

# A Device of Tracking a Single Nanometer-Sized Particle in 3D with Nanometer Resolution and Millisecond Response Time

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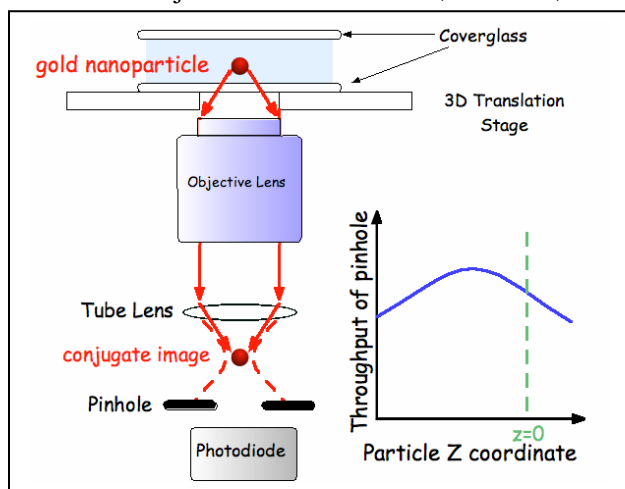
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Scientists often send a tiny 'spy', be it a fluorescence micro-sphere, a dye molecule, a quantum dot, or a metallic nanoparticle to probe a sample that exhibits complexity on multiple time and length scales. The spy reports valuable information about its local environment via emitted photons. A great challenge for scientists is to keep track of the spies as they move in the samples. Analysis of the trajectory yields a great deal of information. This is particularly true in biology where a biochemical process is like a movie with multiple scenes occurring at different places in a sequence.

The most popular noninvasive scheme for keeping track of the spies is to use a fast video camera. The trajectories thus obtained, however, are limited to 2 dimensions; a camera cannot



give the Z position accurately in real time. We demonstrate a simple method shown in the left figure. In our design, an optical pin hole is used to extract the movement in Z direction directly. The idea comes from confocal microscopy. In a confocal microscope, right at the image point of the object at the focus of the objective lens (the conjugate focal point), there is a pin hole. It eliminates out-of-focus light, so that a cross section of a sample can be imaged. We modify this setup slightly, where the pin hole is placed slightly behind the image point. Therefore, when the spy moves up or

down, its image moves farther or closer to the pin hole but not across it. This leads to a change in the intensity of the light through the pin hole as a function of the Z position. Although the change is minute, a sensitive detector can pick it up. The in-plane XY position is detected by a standard quadrant photodiode (a quadrant photodiode is a bundle of four photodiodes placed together like a cross). As the spy moves, its image also moves such that the four photodiodes receive different intensity light. A simple circuit checks the difference between the four units, and gives the signal of movement in XY direction. In our system, the detection of the 3D movement is in real time. We then use a feedback system to control a 3D translation stage to counteract the particle movement. By doing so, we were able to track our spy and maintain it under the focus of optical interrogation. Currently, our system has a 1 millisecond response time which is the fastest so far for a three-dimensional tracking scheme.

To date, we have successfully tracked individual 250-nm gold nano particles in water with 20-nm precision in the XY position and 100-nm precision in the Z direction, using the scattered light from the gold nano particle. By precisely maintaining the position, we could further perform other spectroscopic experiment on the moving particle by illuminating it with a second laser beam. Current work is aimed this direction. We hope our system becomes a useful

platform for the study of intra cellular dynamics, and spectroscopy on freely moving single molecule.