Abstract Submitted
for the MAR14 Meeting of
The American Physical Society

Measuring Conformational Dynamics of Single Biomolecules Using Nanoscale Electronic Devices MAXIM V. AKHTEROV, YONGKI CHOI, PATRICK C. SIMS, Dept. of Physics and Astronomy, Univ. of California Irvine, TIVOLI J. OLSEN, Dept. of Chemistry, Univ. of California Irvine, O. TOLGA GUL, BRAD L. CORSO, Dept. of Physics and Astronomy, Univ. of California Irvine, GREGORY A. WEISS, Dept. of Chemistry, PHILIP G. COLLINS, Dept. of Physics and Astronomy, Univ. of California Irvine — Molecular motion can be a rate-limiting step of enzyme catalysis, but motions are typically too quick to resolve with fluorescent single molecule techniques. Recently, we demonstrated a label-free technique that replaced fluorophores with nano-electronic circuits to monitor protein motions. The solid-state electronic technique used single-walled carbon nanotube (SWNT) transistors to monitor conformational motions of a single molecule of T4 lysozyme while processing its substrate, peptidoglycan. As lysozyme catalyzes the hydrolysis of glycosidic bonds, two protein domains undergo 8 Å hinge bending motion that generates an electronic signal in the SWNT transistor. We describe improvements to the system that have extended our temporal resolution to 2 μs. Electronic recordings at this level of detail directly resolve not just transitions between open and closed conformations but also the durations for those transition events. Statistical analysis of many events determines transition timescales characteristic of enzyme activity and shows a high degree of variability within nominally identical chemical events. The high resolution technique can be readily applied to other complex biomolecules to gain insights into their kinetic parameters and catalytic function.

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Date submitted: 14 Nov 2013 Electronic form version 1.4