Dissecting fast dynamics of single biological molecules with high-speed laser tweezers

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Single molecule techniques such as optical and magnetic tweezers and atomic force microscopy have enabled the investigation of molecular motor mechanics, DNA and RNA processing enzymes, and load-dependent kinetics of molecular interactions. However, they are inadequate to probe short-lived (millisecond and sub -millisecond) molecular complexes. We developed a constant-force laser trap that allows us to investigate molecular interactions and sub-nanometer conformational changes occurring on a time scale of few tens of microseconds. [Capitanio et al., Nature Methods 9, 1013-1019 (2012)]. The method is effective in studying the sequence-dependent affinity of DNA-binding proteins along a single DNA molecule, molecular motors walking on their cytoskeletal filaments, and structural proteins transducing mechanical signals in the cell. We show applications of our technique to the study of transcription factors dynamics on DNA during gene expression regulation and mechanosensitivity of myosin motors in muscle contraction and intracellular transport.