Bio-molecular Imaging using Mass Spectrometry

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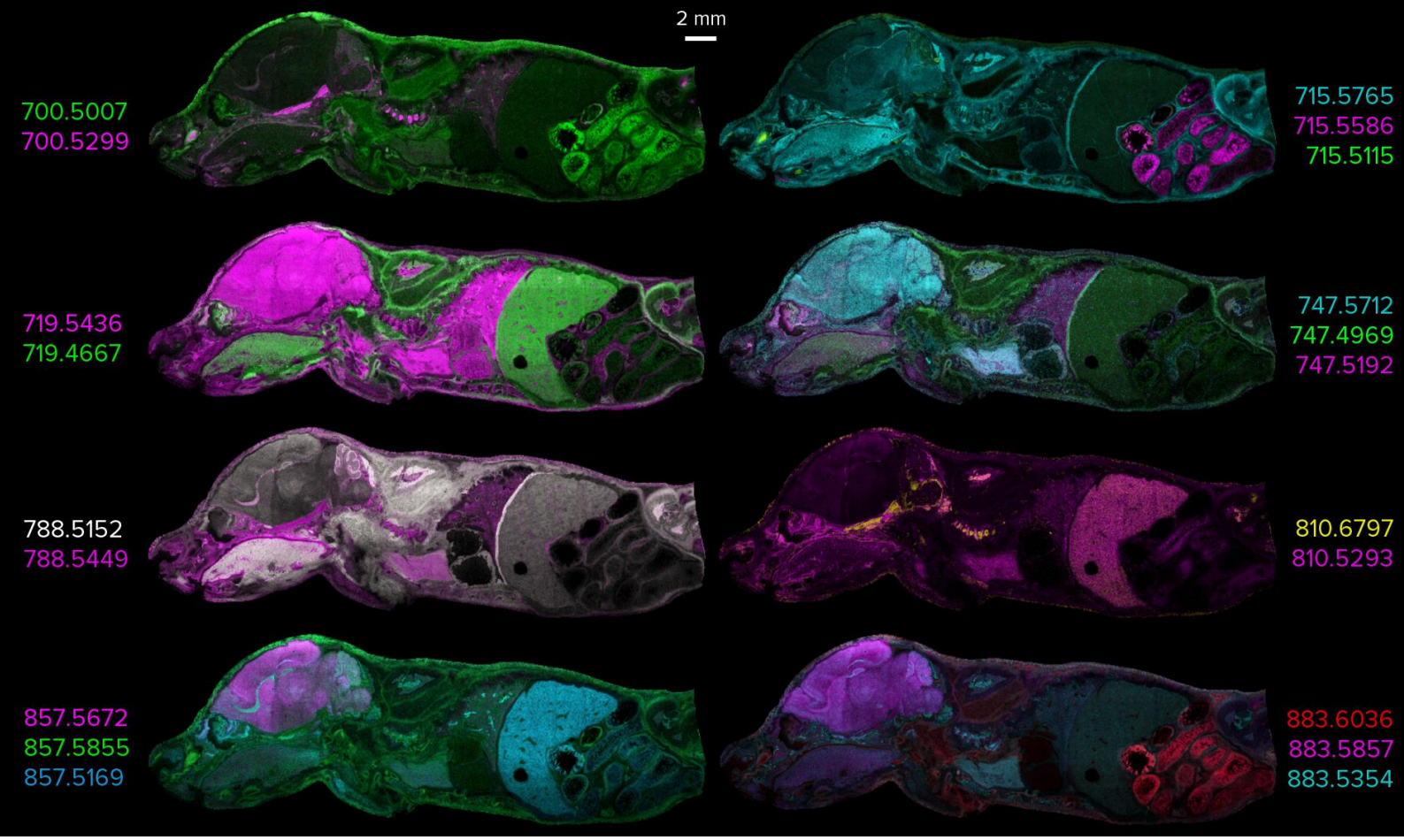

Imaging Mass Spectrometry

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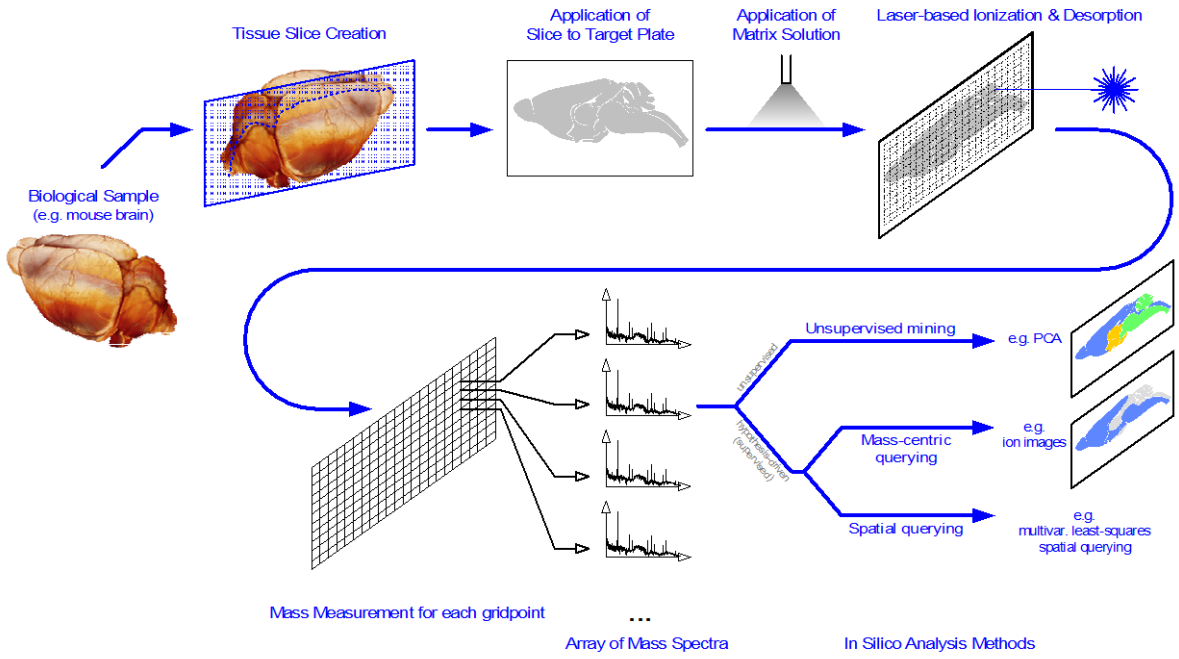
Why this research?

Understanding the spatial context in which molecules interact is becoming increasingly important for biology and medicine. The spatial distribution of biomolecules and the localization of biochemical interactions throughout tissue often hold crucial clues towards determining the biological functions of these biomolecules. Imaging mass spectrometry (IMS)[1,2] is a molecular imaging technology that can deliver such spatial information with high chemical specificity for various classes of biomolecules, including metabolites, lipids, peptides, and proteins. IMS has been gaining considerable momentum in recent years, primarily in the field of tissue biomarkers and drug delivery, and has been successfully applied to tissues of various origin, including insect, mammalian, and human tissue. IMS makes it possible to monitor many hundreds of biomolecules simultaneously, making it a prime technology for exploratory studies. However, this exploratory advantage is currently hampered by the large amount of data that a single IMS experiment can deliver, making interpretation and analysis difficult.

What is Mass Spectrometry?

Mass spectrometry (MS) is a technique that measures the molecular masses found in a sample, and reports them in the form of a mass spectrum. A mass spectrometer uses charged particle optics or ion optics to direct ionized molecules from an ion source, through a mass analyzer, to an ion detector, determining the molecules' mass in the process. In biology, MS is used to characterize the chemical structure of molecules and identify biomolecules such as proteins in organic samples or liquids. Mass spectrometry has become one of the driving technologies in the post-genomic life sciences, particularly in fields such as proteomics, peptidomics, lipidomics, metabolomics, and drug discovery, and its impact has been well recognized (e.g. 2002 Nobel Prize in Chemistry).



What is Imaging Mass Spectrometry?

Imaging mass spectrometry is a molecular imaging modality that uses a mass spectrometer to acquire a full mass spectrum at each pixel location in a tissue section. An overview of the typical workflow of a MALDI-based MSI experiment is shown above. MSI brings the chemical specificity of MS to the spatial domain and is capable of measuring in a single experiment the spatial distribution of hundreds of biomolecules concurrently throughout a tissue section, without the need for tagging (as in other molecular imaging modalities such as fluorescence microscopy) and without requiring any prior knowledge on the molecular species of interest. The spatial distribution measured for a particular mass or molecule species is called an ion image.

Data challenges?

Similar to how a color photograph measures three variables per pixel (red, green, and blue), an IMS experiment measures many variables per pixel. In the case of IMS, the number of variables per pixel can run into more than 16 million distinct features. The data size of a single IMS data set can run into many hundreds if not thousands of gigabytes as a result. As an example, the mouse brain image on the front page is depicting only two of thousands of ion images captured in a single experiment. The total raw data size of this experiment exceeded 1.5 terabyte. Successful IMS analysis depends on dealing with this massive data dimensionality.

Research

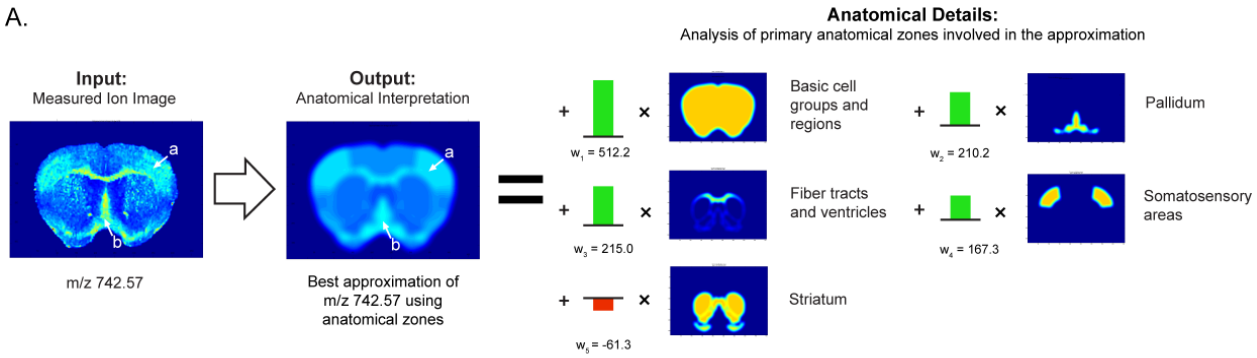
In our group, we explore new ways of acquiring, processing, and data mining the massive data sets that an IMS experiment can produce. The computational foci include:

- **Mass spectral signal processing and ion optics**
  (e.g. removal of multiplicative noise, baseline correction, etc.)

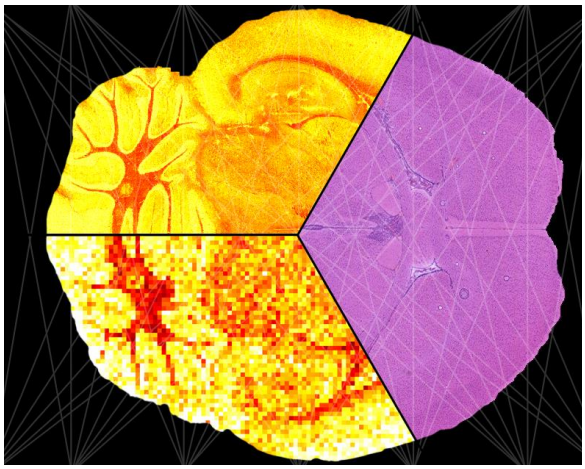
- **Dimensionality reduction and transformations**
  (e.g. wavelet transform, dictionary learning, etc.)

- **Pattern recognition and matrix/tensor factorizations**
  (e.g. non-negative matrix factorization, convex optimization, etc.)

- **High-level biological interpretation**
  (e.g. automated anatomical interpretation)



- **Data mining across different imaging sensors**
  (e.g. image fusion)



Literature

Caprioli, R. M.; Farmer, T. B.; Gile, J. *Anal. Chem*. 1997, 69, 4751–4760.
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