Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Biotechnology

Visualizing life with ambient mass spectrometry

Cheng-Chih Hsu[1] and Pieter C Dorrestein[1,2]

Since the development of desorption electrospray ionization (DESI), many other ionization methods for ambient and atmospheric pressure mass spectrometry have been developed. Ambient ionization mass spectrometry has now been used for a wide variety of biological applications, including plant science, microbiology, neuroscience, and cancer pathology. Multimodal integration of atmospheric ionization sources with the other biotechnologies, as well as high performance computational methods for mass spectrometry data processing is one of the major emerging area's for ambient mass spectrometry. In this opinion article, we will highlight some of the most influential technological advances of ambient mass spectrometry in recent years and their applications to the life sciences.

Addresses
[1] Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA 92093, United States
[2] Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, La Jolla, CA 92093, United States

Corresponding author: Dorrestein, Pieter C (pdorrestein@ucsd.edu)

Current Opinion in Biotechnology 2015, **31**:24–34

This review comes from a themed issue on **Analytical biotechnology**

Edited by **Hadley D Sikes** and **Nicola Zamboni**

http://dx.doi.org/10.1016/j.copbio.2014.07.005

Ambient ionization mass spectrometry

In the late 20th century, acquiring label-free chemical information from the biological systems has became a reality due to the development of biomolecule-compatible ionization methods for mass spectrometry (MS), e.g. electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) [1,2]. The mass spectral data, when acquired in a spatial manner, can be intuitively reconstructed as and image and this has resulted in the booming filed of imaging mass spectrometry (IMS). A large number of ionization methods has been developed over the past decade that combine IMS with biological systems, demonstrating its profound impact on life sciences [3].

One can say that the technological development of ambient ionization methods has entered the golden age. The term "**ambient mass spectrometry**" was first introduced in 2006 [4]. In the past decade, *the analytical science as well as biological and medical science communities have, extensively utilized ambient mass spectrometry, or ambient ionization mass spectrometry*. Each ambient ionization MS technique follows three main principles: (1) ions are generation and maintenance under atmospheric pressure and room temperature (for most of the techniques) before introducing the ions into a mass spectrometer for analysis; (2) samples do not require any pretreatment or only require minimal preparation; (3) analytes are directly desorbed/ionized from the sample surface such that instantaneous or real-time MS measurements becomes possible (Figure 1).

Due to the simplicity and insightful molecular information it can provide, there has been a growing interest in ambient mass spectrometry to be used as new tools for exploration of the chemical dimensions such as searching for new drug leads and signatures of disease. This opinion article is not aimed to be a comprehensive review of ambient ionization methods rather it is aimed to highlight some of the recent tools and how we see they fit into major areas of the life science communities. In the first part of the article we highlight extractive-based ionization methods, including desorption electrospray ionization (DESI) and nanospray desorption electrospray ionization (nanoDESI). Further we highlight representative examples of applications that indicate they have high biomedical potential. We also describe recent technological advancements that strongly indicate one of the future directions of ambient mass spectrometry is toward integration with non-MS based multi-modal interfaces to improve the understanding of the true complexity of biology.

DESI

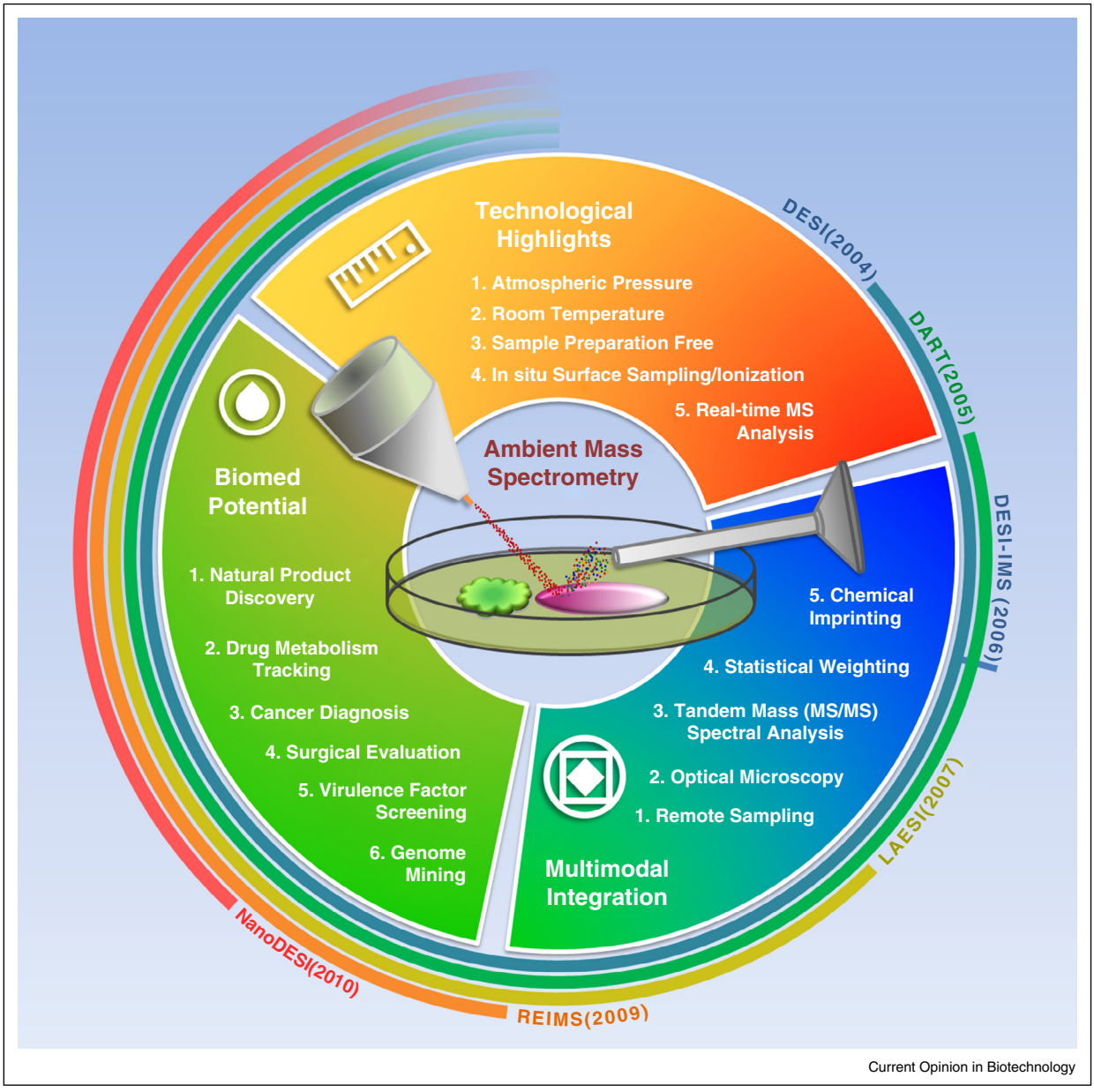
The basics

The introduction of desorption electrospray ionization (DESI) in 2004 is a landmark development in the history of ambient ionization mass spectrometry [5]. DESI utilizes a nebulized electrospray of highly charged microdroplets to pick up the analytes directly from the sample surface. The subsequent secondary droplets carry the dissolved analytes to the mass spectrometry without separation procedures (Figure 1). Similar to conventional ESI of bulk solution, gaseous ions are believed to be created by electrostatic explosion and evaporation [5].

Application on tissues

DESI MS analysis of biological tissues has been used for direct chemical profiling since 2005, when the first

Figure 1



The cycle of major ambient mass spectrometry methods discussed in this opinion article. *Center:* Schematic diagram of desorption electrospray ionization (DESI) source obtaining chemical information from a biological sample surface. A stream of charged micro-droplets (in red) is sprayed onto the sample surface to desorb and ionize compounds (in multiple colors), during which molecules retain in their structural intact states. *Outer strips:* Time frame of the major development in ambient ionization mass spectrometry methods since DESI MS was reported in 2004. The year of the first publication using the indicated ion sources are listed in the parentheses.

ambient mass spectrometry analysis to animal tissue sections without any sample pretreatment was performed [6]. Strong ion signals from phospholipids were found at the mass-to-charge (m/z) range 700–900 from pancreas and brain tissues. The alteration of phospholipid profiles of tumor tissue was also first investigated and described in this paper [6]. The same group also applied DESI MS to the native and freshly cut plant tissue in the same year [7]. Dozens of alkaloids, coniine for example, were identified on different species. In 2006, the first whole-section surface IMS was demonstrated on rat brain tissue [8] showing spatial distributions of different lipid species that reflected the chemical-histological heterogeneity of a brain tissue. Automatic 2-dimensional (2-D) stages are employed with DESI ion sources to generate 2-D MS images [9]. Lateral resolution of a DESI IMS is usually