Japan-Finland Symposium on Future Diagnostics

New principles for in vitro diagnostics - a retrospective review

Erkki Soini, Prof. emer.

Period 1963 - 1989 Wallac Oy (currently Perkin Elmer Life Sciences)

- radiation safety
- nuclear medicine
- RIA counters
- LSC counters

THE VISION 1974:
The use of radioactive material for biomolecule labelling should be limited in future. Nonisotopic method need to be invented. My alternative approach was the use of time-resolved fuorescence of lanthanides.

Wallac should invest on chemistry skills.

Wallac Oy (currently Perkin Elmer Life Sciences)Period 1975 - 1985

- Time resolved fluorescence – "Delfia"

CLIN. CHEM. 25/3, 353–361 (1979)

Fluoroimmunoassay: Present Status and Key Problems

Erkki Soini[1] and Ilkka Hemmilä[2]

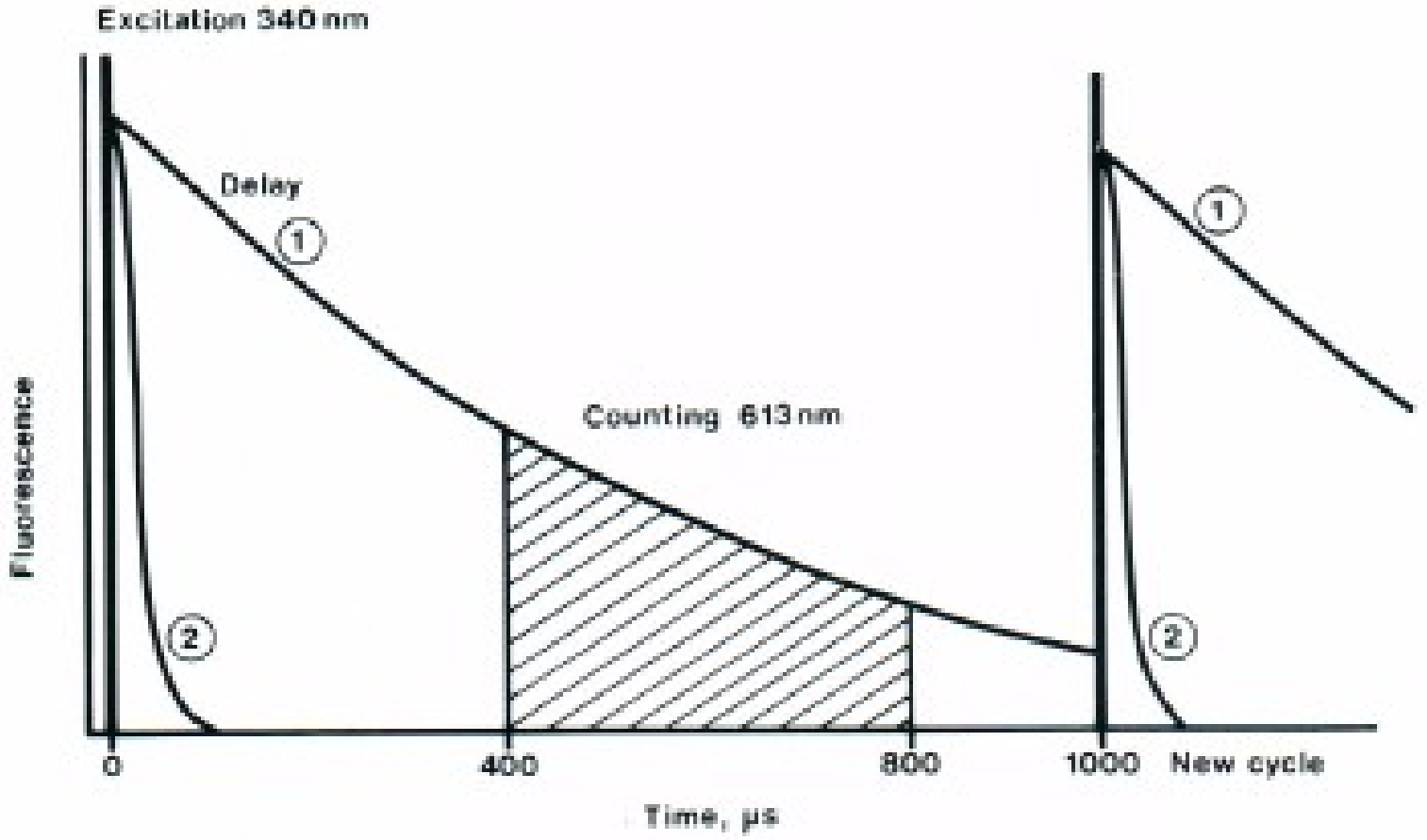
Fluorescence immunoassay of biological fluids (for example, blood samples) is discussed. We attempt to chart present methods of assay as well as new possibilities. Different fluorescent probes, their detection limit, and methods for reduction of background are discussed; methods for separating the free and bound fraction are also reviewed. Special consideration is given to the possibilities of enhancing sensitivity by developing both instruments and chemical methods, and in particular to the possibilities

CLIN. CHEM. 29/1, 65–68 (1983)

Time-Resolved Fluorometer for Lanthanide Chelates—A New Generation of Nonisotopic Immunoassays

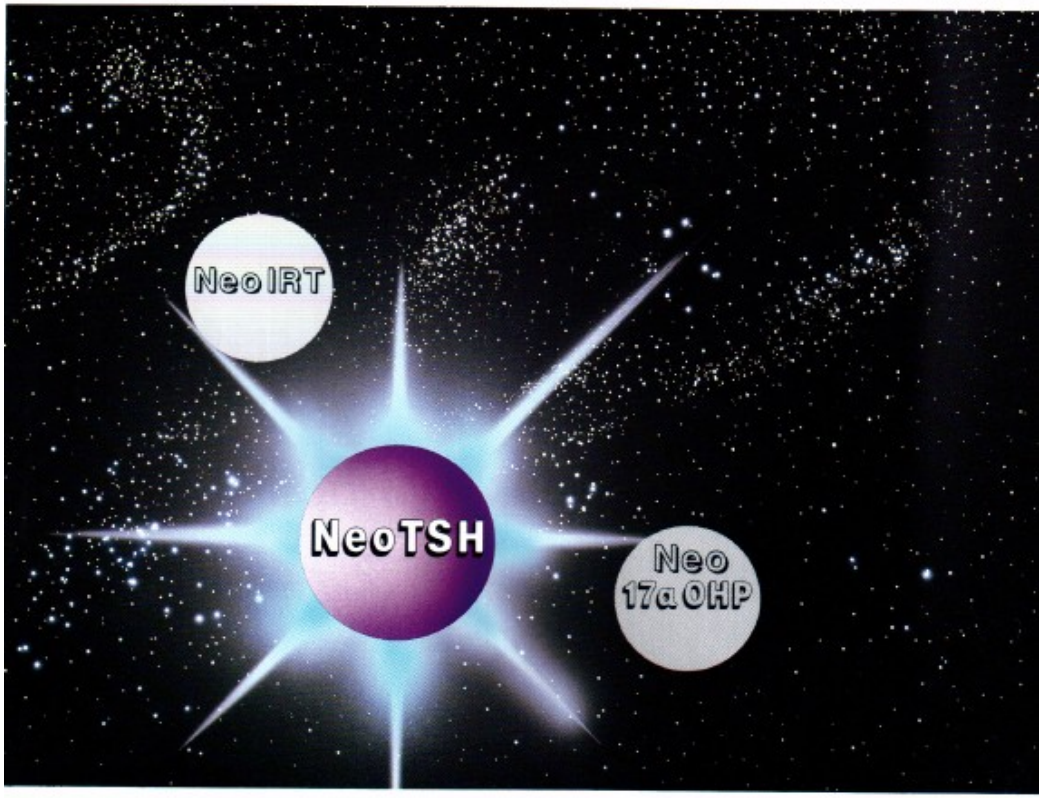
Erkki Soini and Hannu Kojola

Pulsed-light time-resolved fluorometry of lanthanide chelates has proved to be very sensitive for use with nonisotopic immunoassays. We describe a manually operated fluorometer with a conventional xenon flashtube. Sensitivity for 1-s determinations is similar to that of radioisotopic methods.



. Selected counting time (400-800 ms) of Eu chelate fluorescence emission (1) following an excitation light pulse. Background fluorescence ceases after a few nanoseconds.

Pharmacia DELFIA® System



The leading technology in Neonatal Screening

THE VISION 1984:
"Closer to the cell".
Confocal light microscopy was verified to provive better resolution and in addition possibility for 3D imaging of living cell material

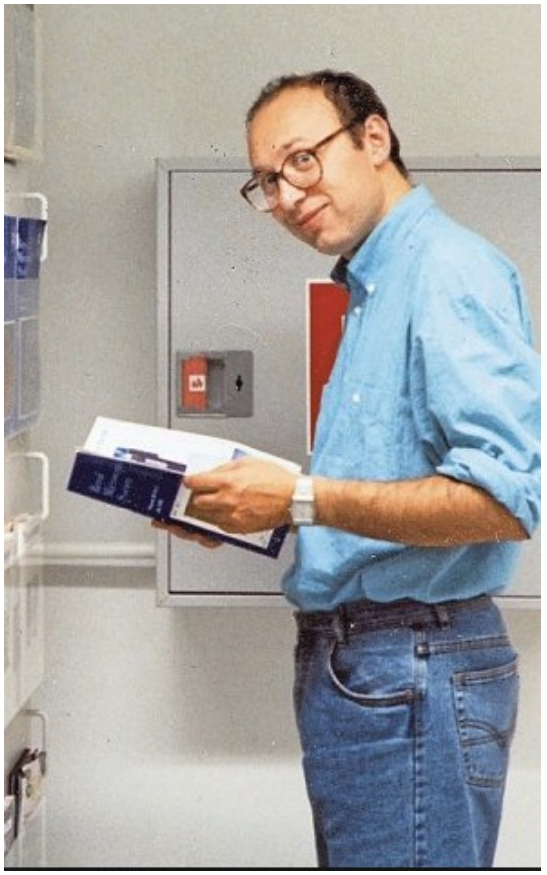
THE VISION 1986

The optics technology Confocal Microscopy could be used not only for imaging but also for other applications, eg. for in-vitro diagnostics

THE VISION 1987:
The new in-vitro diagnostics concept:
- elimination of the multi-step sample preparation
- elimination of separation of free and bound reactants
- making single step assays possible
- microvolumes
- fast results
- multiparameter assays

Pekka Hänninen

Stefan Hell



TECHNICAL SOLUTION 1993:
The use of fluorescence two-photon excitation and microparticles as solid phase -----> TPX-technology

Confocal microcopy technology
Laboratory on Biophysics
University of Turku

1993 – 2003

Important research results:

1) superresolution light microcopy STED

2) in vitro diagnostics concept with two-photon fluorescence excitation (TPX) "mariPOC"

Collaboration with Japan

For the R&D work of TPX we received a substantial financial support from SRL Inc, Tokyo (currently a Fujirebio subsidiary)

Stefan Walter Hell

Stefan W. Hell

Born	23 December 1962 (age 52) Arad, Romania
Citizenship	German
Fields	Physical chemistry
Institutions	European Molecular Biology Laboratory Max Planck Institute for Biophysical Chemistry German Cancer Research Center
Alma mater	Heidelberg University
Thesis	(1990)
Known for	STED microscopy
Notable awards	Nobel Prize in Chemistry (2014) Kavli Prize in Nanoscience (2014) Otto Hahn Prize (2009) Gottfried Wilhelm Leibniz Prize (2008)

Breaking the diffraction resolution limit by stimulated emission: stimulated-emission-depletion fluorescence microscopy

Stefan W. Hell and Jan Wichmann

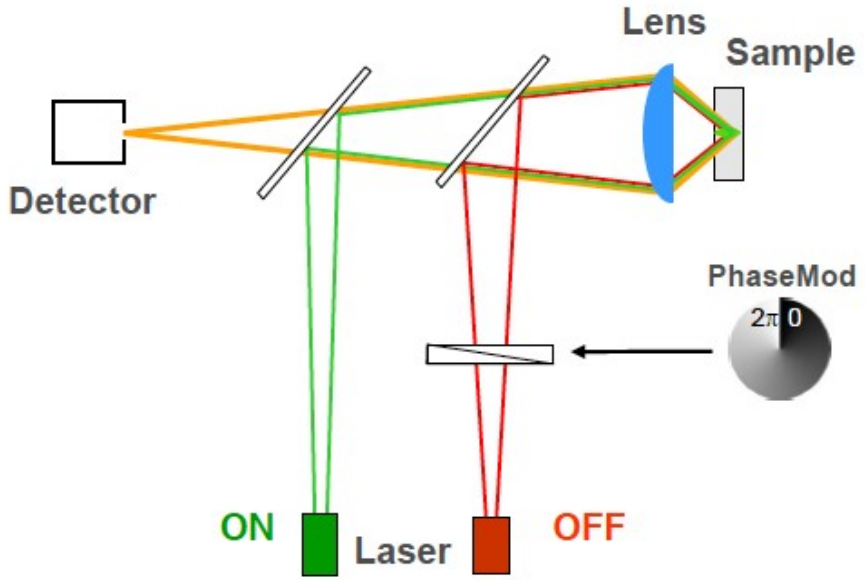
Department of Medical Physics, University of Turku, Tykistökatu 6, 20521 Turku, Finland

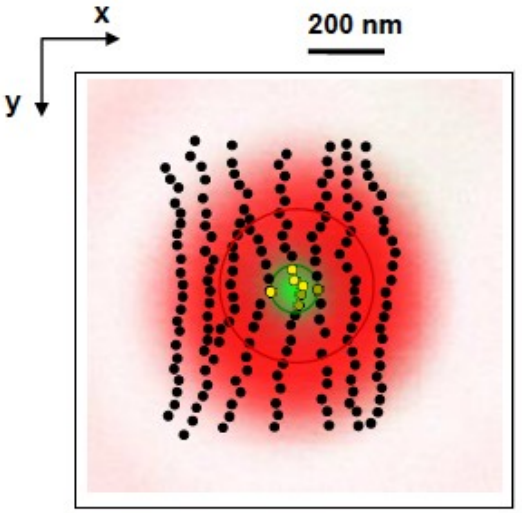
Received March 7, 1994

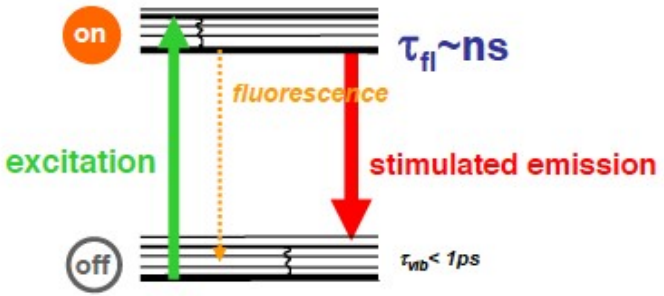
We propose a new type of scanning fluorescence microscope capable of resolving 35 nm in the far field. We overcome the diffraction resolution limit by employing stimulated emission to inhibit the fluorescence process in the outer regions of the excitation point-spread function. In contrast to near-field scanning optical microscopy, this method can produce three-dimensional images of translucent specimens.

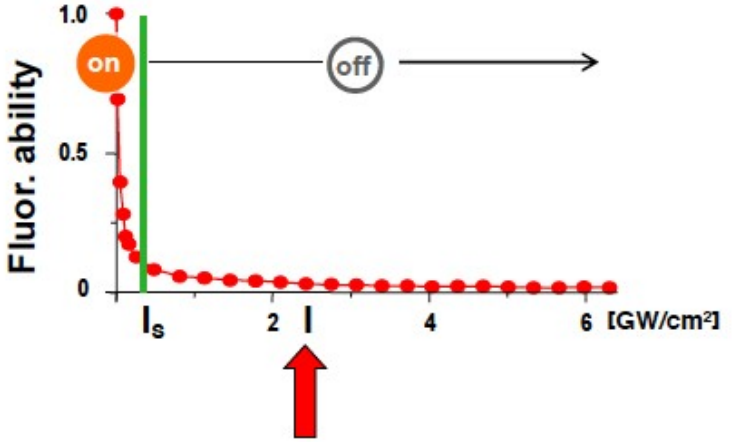
STED microscope:

Hell & Wichmann, Opt. Lett. (1994)

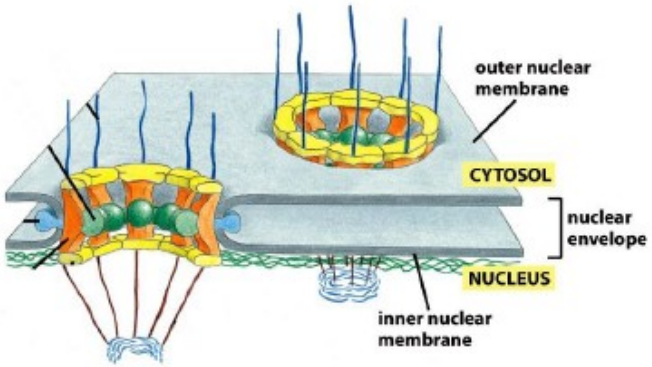






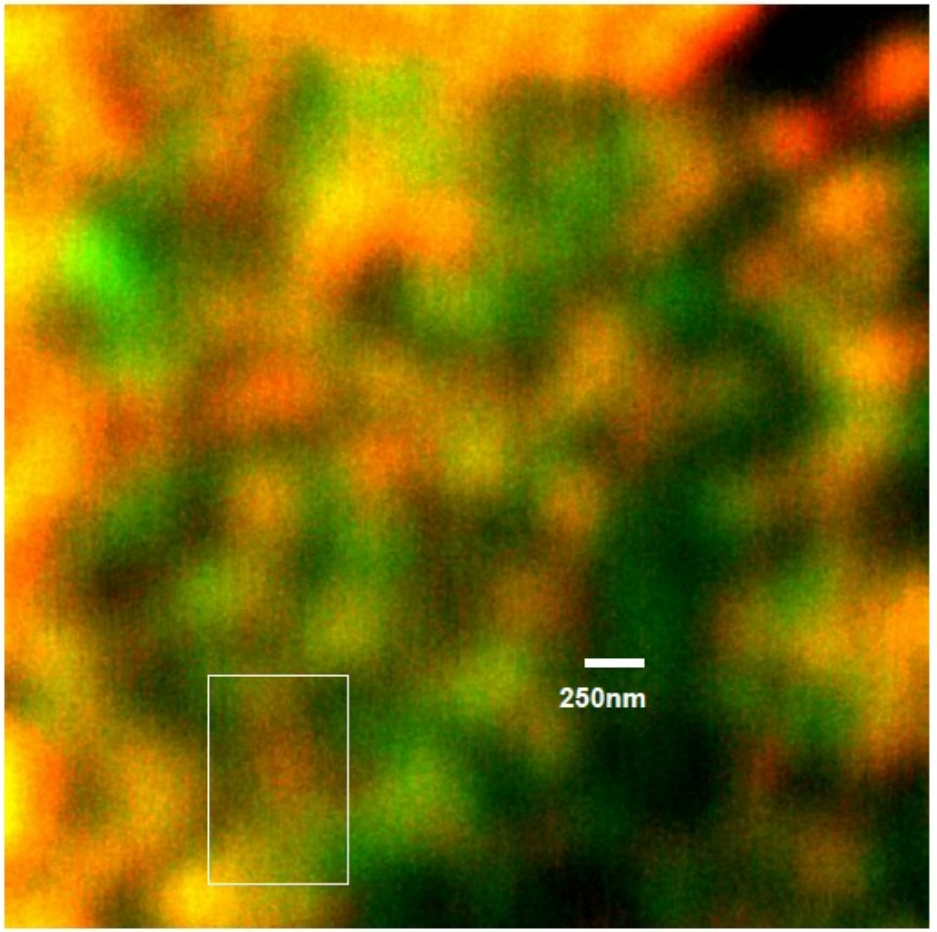


Protein assemblies in cell



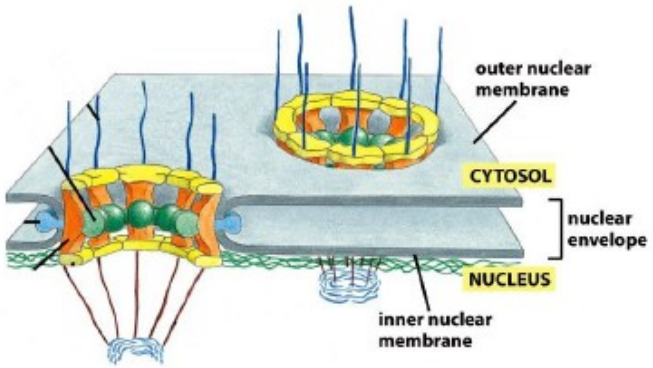
Nuclear pore complex

Standard (Confocal)



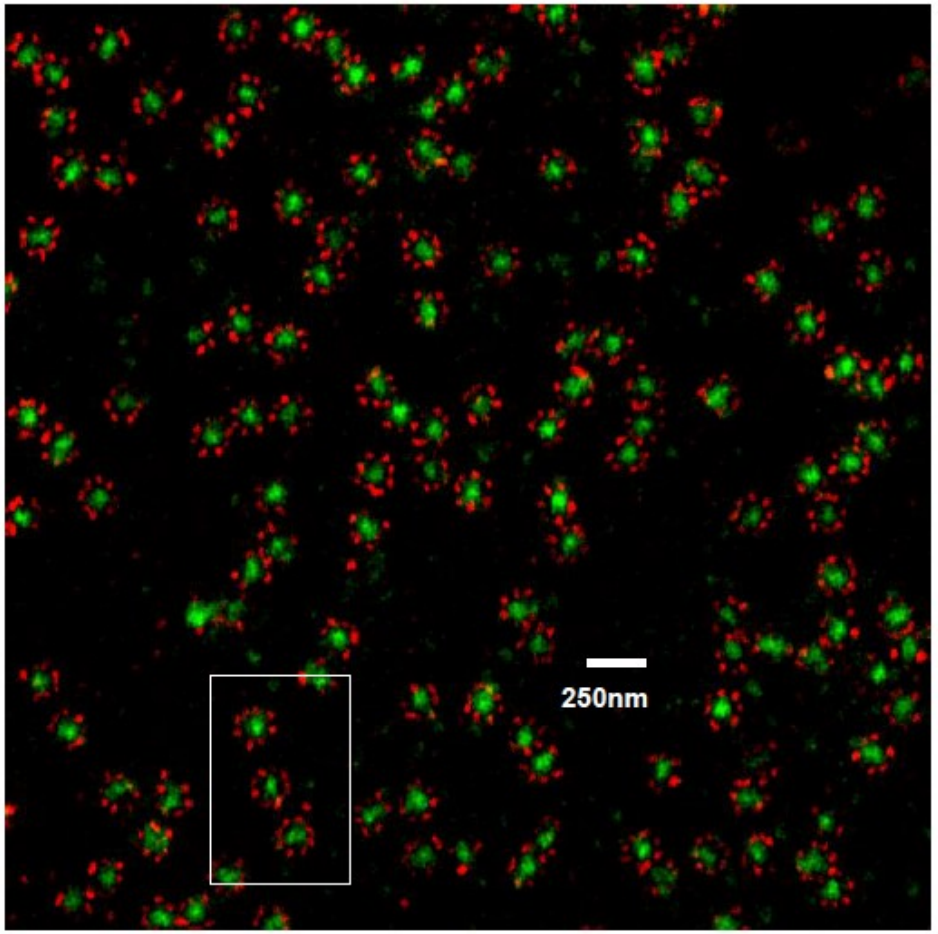
Göttfert, Wurm *et al* Biophys J (2013)

Protein assemblies in cell



Nuclear pore complex

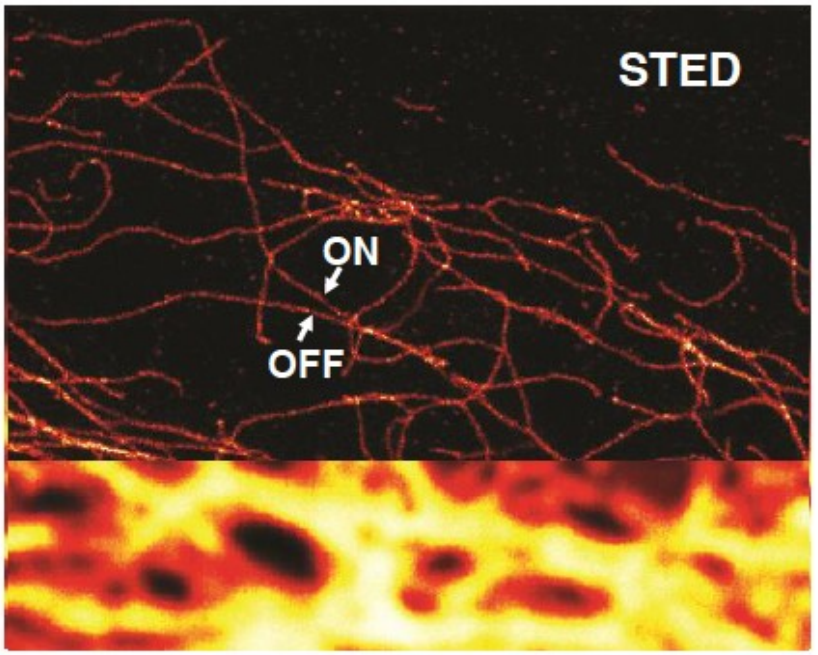
STED



Göttfert, Wurm *et al* Biophys J (2013)

$$d = \frac{\lambda}{2n \sin\alpha \sqrt{1 + I/I_s}} \longrightarrow 0$$

… down to molecular scale.



GOAL 2004
Leica launched very first super-resolution STED microscope.

GOAL 2008

ArcDia International Oy Ltd launched mariPOC (TPX-technology) for rapid test of respiratory infections

•**Nobel Prize for Inventor of Super-Resolution Microscopy**

Stefan Hell

The Nobel Prize in Chemistry

2014