Single Molecule Enzymology Using Carbon Nanotube Circuits

Yongki Choi, Patrick C. Sims, Tivoli Olsen, O. Tolga Gul, Brad L. Corso, Mariam Iftikhar, Gregory A. Weiss, and Philip G. Collins

Departments of Physics, Chemistry, and Molecular Biology and Biochemistry, Univ. of California, Irvine
4129 F. Reines Hall, Irvine CA 92697 USA

Tethering a single biomolecule to a carbon nanotube field effect transistor can produce a stable, high bandwidth transducer for monitoring protein motions, charge transfer events, and enzymatic activity.(*1-3*) Recently, electronic monitoring has been accomplished for multiple variants of three different enzymes, T4 lysozyme, c-AMP dependent protein kinase, and the Klenow fragment of DNA polymerase I.

With all three enzymes, single molecules were electronically monitored for 10 or more minutes, allowing us to directly observe rare transitions to chemically inactive and hyperactive conformations. The high bandwidth of the nanotube transistors further allow every individual chemical event to be clearly resolved, providing excellent statistics from tens of thousands of turnovers by a single enzyme. Besides establishing values for processivity and turnover rates, the measurements also reveal variability, dynamic disorder, and the existence of intermediate states.

Our immediate success generalizing the platform to three enzymes and to multiple variants indicates that this nanotube device technique is versatile and promising for further single molecule studies.

1. Y. Choi *et al.*, *Science* **335**, 319 (2012).
2. Y. Choi *et al.*, *J. of the Am. Chem. Soc.* **134**, 2032 (2012).
3. Y. Choi *et al.*, *in review*.

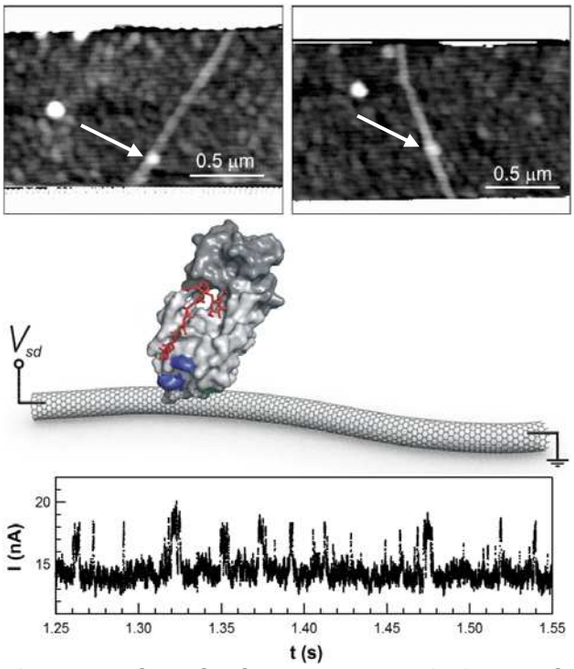

Fig 1. Single molecule nanocircuits. (top) Example AFM images of single-walled carbon nanotube transistors, each labeled with a single lysozyme molecule (arrows). (middle) Schematic representation of a device, showing the relative size of a nanotube to lysozyme. The drawing highlights lysozyme's two active domains (light and dark grey), which move with respect to each other when processing substrate (red). (bottom) The device current fluctuates between two levels in sync with the enzyme domains opening and closing on its substrate, producing a real-time recording of the enzyme's activity.