New instrument for massively parallel single molecule binding measurements

Published date: Feb. 1, 2012

Technology description

Summary

MARKETS ADDRESSED:
The ability to quantify interactions between biomolecules is of great interest for scientific and medical research, as well as for drug development. Currently, measurements of the affinity and the kinetics of biomolecular interactions are typically performed in solution, using methods such as calorimetry, stop-flow imaging, or surface plasmon resonance. However, these bulk measurements are limited in many ways, including 1) they report only average behavior, often losing important details associated with metastable states and rare events, and 2) they measure chemistry in the absence of externally applied mechanical stress, which can be dramatically different from the crowded and dynamic environments of living systems.
The relatively new field of single-molecule manipulation addresses these problems by directly measuring the behavior of single molecular interactions under force. This enables the study of the mechanical properties of biomolecular complexes and cellular targets, yielding valuable information into both the structure and the function of biological systems at the nanoscale. The field has been largely driven by technology such as the atomic force microscope and optical tweezers. However, these technologies are very expensive and characterization of a single biological interaction is slow and painstaking.
Harvard's high-throughput single-molecule measurement device addresses many of the problems of previous single-molecule methods, while retaining single-molecule sensitivity and control. The instrument can be used for quantifying the affinity and force dependent kinetics of a pair of molecules, as well as exploring the internal states of a single molecule by stretching and relaxing it under force. The single molecule probe finds applications in drug discovery and development, and life science research.

Advantages

Harvard researchers have developed a radical new method for making massively-parallel, high-throughput single-molecule force measurements. This approach brings single-molecule

experimentation to the common scientist by overcoming the laborious measurements, high cost and technical skill that other techniques require. The new instrument is a spinning microscope in which the resulting centrifugal force acts simultaneously on a multitude of single molecules (e.g. proteins, DNA) or single molecular complexes (e.g. receptor-ligand pairs). Each single-molecule system can be observed directly and independently for true single-molecule detection. Another advantage of this technology is that it can provide accurate, calibration-free force control in a wide range of directions and magnitudes, enabling the convenient quantification of a wide variety of force-dependent interactions. This invention provides dramatic advantages in cost, versatility, and especially efficiency, reducing experimental time from days to minutes.

Institution

Harvard University