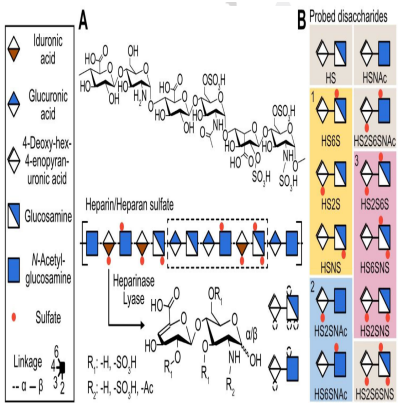
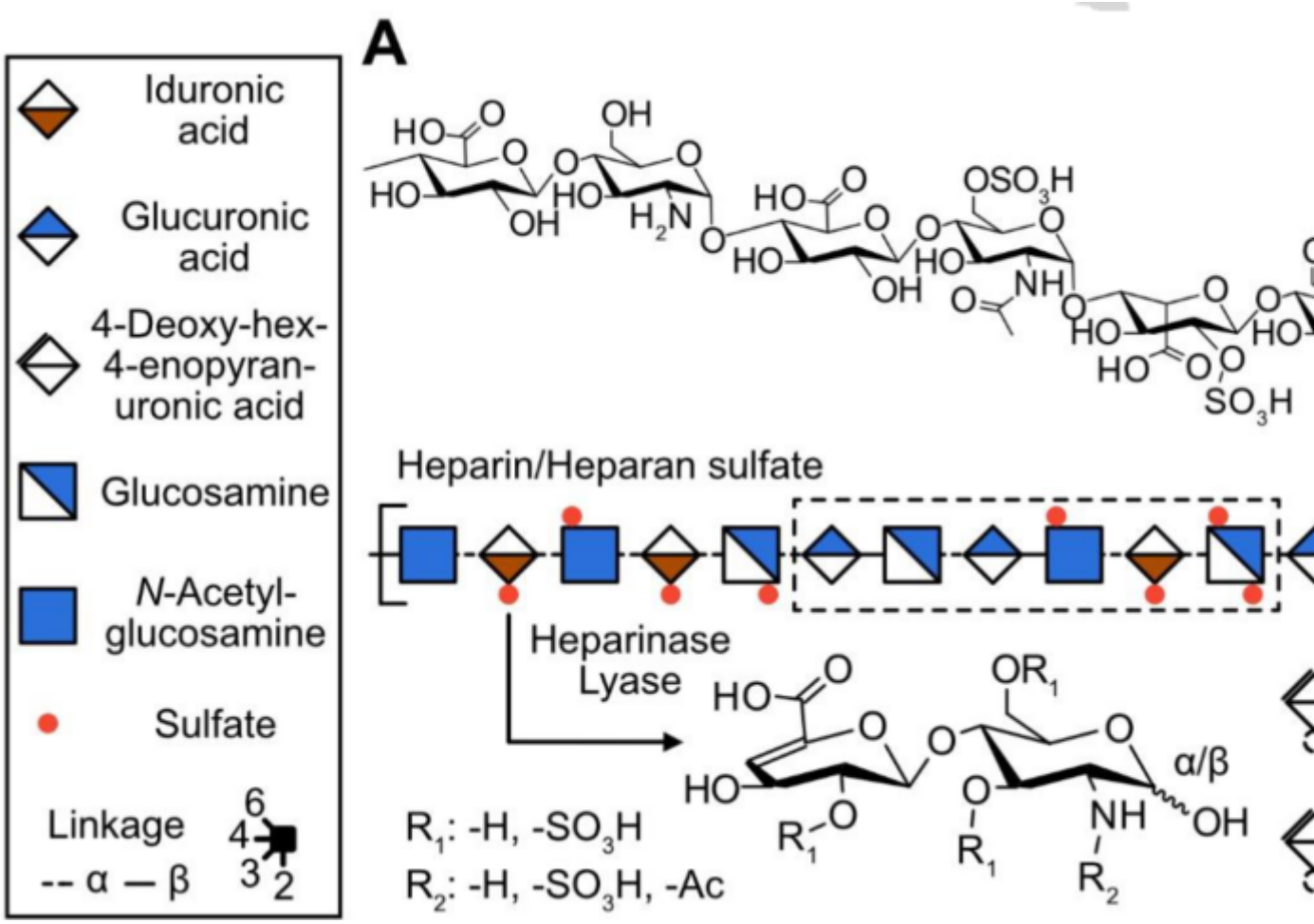


Ion Mobility Mass Spectrometry-based Disaccharide Analysis of Glycosaminoglycans

Description

Glycosaminoglycans (GAGs) are linear acidic polysaccharides, ubiquitous molecules involved in a wide range of biological processes. Despite their seemingly simple structure, with a repeating backbone of alternating hexuronic acid and hexosamine dimers, GAGs present a highly complex structure, mainly due to their heterogeneous sulfation patterns. The commonly used method for compositional analysis of all GAGs is â??disaccharide analysisâ?•. GAGs are enzymatically depolymerized into disaccharides, derivatized with a fluorescent label, and then analysed through liquid chromatography. However, the time-consuming liquid chromatography is the limiting factor in the high throughput analysis of GAG disaccharides. To overcome this limitation, the authors used trapped ion mobility mass spectrometry (TIM-MS) for the separation of isomeric GAG disaccharides, reducing the measurement time from hours to a few minutes. This significant reduction in measurement time could revolutionize the field of GAG analysis.



The glycosaminoglycans (GAGs) heparin/heparan sulfate (HS). A) HS is a simplified chemical structure based on the symbol nomenclature for glycans (SNFG).[19] The example structure (top) can be seen as an SNFG depiction in the dotted box. B) List of probed disaccharides and their nomenclature. Three groups of isomeric disaccharides are present: group 1, monosulfated and non-acetylated (yellow); group 2, monosulfated and acetylated (blue); and group 3, disulfated and non-acetylated (red).

A full set of disaccharides comprises twelve structures, with eight possessing isomers. Most disaccharides cannot be differentiated by TIM-MS in underivatized form. Therefore, chemical modifications to reduce sample complexity and enhance differentiability were developed. Quantification is performed using stable isotope labelled standards, which are easily available due to the nature of the performed modifications.

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