



Light—or optical—microscopy has been around since the 17th century. This type of microscope uses visible light and lenses to magnify an object. In 1873, German physicist Ernst Abbe established that the resolution of a light microscope is limited by the wavelength of the light used to illuminate the object and the aperture (opening) that lets the light in. This “diffraction limit” means that the structures of objects smaller than a few hundred nanometers, such as those of many molecular assemblies inside cells, can’t be resolved with this type of microscope. With her super-resolution microscopy method Stochastic Optical Reconstruction Microscopy (STORM), Zhuang was able to overcome the diffraction limit with the use of fluorescent probes. In conventional light microscopy, the probes are all switched on at the same time, making the determination of individual probes’ locations difficult because the images of the probes overlap. STORM, though, took inspiration from another of Zhuang’s discoveries: photo-switchable fluorescent dyes that can be turned on or off with light. At any given time during STORM imaging, only a subset of the photo-switchable probes are switched on so that the images from the probes will not overlap, allowing their positions to be determined precisely from their images. Combining those positions produces a higher-resolution image than is available with conventional fluorescence microscopy. With Zhuang’s innovations in optical design and fluorescent dyes, she has pushed STORM’s resolution to one-to-two orders of magnitude beyond the diffraction limit. And with this microscope technology, Zhuang and colleagues have been able to make many important discoveries, for instance, uncovering the periodic membrane skeleton structure in the axons of neurons and elucidating the molecular structure of synapses in the brain.