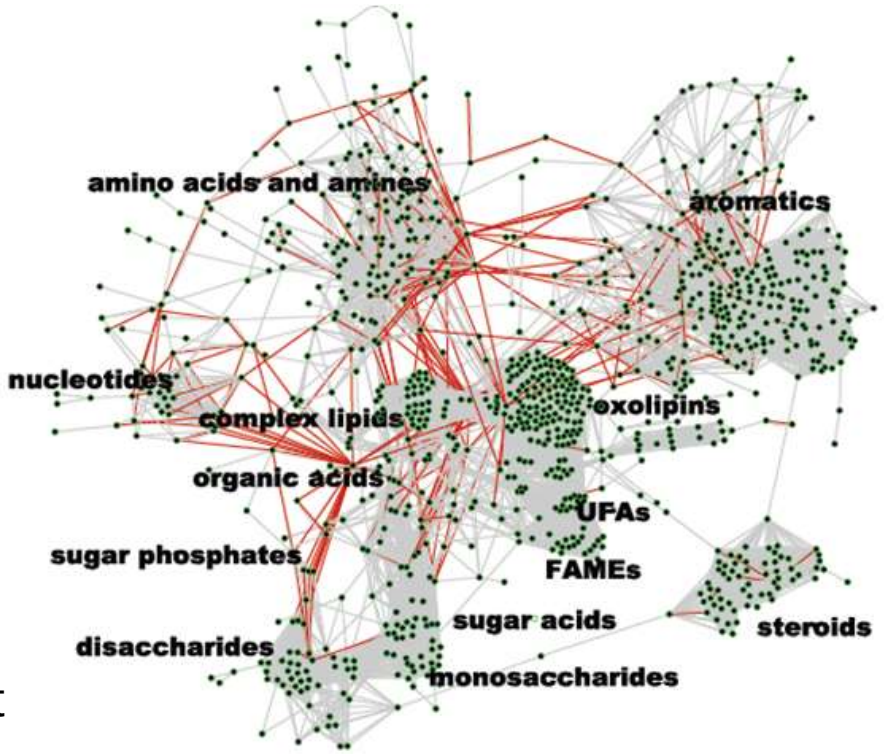


Opportunities: To measure and understand the consequences of the multiple forms a single protein (post-translational modifications) can have and what effect each has on the protein's activity and its distribution in the cell.

Vision: To monitor the health of human cells in response to various stimuli.

Metabolomics towards 2040 – challenges and opportunities

Challenge: Enormous number of unidentified metabolite signals in human tissues and fluids. The human Metabolome Database includes >140,000 metabolites in human tissues, for which only 20% have been detected. Currently we can only detect a minority of all predicted metabolites and and there is a vast excess of unknown metabolites.



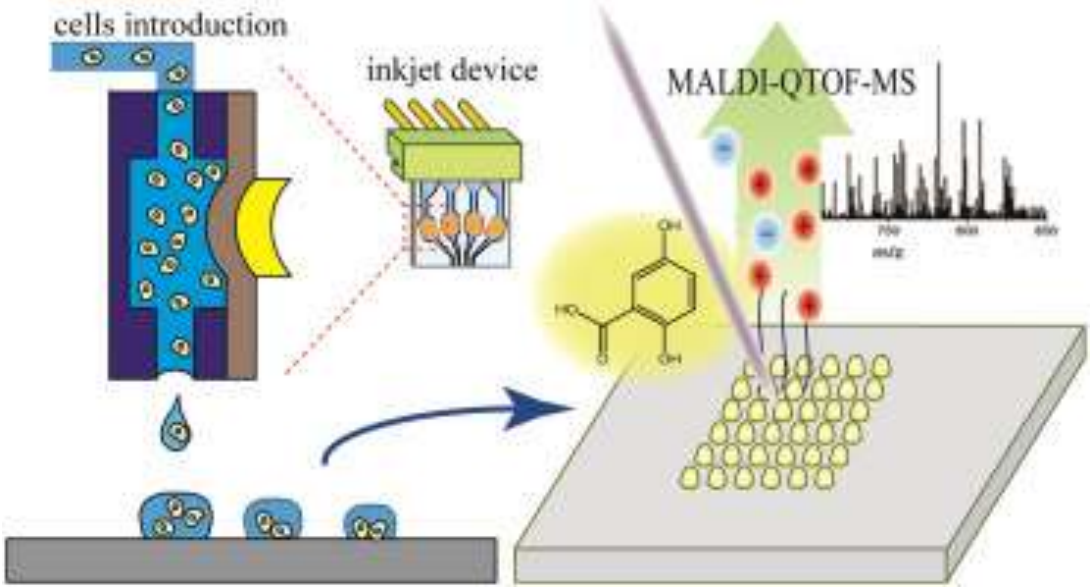
Opportunity: Over the next 20 years we will identify/account for all metabolites, which will massively expand our current view of human metabolism and the impact that environmental metabolites (drugs, pollutants, food, microbiota) on human metabolism.

Vision: Able to routinely detect (with absolute quantitation) >20,000 endogenous and exogenous metabolites in easy-to-sample biofluids (blood, urine, saliva) using bench top (relatively inexpensive) instruments - providing an immediate and global picture of the health and performance of an individual.

Metabolomics towards 2040 – challenges and opportunities

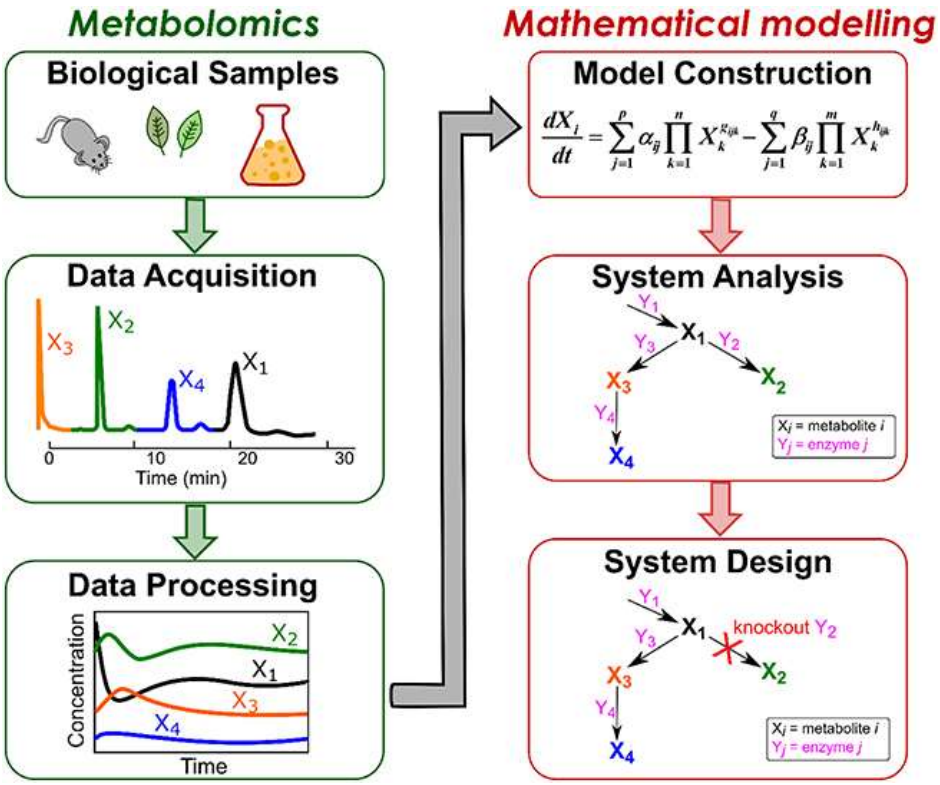
Challenge: To develop real-time, highly sensitive analytical methods on biofluids and tissues.

Opportunities: (1) increase through-put (such as direct infusion MS, ambient pressure MS) to allow regular, facile and rapid screening of whole populations, (2) allow real time measurements of metabolic changes on the scale of seconds to minutes (using direct infusion of cells) and (3) single cell metabolomics.



Vision: Sampling will be cheap and simple enough to do daily (or even continously) allowing monitoring of wellness, alertness and general performance (aside from diseases states) eg. we are already looking for biomarkers for alertness that would allow long haul drivers to self assess. Continuous monitoring through the skin (sweat) or by on-line monitoring of breath in future (breathomics is already here)

Metabolomics towards 2040 – challenges and opportunities



*Challenge: C*omputational modelling of non-linear metabolic networks.

Opportunities: Understand molecular communications in cells.

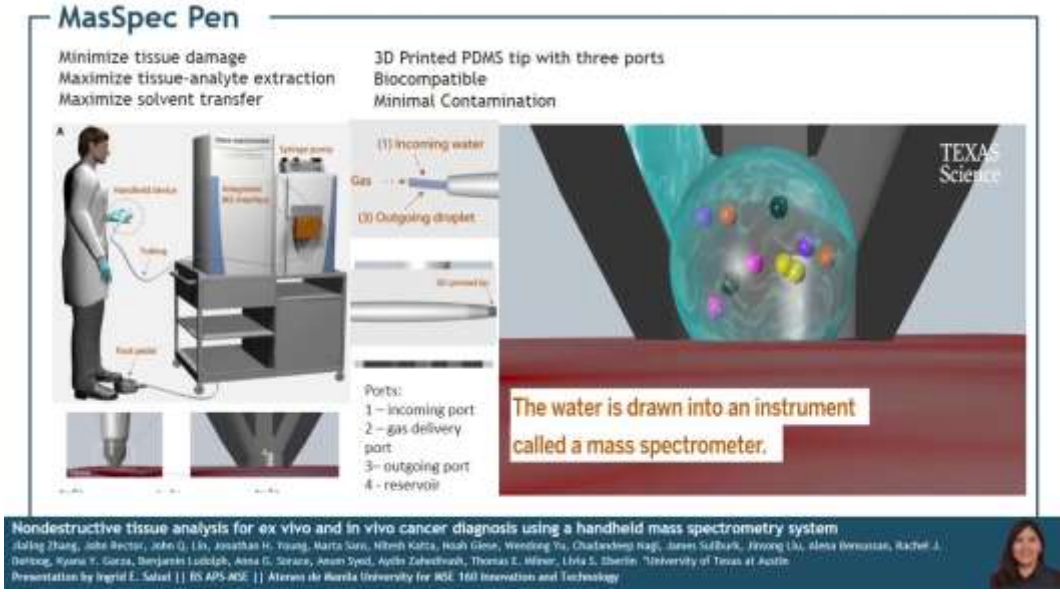
Vision: We will master synthetic biology – ie. we will be able to manipulate bugs or design synthetic cells that could be used to colonise our bodies and optimise performance/protect us from pathogens, chemicals etc.
Advanced, rapid global metabolite profiling/modelling will revolutionise drug development as new compounds could initially be tested *in silico* and then *in vivo* at very low concentrations to test for potential toxicity and appropriate mode of action.

Metabolomics towards 2040 – challenges and opportunities

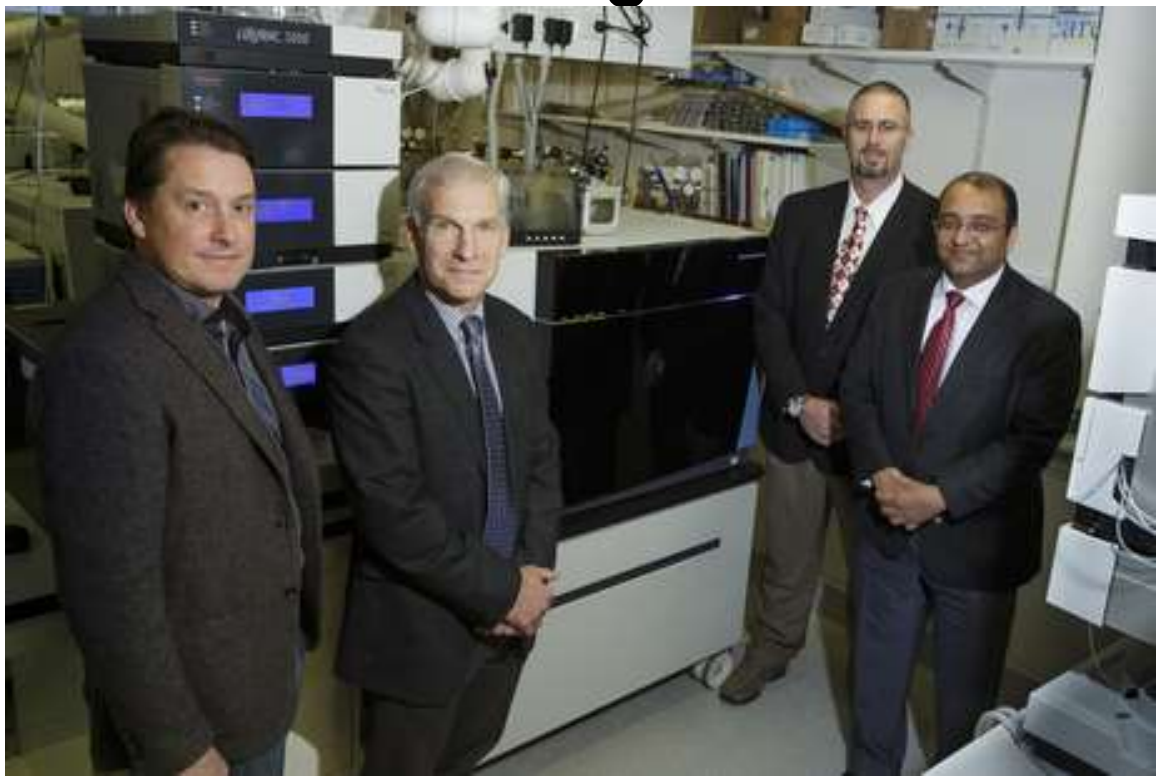
Challenge: Democratize mass spectrometry in the form of simple hand-held devices (using ambient DESI sources).

Opportunities: Disease diagnosis in real-time (ie. in the field/doctors rooms), intra-operatively, continuous environmental monitoring of chemicals, food/water quality…

Vision: Minaturised MS (or new analytical) technology to allow to continuously monitoring of the chemical environment around us (useful in the battlefield) and to provide early warning for pathogens, epidemics, …



Acknowledgements



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