

# **LABEL-FREE SINGLE MOLECULE QUANTIFICATION OF DNA BY MASS PHOTOMETRY**

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## **Abstract:**

A primary advantage of label-free detection methods over fluorescent measurements is its quantitative detection capability, since an absolute measure of material facilitates kinetic characterisation of biomolecular interactions. Mass photometry based on interferometric scattering microscopy (iSCAT) is a novel, label-free imaging and quantification approach, having demonstrated accurate mass measurement of single biomolecules in solution. Here, we show that mass photometry is equally applicable to nucleic acid detection and mass quantification. Individual ds-DNA molecules binding to a cover glass surface produce strong interferometric contrast, with a detection limit on the order of 60 base pairs. Characterisation of standard DNA ladders yields mass distributions with well-resolved peaks, exhibiting a clear correlation between interferometric contrast and the number of base pairs resulting in 5 base pair accuracy and 10 base pair precision. Combined with the capabilities of mass photometry to study soluble proteins, these results furthermore pave the way towards label-free, single molecule, solution-based quantification of protein-DNA interactions.