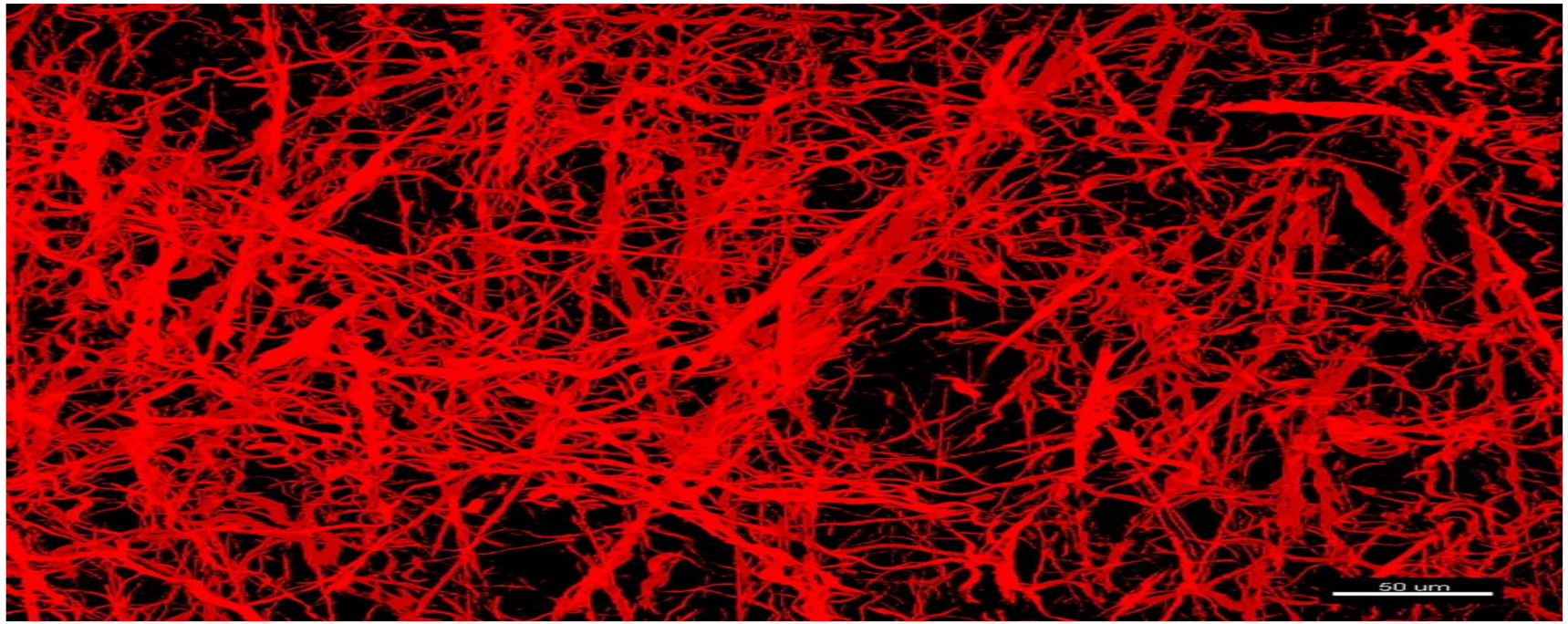
Nanostructured Copper-functionalized silica-based materials for NLO applications:

SHG nanoprobes: advancing harmonic imaging in living tissue



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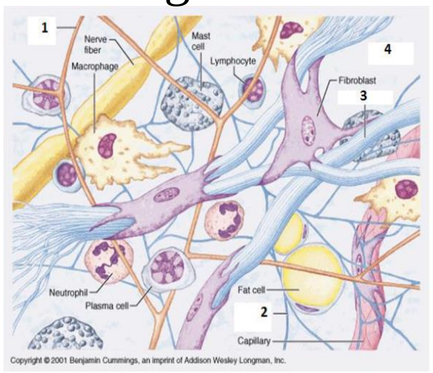
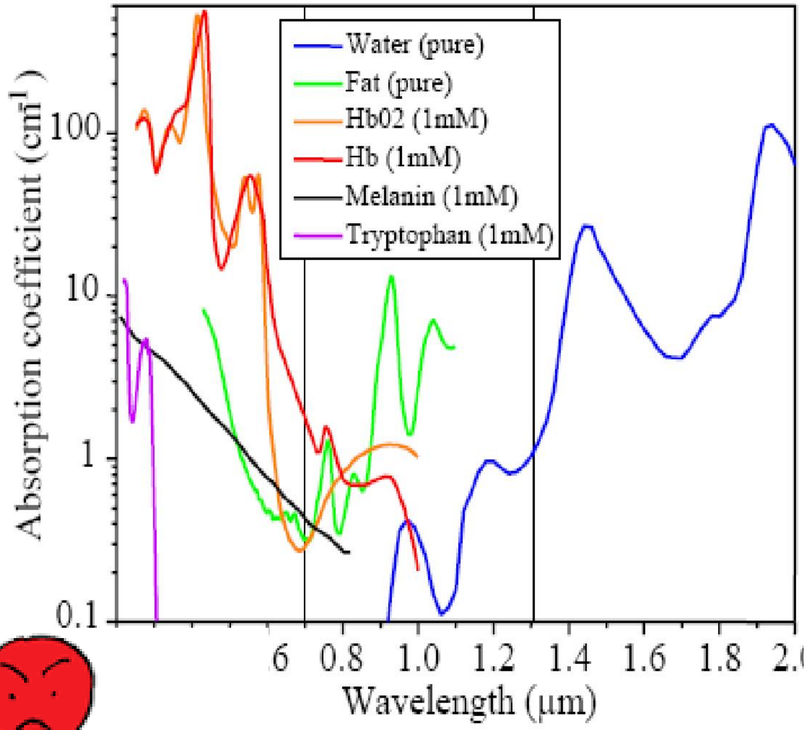
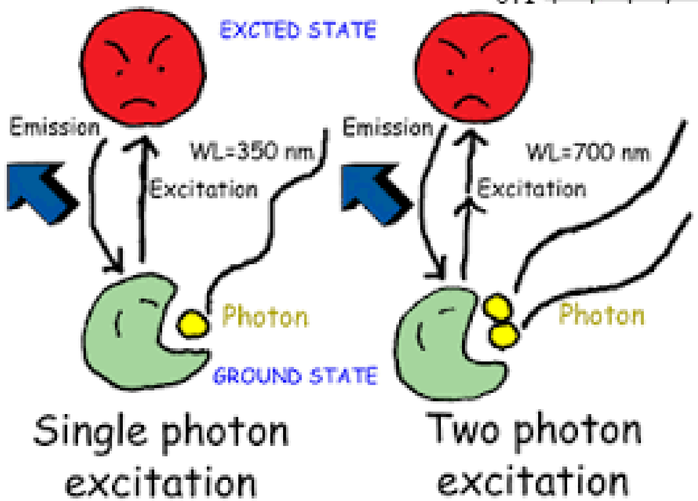
Fundamental limit of optics: what limits imaging depth

Absorption in tissues

0.7 – 1.2 um: reduced absorption compared to VIS light







Scattering in tissues

0.7 – 1.2 um: reduced Rayleigh scattering compared to VIS light

But strong Mie scattering at a few 100's um depth

Light Scattering

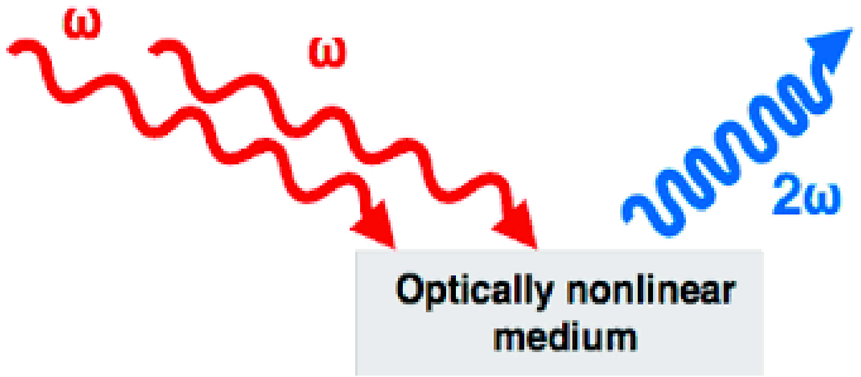
Type	Result	Relevance
Rayleigh Scattering	Blue light is scattered more	Why the sky is blue!
Particles *smaller* than wavelength of light		
Mie Scattering	Scattered light is white	Sclera, cataracts, and clouds appear white
Particles the *same or larger* as wavelength of light		
Tyndall Scattering	Blue light is scattered more	Blue irides (stroma without melanin is clolorless; scattering makes it appear blue)
Colloidal particles *same order* as wavelength of light		Flare appears blue

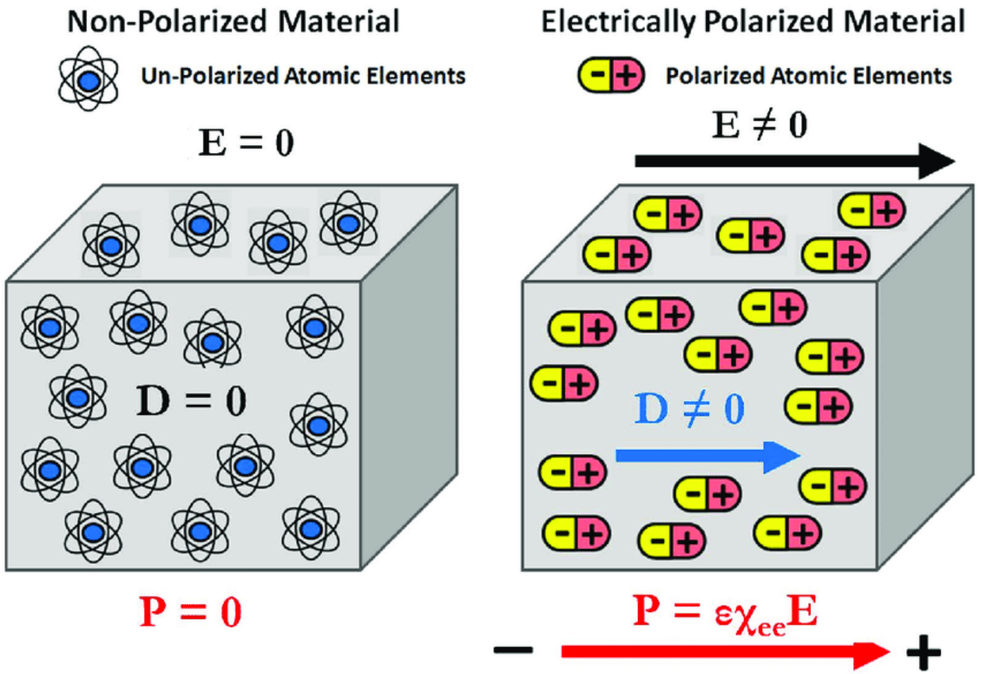
Motivation: find a solution to all these issues that stop tissue imaging.

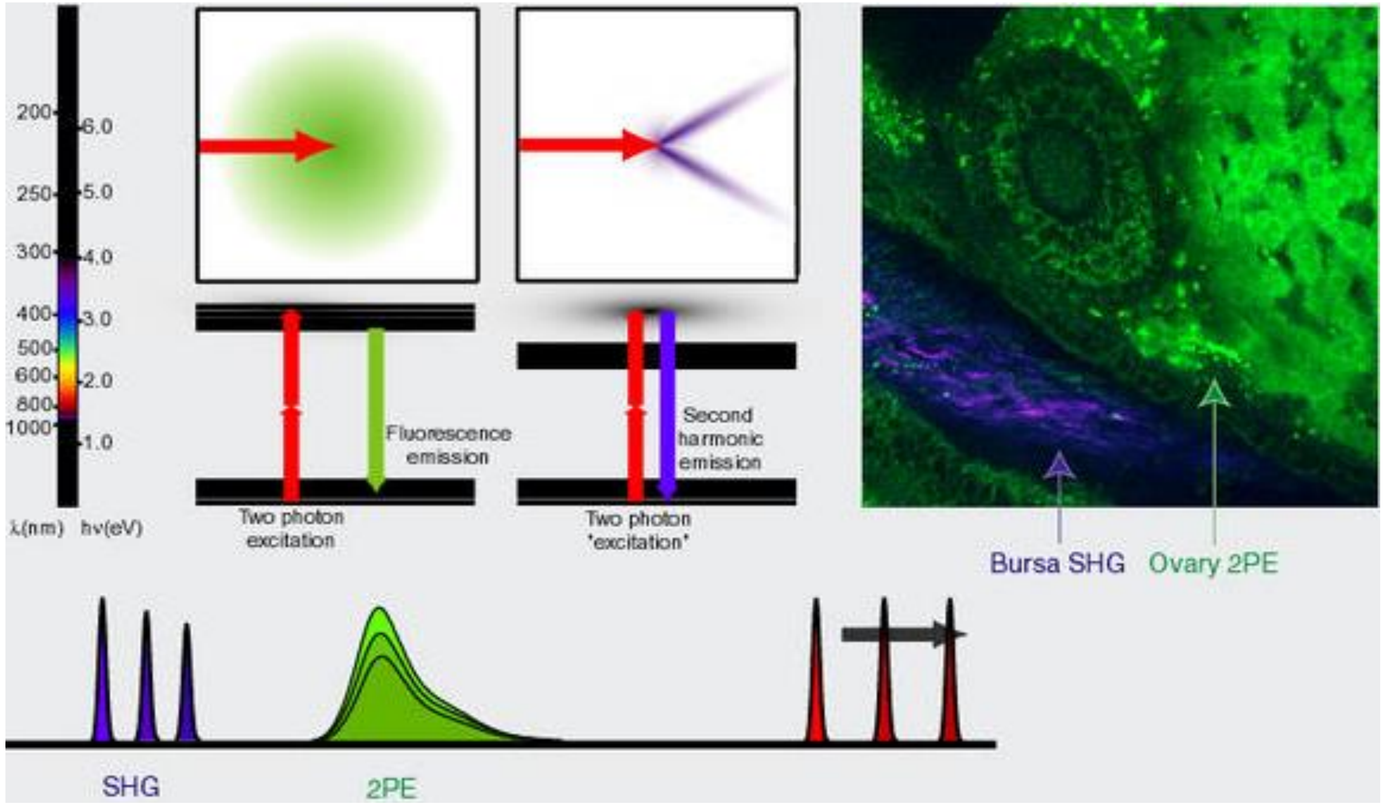
IR-Excitation: The longer wavelength penetrates deeper into the tissue

Clearing the tissue (Bleaching the pigments)

Second Harmonic generation (SHG) is a second-order nonlinear optical process in which two photons at the frequency ω interacting with **noncentrosymmetric** media (i.e., material lacking a generalized mirror symmetry) combine to form a new photon with twice the Energy.







$$P(\omega) = \chi^{(1)} \cdot E(\omega) + \chi^{(2)} \cdot E(\omega)^2 + \chi^{(3)} \cdot E(\omega)^3 + \cdots$$

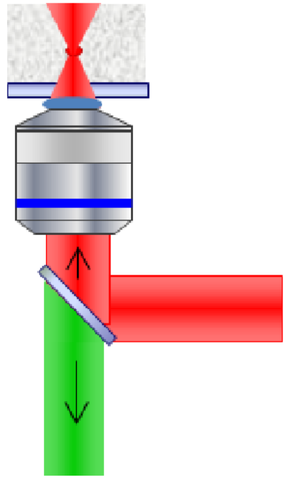
$E_{ext} = E_{at} = 5.14 \times 10^{11}$ V/m ……Atomic electric field strength

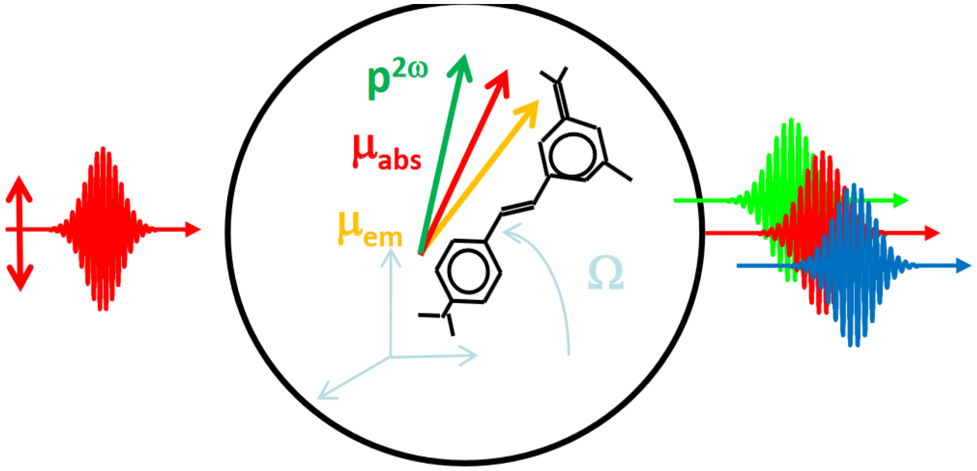
$\chi(1) = 1$

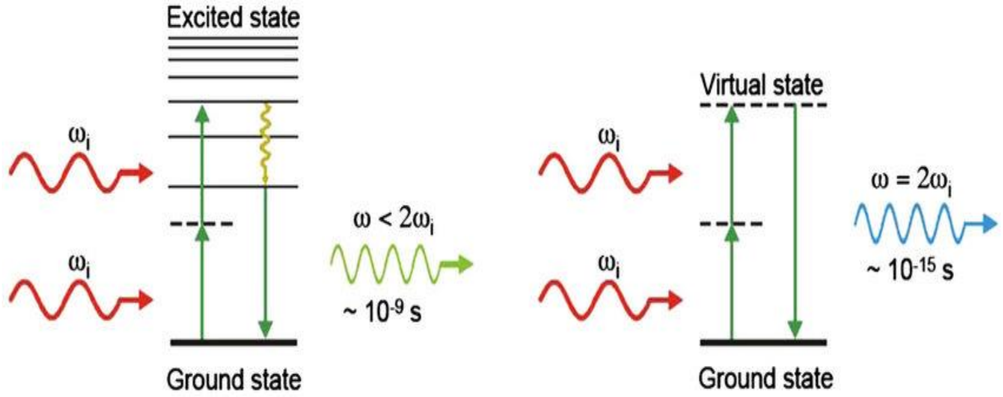
$\chi(2) = 1.94 \times 10^{-12}$ m/V.

$\chi(3) = 3.78 \times 10^{-24}$ m²/V²

From incoherent two-photon fluorescence (2PF) to coherent NLO

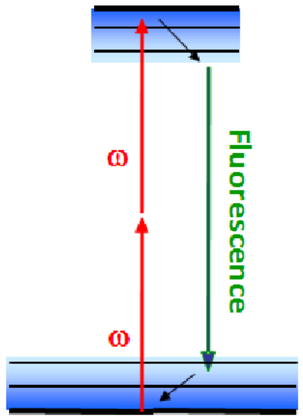


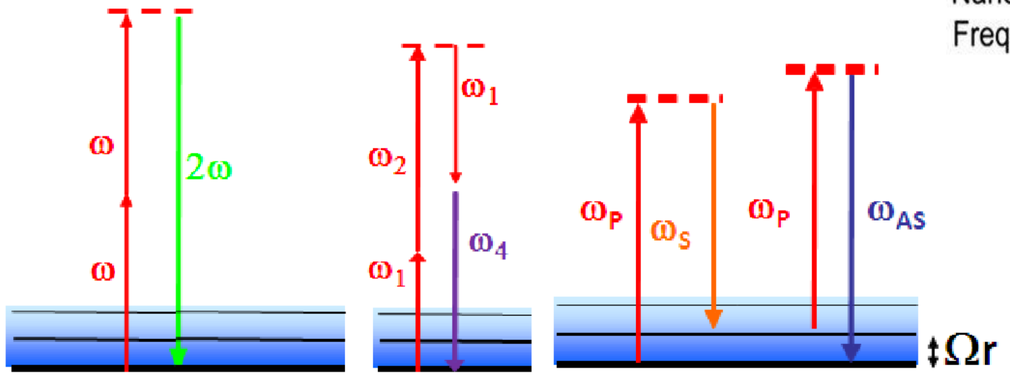




Incoherent process:
2PF

Coherent nonlinear processes :
SHG-THG, FWM, CARS





Two-Photon Excited Fluorescence

Involves real transition
Energy is partially lost
Nanosecond response time
Frequency lower than SHG

Second Harmonic Generation

Involves virtual transition
Energy is conserved
Femtosecond response time
Frequency exactly doubled

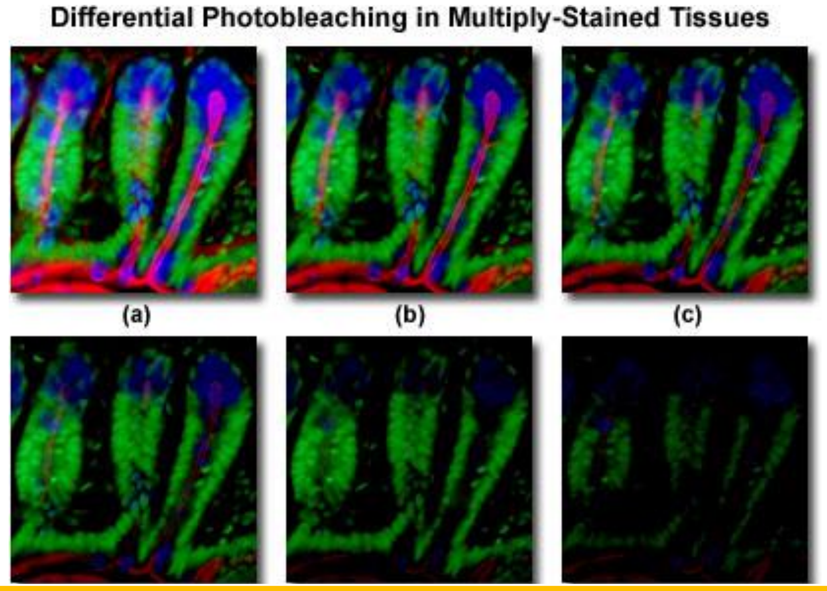
Single-molecule detection
- Biological systems are labelled

In-depth detection in tissues
- No labelling(collagen,and other molecules that show a specific orientations)

https://www.researchgate.net/publication/45406617_Second_harmonic_generating_SHG_nanoprobes_for_in_vivo_imaging

Challenges of 2PF

Bleaching: multiple excitations of the Fluorophore lead to weak photons
➔
phototoxicity



Dye saturation

Fluorescent dyes are limited in the maximum number of photons that they can emit in a given time

Blinking

large intensity fluctuations of fluorescence, whereby photon emission turns “on” and “off” intermittently➔over blocks of time during which the tagged molecule cannot be followed

Fluorescent probes fall short of their potential due to dye bleaching, dye signal saturation, and tissue autofluorescence

SHG nano-probes outperform fluorescent counterparts: no bleaching or blinking, the signal remains strong under intense illumination, offering superior contrast for molecular imaging of live cells and tissues

Better alternatives of Fluorophore dyes are SHG probes

- Long-term observation without photobleaching, flexibility in the choice of the excitation wavelength, and coherent signals.
- Narrow signal bandwidth for greater noise rejection, ultrafast response time, and excellent biocompatibility

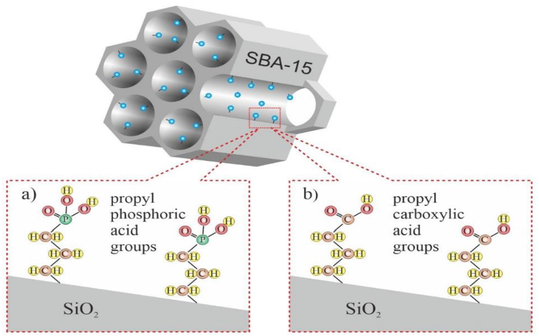
Where we are standing

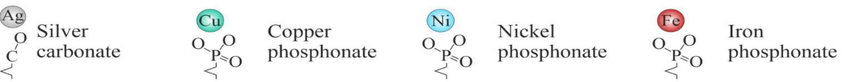
Barium titanate nanoparticles

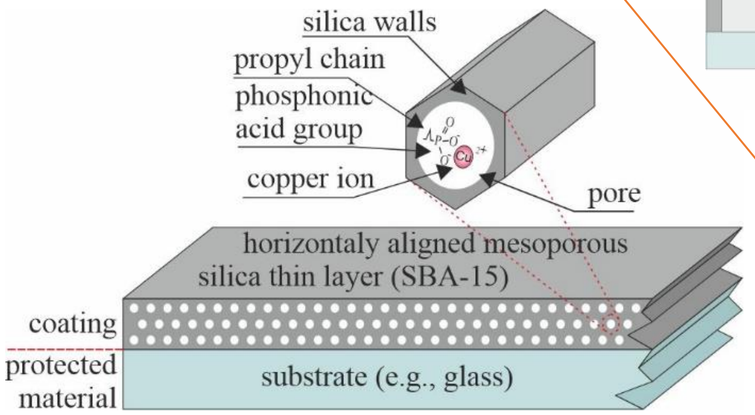
$BaTiO_3$

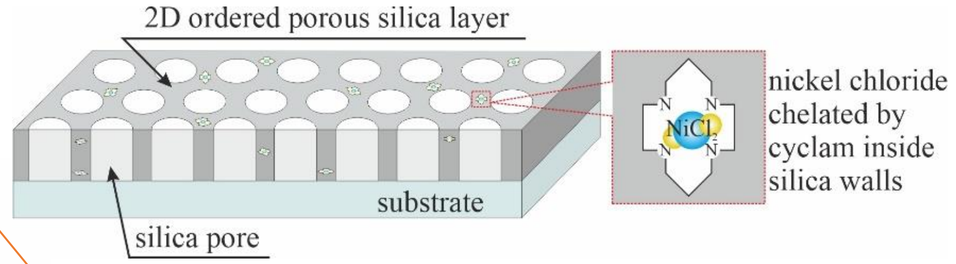
Zinc oxide (ZnO)

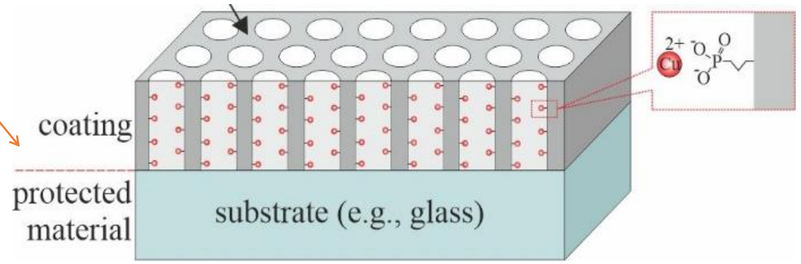
Can we use functionalized mesoporous silica?



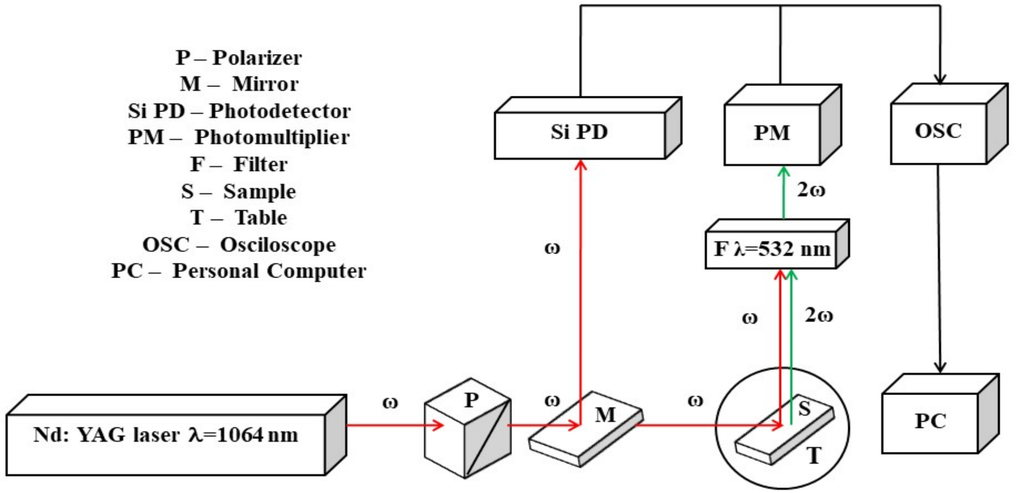


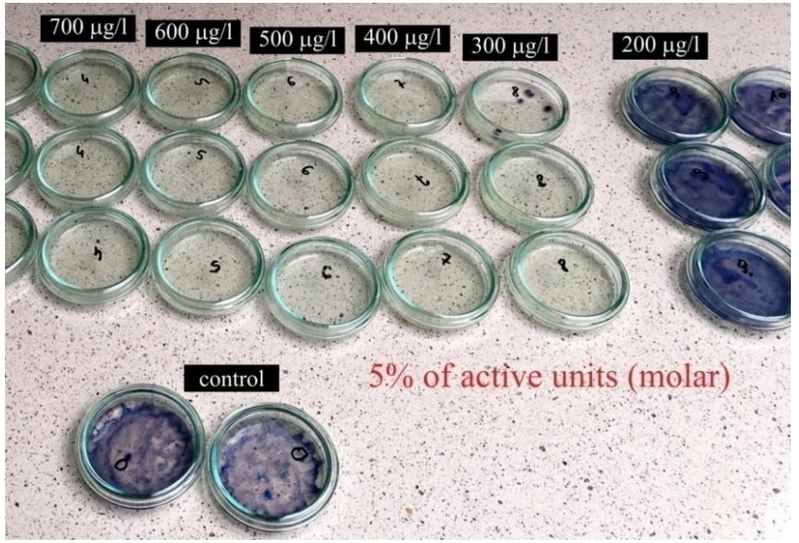


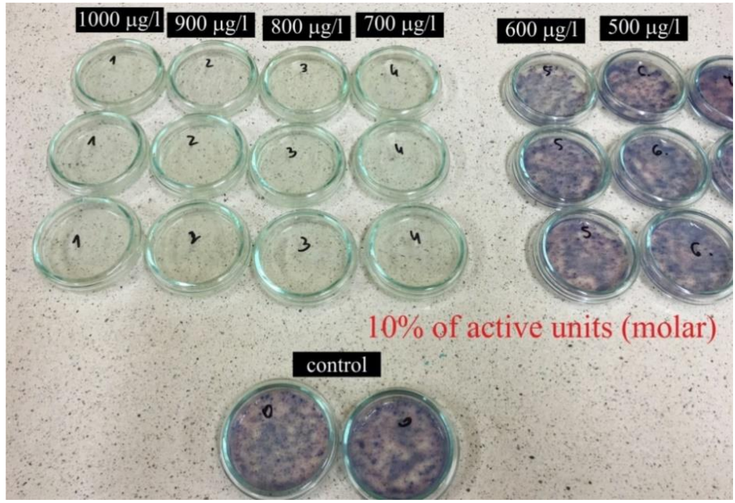




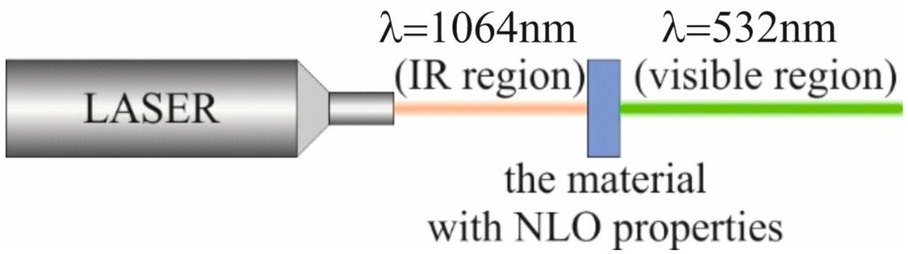
Properties of SBA-POO2Cu as a function of the concentration of functional groups



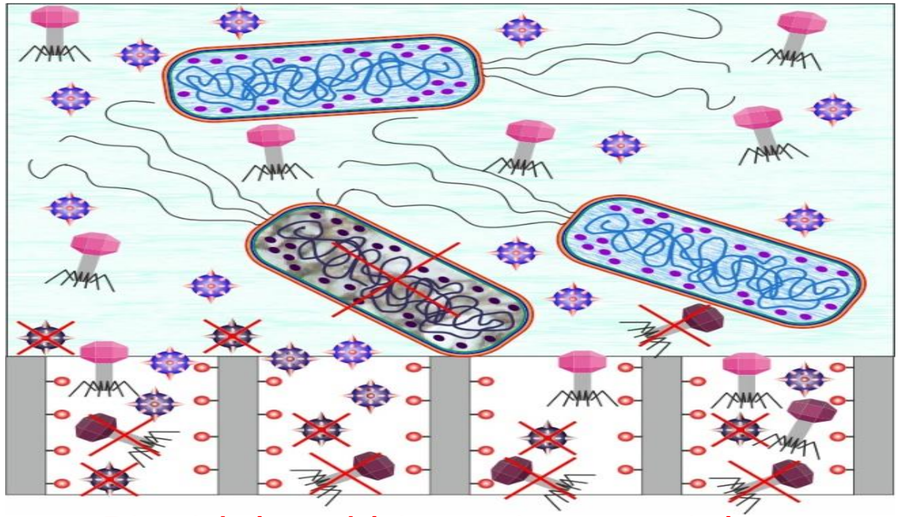




Applications

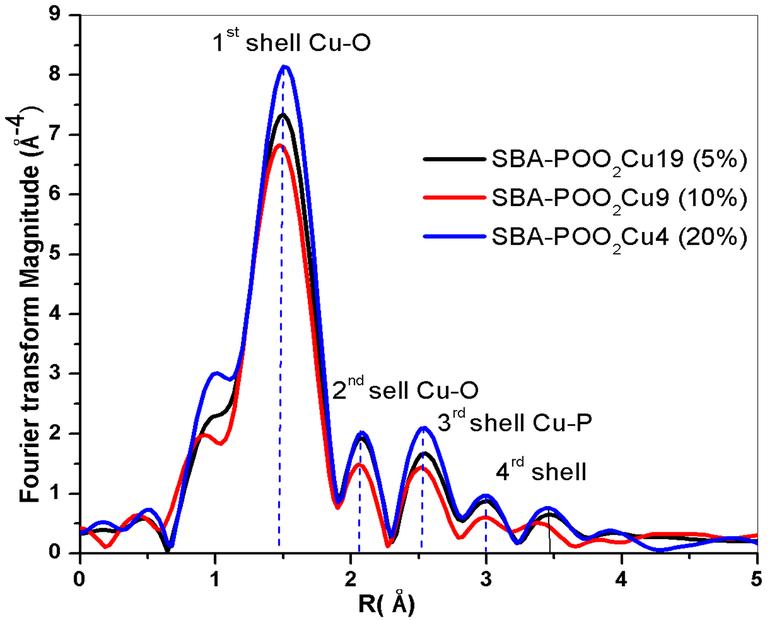


Modulators of the laser light and frequency transformers

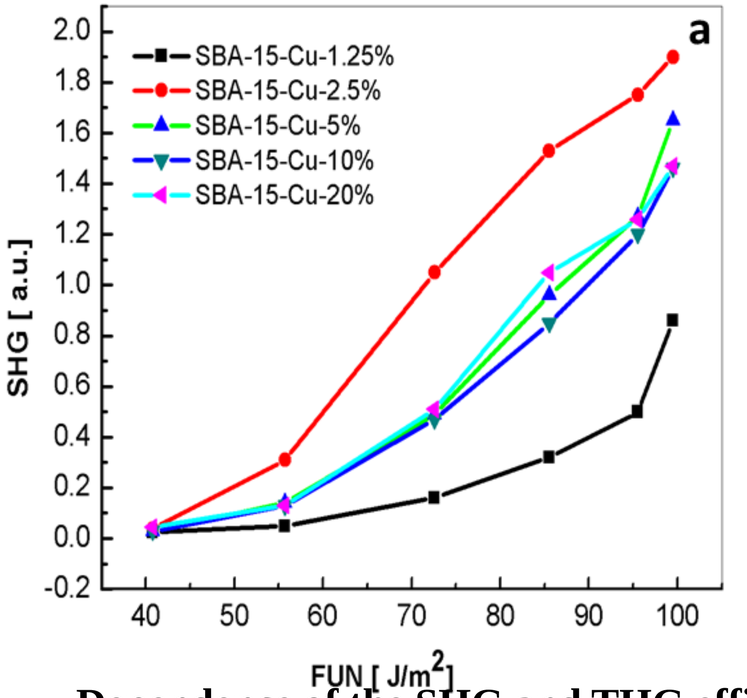


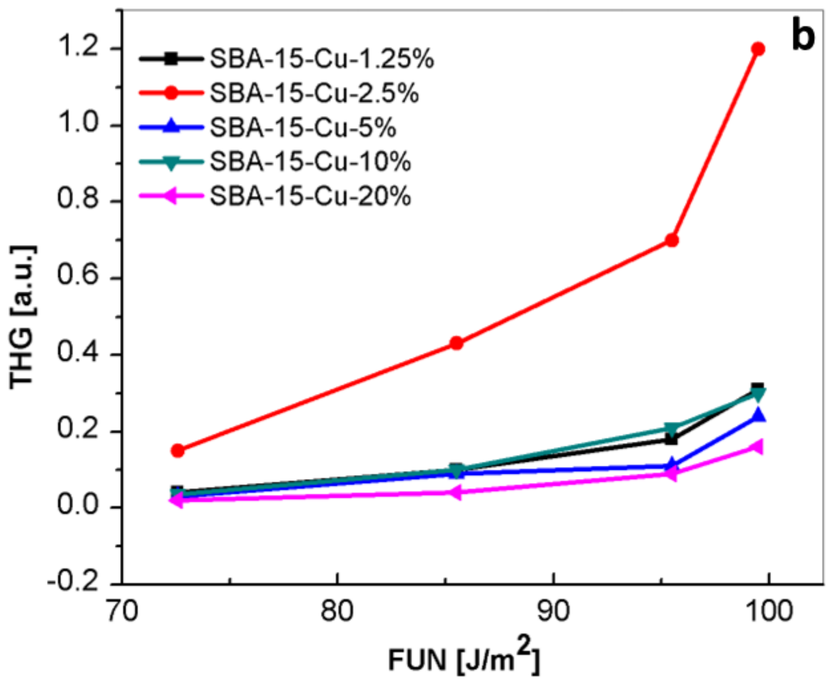
Biocidal and biostatic materials

Dependence of the SHG (a) and THG (b) on different degrees of functionalization.



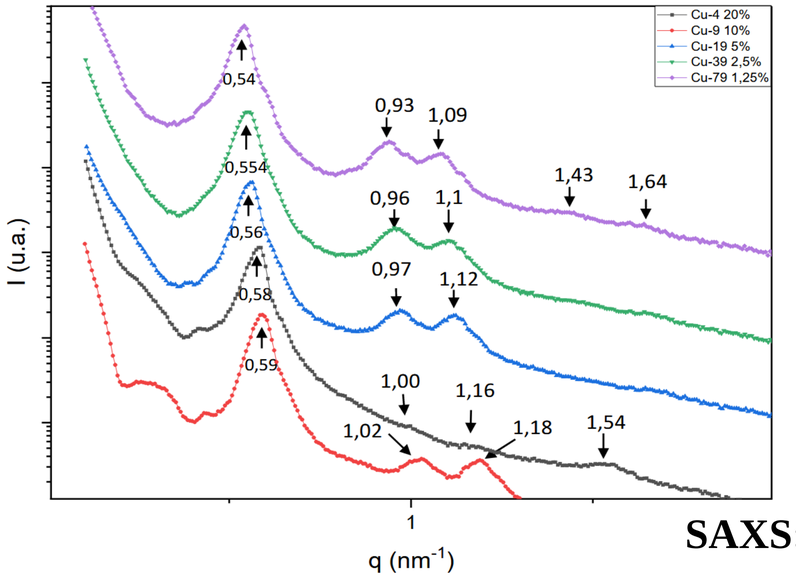
A Fourier Transform of the EXAFS signal provides a photoelectron scattering profile as a function of the radial distance from the Copper





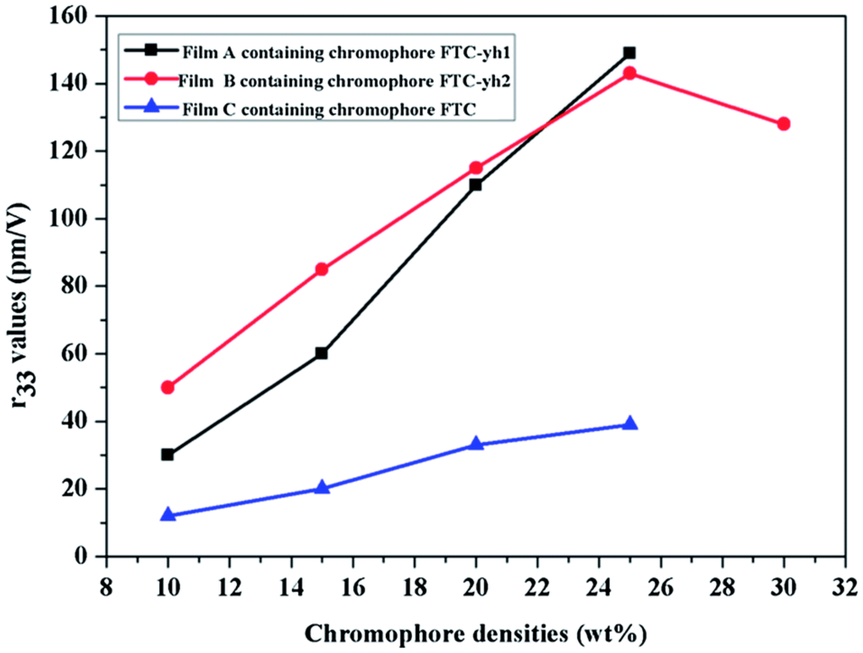
Dependence of the SHG and THG efficiency versus the fundamental power density

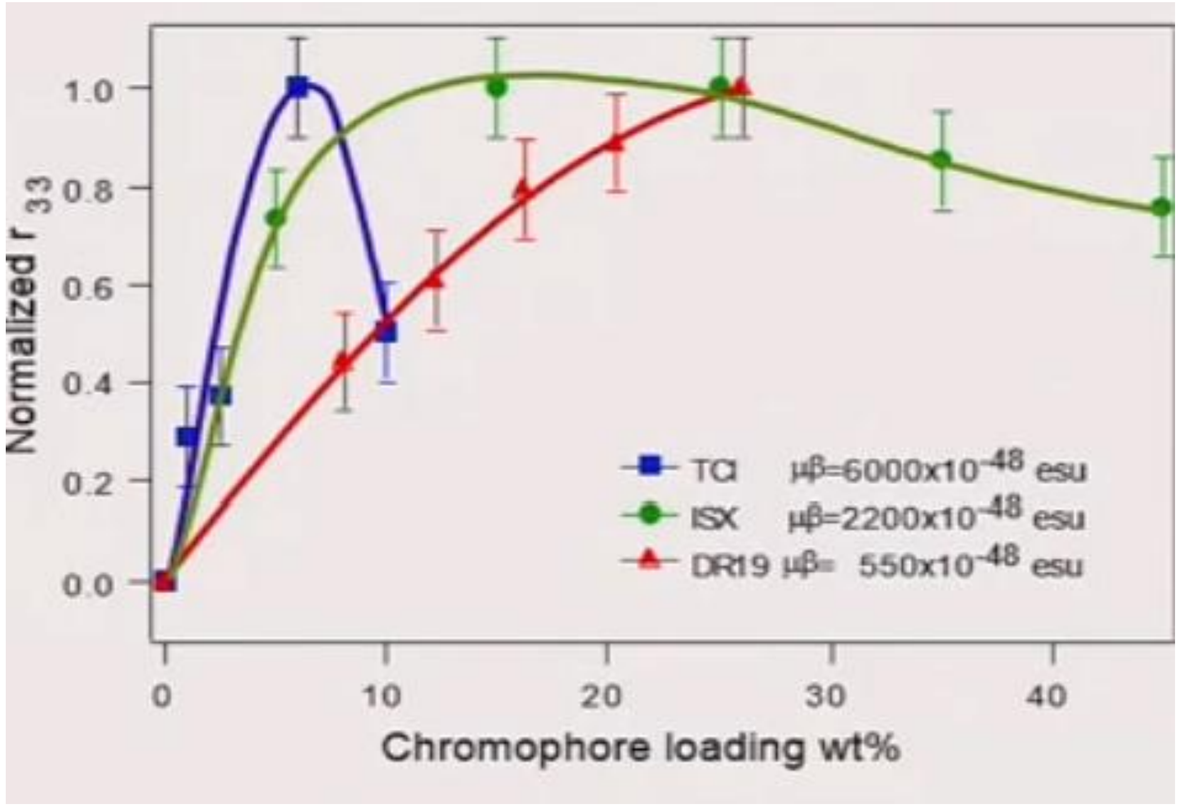
Nonlinear optical methods are sensitive to charge density acentricity, unlike X-ray diffraction. Even small changes below several nanometers affect charge transport between functionalized groups. Studying nanoparticles and ligand coordination is vital for understanding these effects

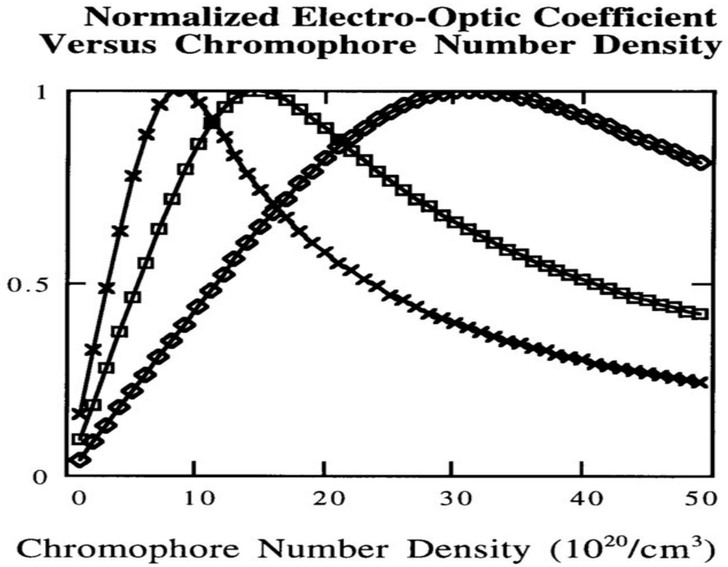


SAXS: small angle X-ray scattering

Centrosymmeric aggregation







When we're dealing with highly concentrated systems, like in certain materials used for optics, molecular groups tend to get a bit too cosy with each other

Summary

- Second harmonic generating (SHG) nanoprobes are innovative and robust labels ideal for in vivo imaging, offering advantages over traditional fluorescent probes. They neither bleach nor blink, and the signal does not saturate with increasing illumination intensity

- Their nanocrystalline structure lacks a central point of symmetry, enabling them to produce second harmonic signals under intense illumination. This process involves converting two photons into one photon with half the incident wavelength.

- These nanoprobes are detectable using conventional two-photon microscopy techniques, facilitating high-resolution imaging in living organisms.


Thank you
For your
Attention