

Weighing single molecules with light

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The cellular processes underpinning life are orchestrated by proteins and the interactions they make with themselves and other biomolecules. A range of techniques has been developed to characterise these associations, but structural and dynamic heterogeneity remain a fundamental challenge. I will show that mass photometry based on interferometric scattering microscopy can mass-image single biomolecules in solution with nanometre precision and mass accuracy comparable to native mass spectrometry in the gas phase. Thereby, we can resolve oligomeric distributions at high dynamic range, detect small-molecule binding, and mass-measure polypeptides, glyco- and lipoproteins. These capabilities enable us to quantify the molecular mechanisms of processes as diverse as homo- and hetero-oligomeric protein assembly, amyloidogenic protein aggregation and actin polymerisation [1,2]. Our results illustrate how single molecule mass imaging provides access to protein dynamics and interactions and introduces a third, light-based approach to measuring mass in addition to the historical mechanical and spectrometric methodologies. This ability to investigate biomolecules in their native state with high mass accuracy and resolution provides critical, complementary information to static structural techniques in the context of protein function and regulation.



1. Young G, Hundt N, Cole D, Fineberg A, Andrecka J, Tyler A, Olerinyova A, Ansari A, Marklund EG, Collier MP, Chandler SA, Tkachenko O, Allen J, Crispin M, Billington N, Takagi Y, Sellers JR, Eichmann C, Selenko P, Frey L, Riek R, Galpin MR, Struwe WB, Benesch JLP, Kukura P. Quantitative mass imaging of single biological macromolecules. *Science* **2018** 360: 423-327