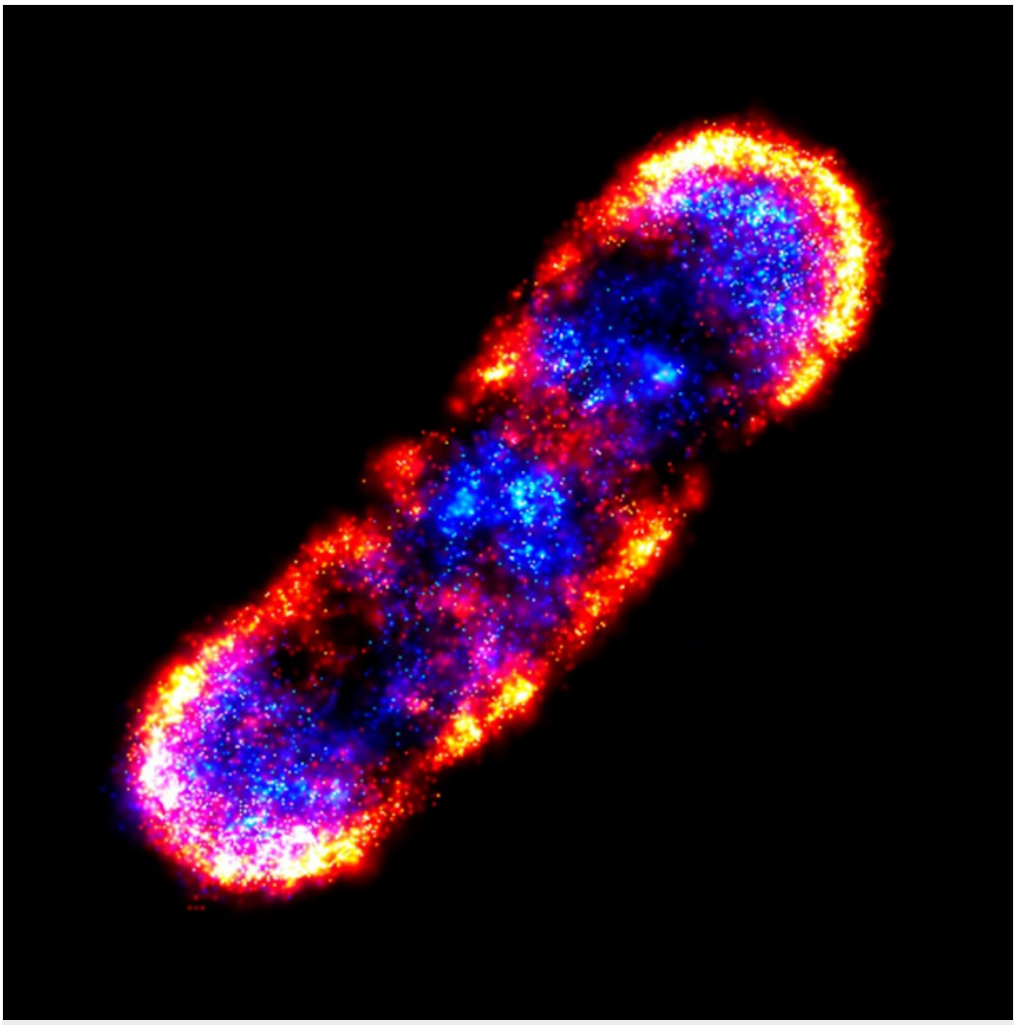
Through the nanoscope: A Nobel Prize gallery

A selection of 'super-resolution' images taken with the techniques that won the 2014 Nobel Prize for Chemistry.

Richard Van Noorden

14 October 2014

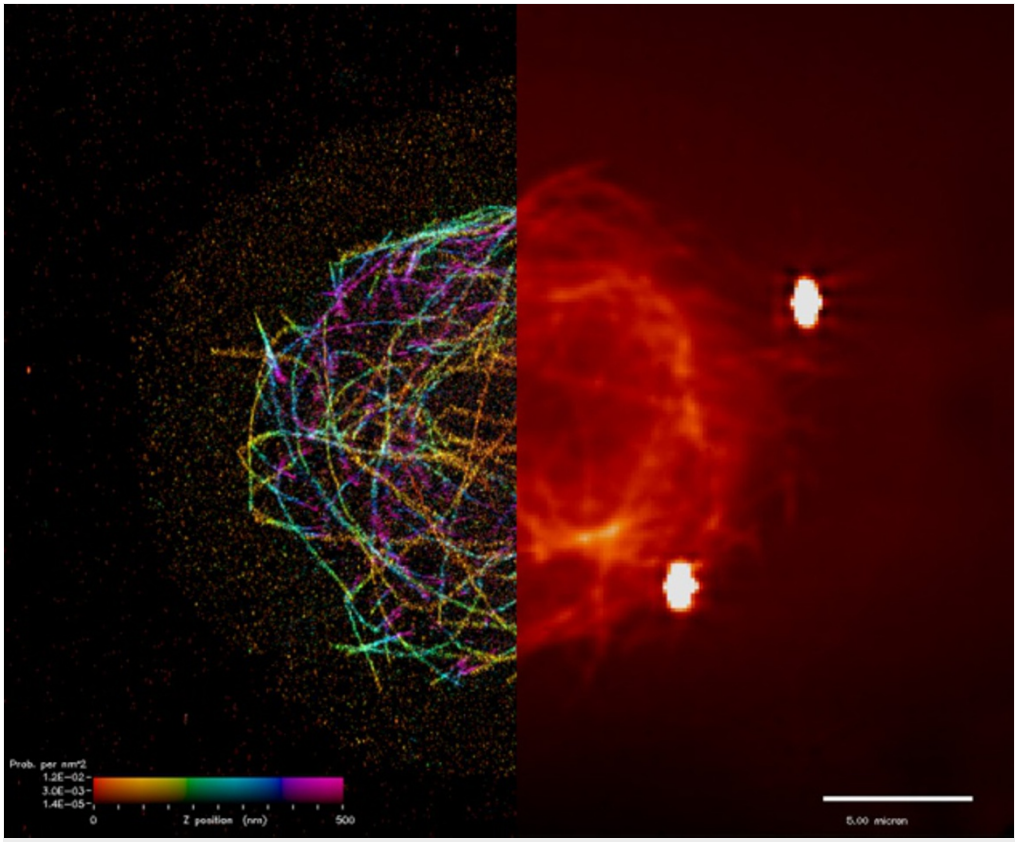
This year's Nobel Prize for Chemistry was awarded to three researchers who developed ways to capture images of living cells at nanoscale resolution — well below the 200 nanometres thought to be the best possible resolution for visible-light microscopes.



LBNL/SPL

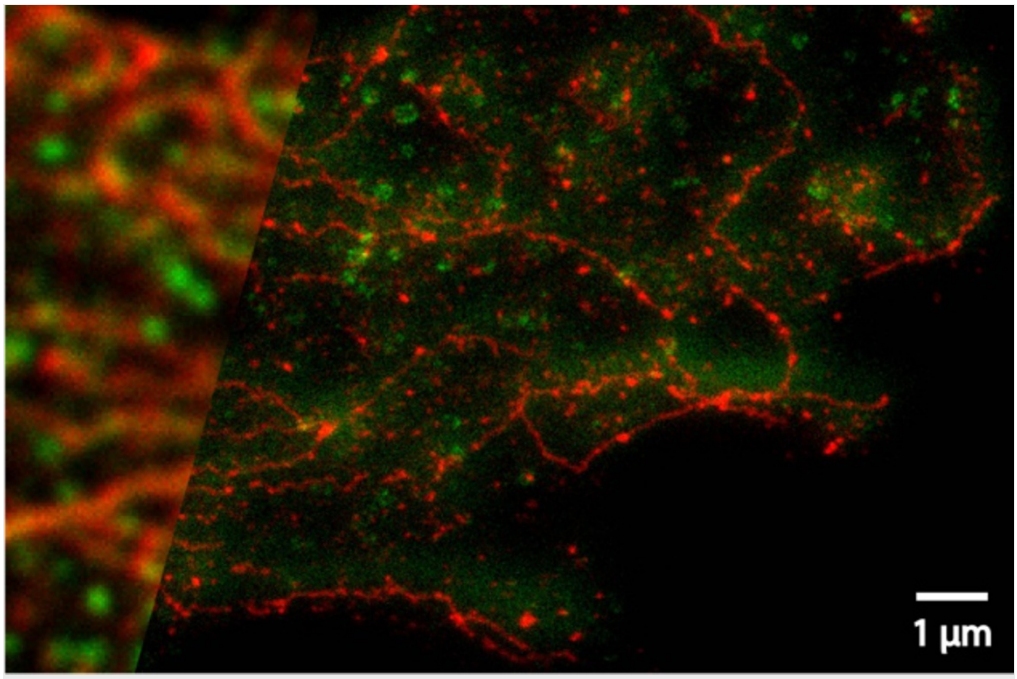
Nobel laureate Eric Betzig, at the Howard Hughes Medical Institute in Ashburn, Virginia, took this picture to

understand how an Escherichia coli bacterium organizes three receptor proteins in its membrane. The bright lights come from fluorescent molecules, which the researchers tagged like beacons onto the proteins of interest. Betzig, together with William Moerner at Stanford University in California, developed 'photoactivated localization microscopy' (PALM), which here reveals the cellular locations of the proteins to within 15 nanometres[1].



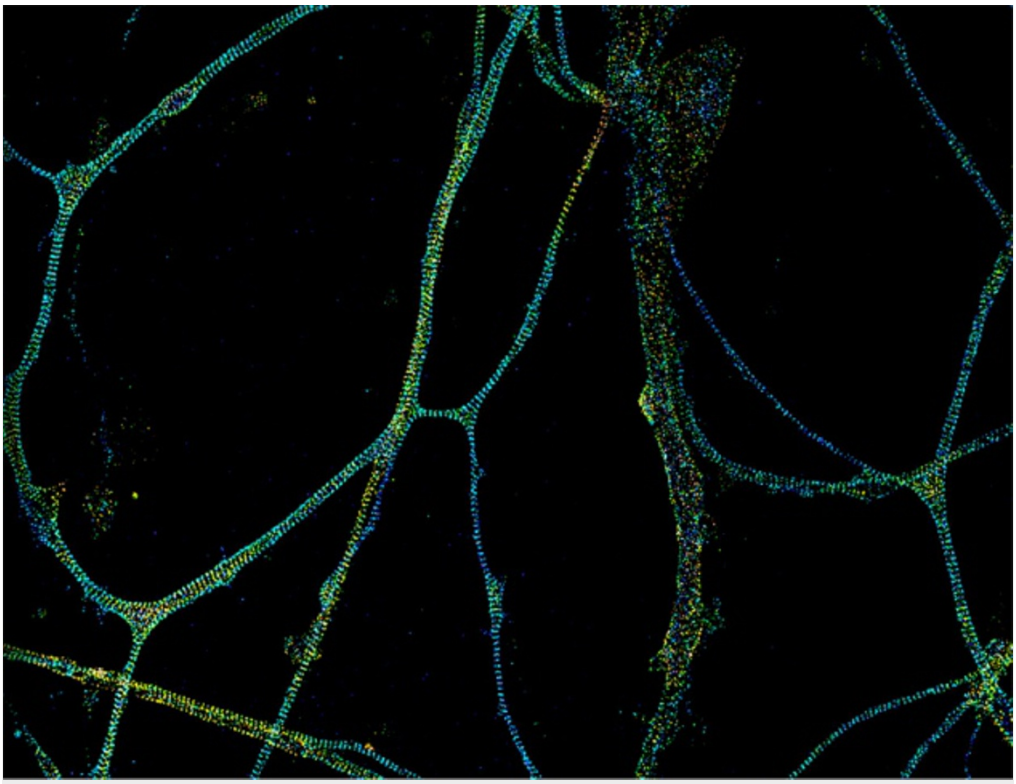
Jimand Cathy Galbraith, Gleb Shtengel, Harald Hess/HHMI/Janelia Research Campus

A three-dimensional version of PALM (left) shows the molecular scaffolding known as microtubules in cells from fruit flies (*Drosophila melanogaster*). The tubules are labelled for depth, with red lower and blue and violet higher, over a 0.5 micrometre range. A regular microscopy image of the same cell is also displayed for comparison (right).



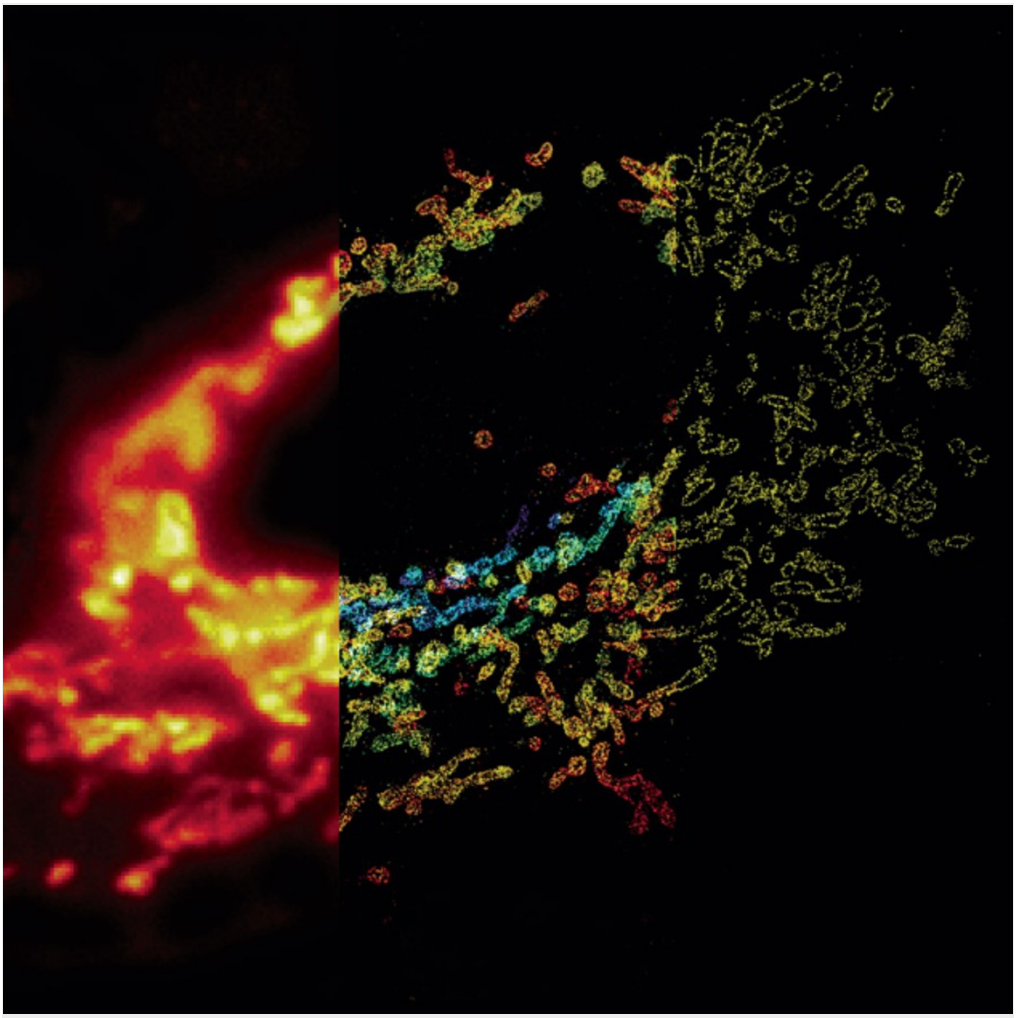
J. Bückers, D. Wildanger, L. Kastrup, R. Medda/Max Planck Inst. for Biophysical Chemistry

A sample from a human brain tumour looks blurred under a confocal microscope (left) but is much sharper in images using a stimulated emission depletion microscope (STED, right) invented by Nobel laureate Stefan Hell of the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany.



Xiaowei Zhuang Lab/HHMI/Harvard Univ.

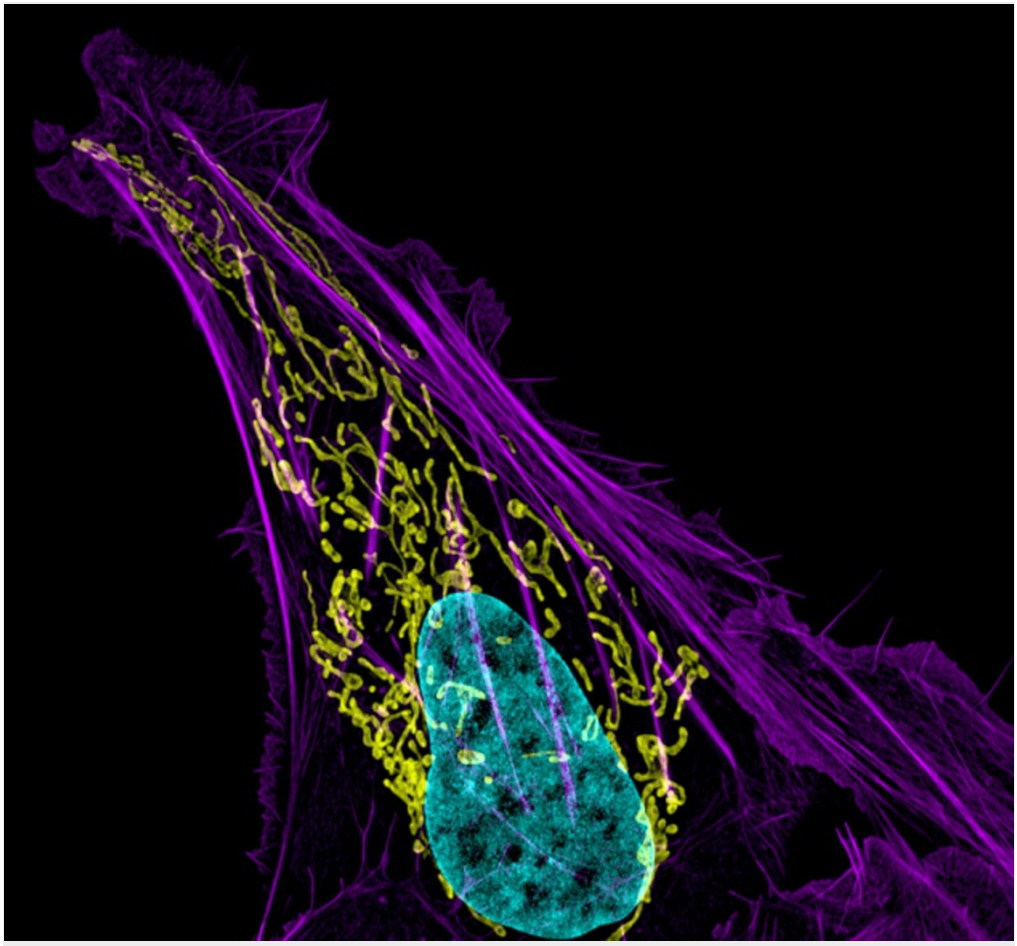
After the work of the Nobel laureates, others invented nanoscopes that work on similar principles. Here Xiaowei Zhuang, at Harvard University in Cambridge, Massachusetts, used stochastic optical reconstruction microscopy (STORM), a technique she developed that is related to PALM, to show how the long, skinny nerve fibres known as axons are reinforced by rings of the protein actin spaced every 180 nanometres along the axon shaft[2].



Xiaowei Zhuang Lab/HHMI/Harvard Univ.

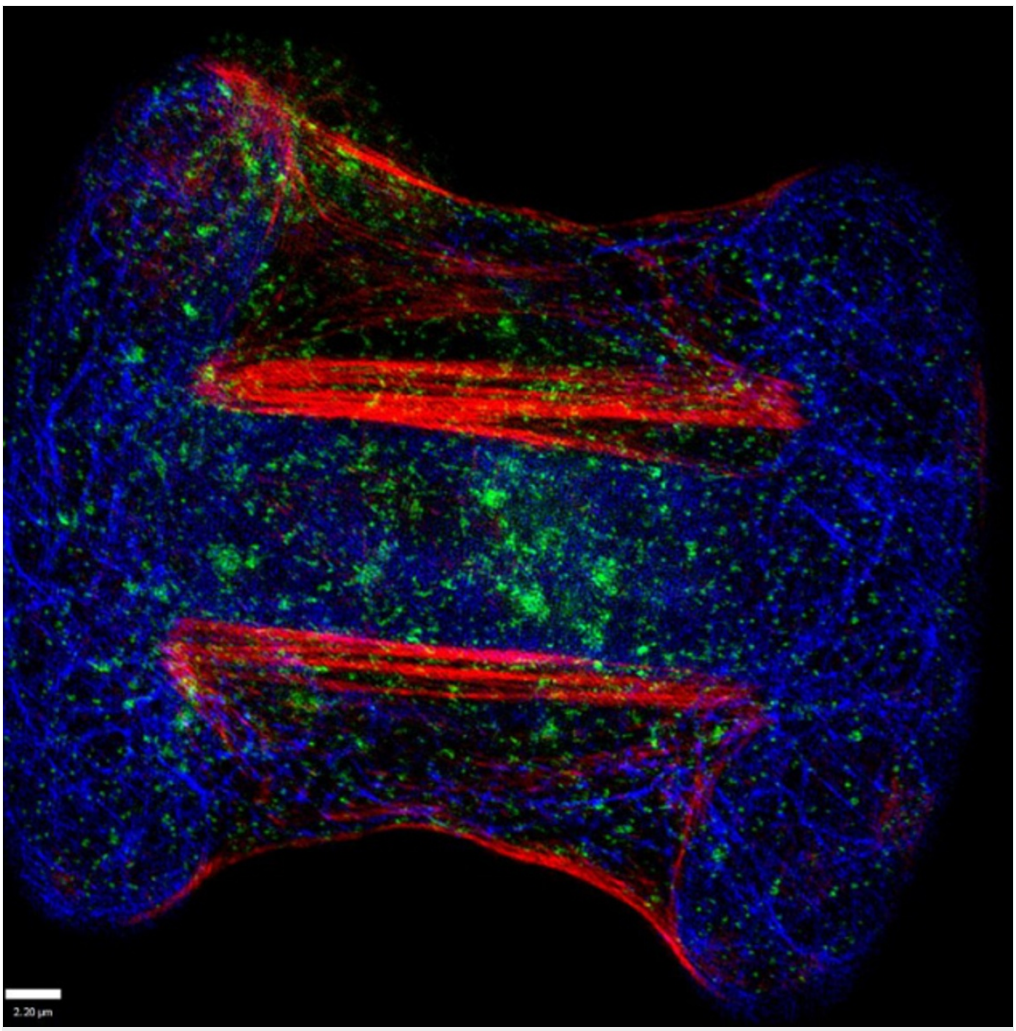
In this image of mitochondria in a cell, the left panel shows an image taken using conventional microscopy;

the middle panel shows a super-resolution STORM image (in three dimensions, with colour indicating depth); and the right panel shows a STORM cross-section through the cell.



Dylan Burnette/NIH/Courtesy of Nikon Small World

A fourth recently-developed super-resolution technique, called structured illumination microscopy (SIM), illuminates samples with stripes of light. A computer program analyses the interference patterns formed by the stripes (usually combining composite pictures with stripes in different orientations) to reconstruct a picture of a cell at about double the resolution limit of optical microscopy. This SIM image shows a three-dimensional view of a human bone cancer cell with actin in purple, DNA in blue, and mitochondria in yellow.



Derek Toomre, Yale Univ./2013 GE Healthcare Life Sciences Cell Imaging Competition

SIM produces some of the prettiest images of cells. Here is one of a cancer cell with actin in red, microtubules in blue, and the transferrin receptor protein (used to carry iron into a cell) in green.

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References

1. Greenfield, D. *et al*. *PLOS Biol.* **7**, e1000137 (2009).
2. Zu, K., Zhong, G. & Zhuang, X. *Science* **339**, 452–456 (2013).

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