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Optical microscopy: the resolution revolution

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Throughout the 20th century it was widely accepted that a light microscope relying on conventional optical lenses cannot discern details that are much finer than about half the wavelength of light (200-400 nm), due to diffraction. However, in the 1990s, the viability to overcome the diffraction barrier was realized and microscopy concepts defined, that can resolve fluorescent features down to molecular dimensions. In this lecture, I will discuss the simple yet powerful principles that allow neutralizing the limiting role of diffraction^{1,2}. In a nutshell, feature molecules residing closer than the diffraction barrier are transferred to different (quantum) states, usually a bright fluorescent state and a dark state, so that they become discernible for a brief period of detection. Thus, the resolution-limiting role of diffraction is overcome, and the interior of transparent samples, such as living cells and tissues, can be imaged at the nanoscale.

1. Hell, S.W. Far-Field Optical Nanoscopy. *Science* **316**, 1153-1158 (2007).

2. Hell, S.W. Microscopy and its focal switch. *Nature Methods* **6**, 24-32 (2009).