Abstract Submitted
for the MAR13 Meeting of
The American Physical Society

Electronic measurements of single-molecule processing by DNA polymerase I YONGKI CHOI, Department of Physics and Astronomy, University of California, Irvine, TIVOLI OLSEN, Department of Chemistry, University of California, Irvine, TOLGA GUL, BRAD CORSO, CHENGJUN DONG, Department of Physics and Astronomy, University of California, Irvine, WILLIAM BROWN, Department of Chemistry, University of California, Irvine, GREGORY WEISS, Department of Molecular Biology, University of California, Irvine, PHILIP COLLINS, Department of Physics and Astronomy, University of California, Irvine — A single-molecule nanocircuit technique is applied to continuously monitor DNA replication activity by the enzyme DNA polymerase I (Pol I). Using single copies of Pol I bound to a single-walled carbon nanotube device, an electrical signal was generated to reveal enzymatic function and dynamic variability. Continuous, single-molecule-resolution recordings were obtained for Pol I processing homopolymeric DNA templates over 10 minutes and through >10,000 DNA replication events. Processivity of up to 40 nucleotide bases was directly observed, and statistical analysis of the recordings determined key kinetic parameters for the enzyme's open and closed conformations. We observe that the closed complex forms a phosphodiester bond in a highly efficient process >99.8% of the time, with a mean duration of only 0.3 ms for all four dNTPs. The rate-limiting step for replication occurs during the enzyme's open state, but with a duration that is nearly twice as long for dATP or dTTP incorporation than for dCTP or dGTP. Taken together, the results provide a wealth of new information complementing prior work on the mechanism and dynamics of DNA polymerase.

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Date submitted: 09 Nov 2012 Electronic form version 1.4