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**High-Bandwidth Atomic Force Microscopy Reveals A Mechanical spike Accompanying the Action Potential in mammalian Nerve Terminals<sup>1</sup>**  
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Information transfer from neuron to neuron within nervous systems occurs when the action potential arrives at a nerve terminal and initiates the release of a chemical messenger (neurotransmitter). In the mammalian neurohypophysis (posterior pituitary), large and rapid changes in light scattering accompany secretion of transmitter-like neuropeptides. In the mouse, these intrinsic optical signals are intimately related to the arrival of the action potential (E-wave) and the release of arginine vasopressin and oxytocin (S-wave). We have used a high bandwidth (20 kHz) atomic force microscope (AFM) to demonstrate that these light scattering signals are associated with changes in nerve terminal volume, detected as nanometer-scale movements of a cantilever positioned on top of the neurohypophysis. The most rapid mechanical response, the “spike”, has duration comparable to that of the action potential ( $\sim 2$  ms) and probably reflects an increase in terminal volume due to  $\text{H}_2\text{O}$  movement associated with  $\text{Na}^+$ -influx. Elementary calculations suggest that two  $\text{H}_2\text{O}$  molecules accompanying each  $\text{Na}^+$ -ion could account for the  $\sim 0.5$ - $1.0$  Å increase in the diameter of each terminal during the action potential. Distinguishable from the mechanical “spike”, a slower mechanical event, the “dip”, represents a decrease in nerve terminal volume, depends upon  $\text{Ca}^{2+}$ -entry, as well as on intra-terminal  $\text{Ca}^{2+}$ -transients, and appears to monitor events associated with secretion. A simple hypothesis is that this “dip” reflects the extrusion of the dense core granule that comprises the secretory products. These dynamic high bandwidth AFM recordings are the first to monitor mechanical events in nervous systems and may provide novel insights into the mechanism(s) by which excitation is coupled to secretion at nerve terminals.

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