

Showcasing research from Professor Josephine Bunch's laboratory, National Centre of Excellence in Mass Spectrometry Imaging, National Physical Laboratory, Teddington, UK.

A straightforward method for measuring binding affinities of ligands to proteins of unknown concentration in biological tissues

We present a simple native mass spectrometry method for determining the binding affinity ( $K_{\rm d}$ ) of ligands to proteins directly from biological tissues, without requiring knowledge of protein concentration. This dilution-based approach enables rapid, label-free analysis using minimal sample manipulation. The method is suitable for analysis of complex biological matrices and for review of competitive binding scenarios, facilitating drug screening and target validation under near-native conditions. The method is high-throughput, requires no protein purification, and is compatible with other biophysical techniques for  $K_{\rm d}$  estimation.

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