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Multiorder Nonlinear Mixing in Metal Oxide Nanoparticles

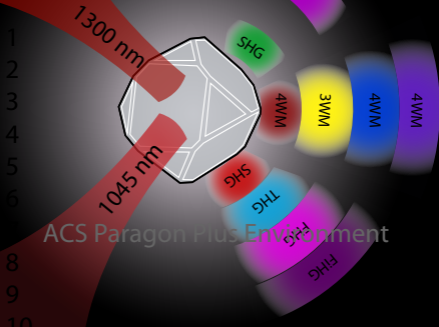
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Multi-order Nonlinear Mixing in Metal Oxide Nanoparticles

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Abstract

While most of the reports on the nonlinear properties of micro- and nano-structures address the generation of distinct signals, such as second or third harmonic, here we demonstrate that the novel generation of dual output lasers recently developed for microscopy can readily increase the accessible parameter space and enable the simultaneous excitation and detection of multiple emission orders such as several harmonics and signals stemming from various sum and difference frequency mixing processes. This rich response, which, in our case, features ten distinct emissions and encompasses the whole spectral range from the deep ultraviolet to the short-wave infrared region, is demonstrated using various nonlinear oxide nanomaterials while being characterized

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3 and simulated temporally and spectrally. Notably, we show that the response is con-
4 served when the particles are embedded in biological media opening the way to novel
5 biolabelling and photo-triggering strategies.
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11 Keywords

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14 Dielectric Nanoparticles, Metal Oxides, Nonlinear Microscopy, Harmonic Generation, Fre-
15 quency Mixing, Ultrafast Optics
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21 Introduction

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24 Within the perturbative approach of nonlinear optics, no more than the few lowest orders
25 of the susceptibility development ($\chi^{(n)}$ with $n \leq 5$) can engender a large manifold of para-
26 metric interactions. However, the comprehensive investigation of this extremely rich and
27 multi-faceted response has been so far hindered by the use of phase-matched crystals, which
28 provide sizeable signals only at selected frequencies.¹ Likewise, spectral broadening by Self-
29 Phase-Modulation (SPM)² might hamper the detection of these signals. Nowadays, the com-
30 bination of tunable ultrafast high repetition rate laser sources with sub-wavelength dielectric
31 structures is disclosing a largely unexplored territory. The research focus has been so far set
32 on nano-engineering dielectric substrates to exploit specific resonance modes, with the ma-
33 jor goal of embedding micrometric frequency-mixers in optoelectronic components.³⁻⁵ In this
34 work, we show that metal oxide nanoparticles of various chemical compositions (harmonic
35 nanoparticles, HNPs) and with no prior morphology- or size-selection can readily generate
36 multiple signals spanning from the deep ultraviolet (DUV) to the shortwave infrared (SWIR)
37 region. Their optical response includes various harmonic orders, and, upon two-color exci-
38 tation, several frequency-sum and difference combinations. Some of these signals exerted on
39 micro- and nano-structures have been previously observed individually⁶⁻⁸ or in combinations
40 of two or three of them.⁹⁻¹⁵ Very recently, Liu *et al.* reported the simultaneous emission of
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3 harmonics and wave-mixing signals from a 3 μm diameter region of a GaAs-based dielectric
4 metasurface optimized for 1.24 and 1.57 μm excitation using a kHz source.¹⁶ Here, using
5 a dual output laser developed for microscopy and sub-micron particles, we demonstrate a
6 similar multi-order phase-coherent response spanning from fifth harmonic generation (FiHG)
7 of a 1300 nm pulse (260 nm) to four-wave mixing (4WM) leading to emission at 2061 nm.
8 Notably, the response is conserved when the particles are embedded in biological media and
9 under laser-scanning conditions accessible thanks to the MHz repetition rate of the source,
10 which opens the way to bio-imaging and photo-interaction schemes.
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21 Results

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24 In Fig. 1, we present the multi-order response detected from a KNbO₃ HNP, upon two-color
25 excitation at 1045 and 1300 nm resolved spectrally from DUV (260 nm) to NIR (874 nm)
26 (horizontal axis) and as a function of the delay Δt between the two excitation pulses (vertical
27 axis). The peak intensity at the focus is 5.5 and 1.7 TW/cm² for the 1045 and 1300 nm
28 excitation, respectively. Details on the experimental set-up together with the protocols for
29 sample preparation are provided in sections S.I. 1 and 2. In S.I. 3, we describe the procedure
30 followed to compose the dataset in Fig. 1. Note that, differently from previous reports,^{17–19}
31 here we did not apply specific protocols to ensure to have a single nanocrystal in the focus of
32 the objective (*e.g.*, correlation with electron/atomic force microscopy, polarization analysis).
33 Therefore, although we systematically searched for objects smaller than the point spread
34 function of the set-up, we cannot exclude the presence of small aggregates instead of isolated
35 nanoparticles (see Fig. S.I. 2 and S.I. 3).
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48 In the image, the mechanism leading to each emission is reported as a combination of
49 upwards and downwards arrows, indicating the addition or the subtraction of a photon from
50 the 1045 nm (light brown) and 1300 nm (black) laser beam. Direct harmonic signals, such as
51 second harmonic generation (SHG) at 522 and 650 nm, or third harmonic generation (THG)
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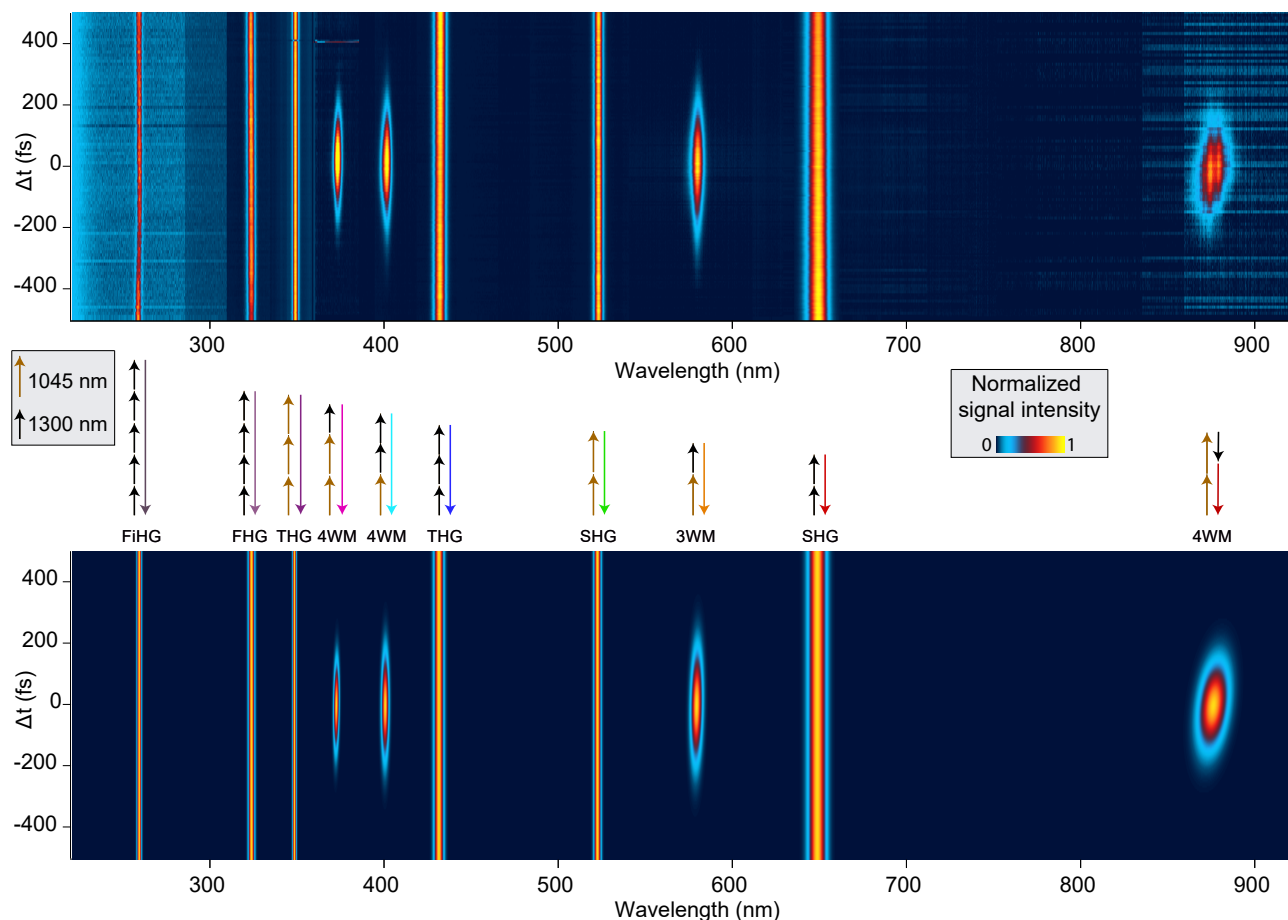


Figure 1: *Top*: Intensity-normalized spectrograms obtained from a sub-diffraction limited KNbO_3 HNP upon simultaneous 1300 and 1045 nm excitation. Direct harmonic signals (SHG, THG, FHG, FiHG) appear as continuous vertical stripes as they do not depend on the relative pulse delay Δt , contrary to signals generated by the superposition of the 1300 and 1045 nm pulses (3WM and 4WM) which display a clear Δt dependence. Note the absence of supercontinuum background and luminescence in the response. *Center*: Photon-combinations leading to each distinct spectral element of the response. *Bottom*: Simulated spectrograms.

at 348 and 433 nm, appear as continuous vertical stripes as they do not depend on the relative pulse delay, Δt .

The spectrogram at 579 nm, obtained by 1045 and 1300 nm sum frequency mixing, corresponds to the well-known Cross Frequency Resolved Optical Gating (XFROG)²⁰ of the two excitation pulses and its duration is determined by the cross-convolution of their temporal envelopes.²¹ The complete response from the KNbO_3 particle includes two harmonics generated by the 1045 nm beam (523 and 348 nm) and four by the 1300 nm (650, 433, 325 and

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3 260 nm), frequency sums involving three-wave mixing (3WM, 586 nm) and four-wave mixing
4 (373 and 401 nm) processes, associated with $\chi^{(2)}$ and $\chi^{(3)}$, respectively, and, finally, a 4WM,
5 involving a negative wave contribution, leading to 874 nm emission. We were not able to
6 detect the fourth harmonic (FHG) of the 1045 nm pulse, which should lie very close to the
7 fifth harmonic (FiHG) of the 1300 nm pulse.
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13 Within our experimental sensitivity, we did not observe any time-dependent intensity
14 variation of the traces associated with the $\chi^{(2)}$ response, which could have been assigned to
15 multi-step generation (see section S.I. 5). Similarly, we do not report any intensity decrease
16 with picosecond-time recovery, such as those that Liu *et al.* attributed to the recombination
17 of pump-generated free-carriers in a GaAs metasurface.¹⁶ We also do not observe supercon-
18 tinuum generation by SPM nor, consistently with previous assessments, fluorescence from
19 the particles. In general, we highlight the high photostability of the KNbO₃ sample. For a
20 reference, the acquisition of each spectral slice (as delimited by the vertical dashed lines in
21 Fig. S.I. 4) took between 30 seconds and 5 minutes depending on signal intensity (the longest
22 acquisitions apply to FHG and FiHG). All spectrograms were sequentially performed on the
23 same object. On the other hand, other materials tested, such as BiFeO₃, display a markedly
24 lower photo-stability when excited at wavelengths ≤ 980 nm as previously reported.²²
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37 The assignments of the temporal and spectral features observed are in line with the simu-
38 lated response presented in the lower panel of Fig. 1. The traces were analytically calculated
39 assuming Gaussian temporal and spectral profiles for the two fundamental pulses and ne-
40 glecting phase-matching effects, in agreement with the sub-coherence length dimensions of
41 the emitters. The spectral widths were set to the experimental values (9.35 nm at 1045 nm,
42 and 16.96 nm at 1300 nm). For the temporal component, we calculated the Fourier-transform
43 duration from the laser spectra and assumed exclusively second-order phase-distortions (*i.e.*,
44 linear chirp) described by the quadratic phase parameter ϕ adjusted to yield the largest
45 overlap with the experimental spectrograms in the wavelength/ Δt space (see section S.I. 4).
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55 Note that the model we devised did not include field confinement effects, Mie resonances^{23,24}
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nor absorption or refraction by the particles or the optical elements in the set-up. The best agreement was found for the quadratic phase values -5053 fs^2 and -2250 fs^2 for the fixed and tunable output, leading to pulse duration at the focus of 190 fs and 153 fs, respectively. Incidentally, we remark that negative delay dispersion is consistent with the large precompensation values of the laser set by the manufacturer, which is designed to be coupled with microscope systems containing more transmissive optical components than our custom set-up. Indeed, we systematically observed that working at the lower edge of the precompressor unit of the tunable output yielded the highest nonlinear conversion.

Being ω_1 and ω_2 the carrier frequencies of the two laser outputs and n_1 and $n_2 \in \mathbb{Z}$ their weight in the non-linear combination, the temporal duration of the i^{th} non-linear emission, centred at the frequency $\omega_i = n_1\omega_1 + n_2\omega_2$, can be readily calculated as

$$\tau_i = \left(\frac{|n_1|}{\tau_{1c}^2} + \frac{|n_2|}{\tau_{2c}^2} \right)^{-\frac{1}{2}} \quad (1)$$

where τ_{1c} and τ_{2c} are the temporal duration of the input pulses, which depends on their chirp, $\tau_c = \tau \sqrt{1 + \frac{\phi^2}{4\tau^4}}$ with τ being their Fourier-transform-limited duration and ϕ the quadratic phase. The pulse duration of each non-linear emission is therefore modulated by the weight of each input pulse in the nonlinear combinations. For example, the calculated duration of the two 4WM presented in Fig. 1 at 373 nm and 401 nm are 101 fs and 94 fs, respectively. These durations should not be confused with the different temporal spread of the 3WM and 4WM spectrograms in Fig.1, which are function of the time delay Δt between the two input pulses. More examples can be found in Fig. S.I. 5.

The frequency mixing schemes one can apply are not limited to the spectral range covered by Fig. 1. In fact, as reported in Fig. 2, by choosing a different wavelength for the tunable output (780 nm instead of 1300 nm), the same sub-diffraction limited KNbO₃ HNP emits also in the short-wave infrared region (SWIR, 1-2.5 μm) at 1583 nm (green trace) by the

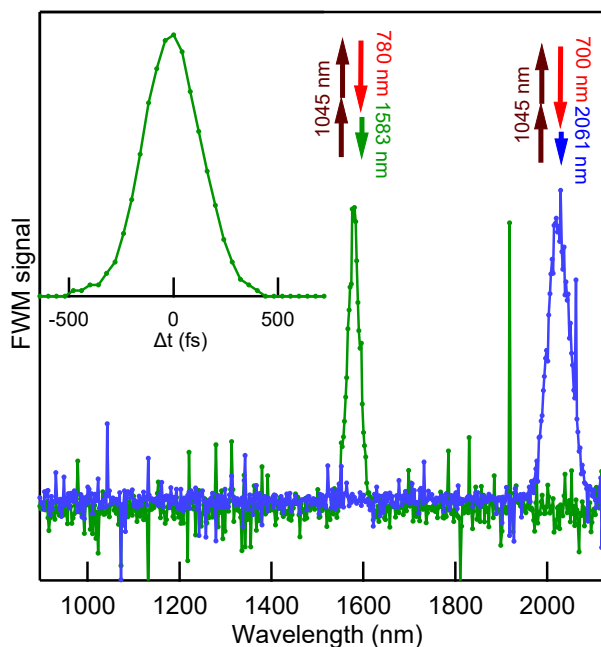


Figure 2: SWIR emission by a diffraction limited KNbO₃ HNP upon two-color excitation. *Green trace*: 4WM spectrum at zero time-delay centered at 1583 nm upon 780 and 1045 nm excitation. *Inset*: corresponding temporal cross correlation. *Blue trace*: 4WM spectrum at 2061 nm upon 700 and 1045 nm excitation.

following 4WM process:

$$\begin{aligned}\lambda_{4WM} &= \frac{1}{\frac{2}{\lambda_1} - \frac{1}{\lambda_2}} \\ &= \frac{1}{\frac{2}{1045 \text{ nm}} - \frac{1}{780 \text{ nm}}} = 1583 \text{ nm}\end{aligned}\quad (2)$$

In the inset, we report the corresponding temporal cross-correlation. This specific wavelength combination was chosen to generate an exemplary signal in the telecom range. By tuning the laser output to 700 nm, we produced an emission at 2061 nm (blue trace), at the long-wavelength detection edge of our set-up.

A critical aspect to carefully consider (in particular in view of applications) concerns the relative intensities of the emission peaks. The yellow traces in Fig. 3 indicate that for KNbO₃ the peak maxima span several orders of magnitude for a given set of excitation pulse inten-

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sities. It is known that the nonlinear response of dielectric nanoparticles depends on the interplay of numerous spectral, material, morphological, and polarization-dependent parameters. In Fig. 3, along with KNbO₃ (average dynamic light scattering (DLS) size 100 nm, see section S.I. 2), we report also the response of BiFeO₃ (green, average DLS size 100 nm), LiNbO₃ (red, average DLS size 60 nm), and ZnO particles (blue, average DLS size 140 nm) under similar excitation settings. The signals are expected to increase as the volume squared, as previously shown for $\chi^{(2)}$ processes in noncentrosymmetric oxides larger than 20 nm in SHG microscopy¹⁸ and ensemble measurements.²⁵ Such volume dependence could explain, for instance, the two orders of magnitude difference for SHG between LiNbO₃ and KNbO₃. In fact these two materials possess a similar orientation-averaged second-order bulk susceptibility²⁶ ($\langle\chi^{(2)}\rangle \approx 30\text{-}35$ pm/V) and their diameters determined by DLS differ by a factor two in our experiment. Likewise, the similar SHG and 3WM traces obtained for KNbO₃ and ZnO result from a larger nanoparticle size for ZnO since its $\langle\chi^{(2)}\rangle$ is below 6 pm/V.^{27,28} Finally, for BiFeO₃, the stronger SHG and 3WM traces could be attributed to its higher $\langle\chi^{(2)}\rangle$ of 100 pm/V and the trend of decreasing conversion efficiency for longer excitation wavelength previously observed within the 800-1300 nm range.²⁵ Nonetheless, the overall spectral responses of Fig. 3 and comparison between nanomaterials are to be considered with great caution. In fact, parametric signals depend on the 3D orientation of the crystallographic axis of the nanoparticles.^{17,29} In addition, we cannot exclude that slightly different focusing of the two interacting beams at 1045 nm and 1300 nm play a role in the differences between the SHG and 3WM amplitudes observed for BiFeO₃ and LiNbO₃. Therefore, it deems extremely complicated to extract reliable information without either i) following an ensemble characterization approach by extending the Hyper Rayleigh Scattering (HRS) formalism to higher nonlinear orders, or ii) proceeding with a bottom up approach concentrating the analysis on emitters well defined in terms of shape, size, and orientation. On the other hand, it is remarkable how under standard excitation and detection conditions and with no particle pre-selection, we are able to easily observe nine nonlinear processes (with the exclusion of

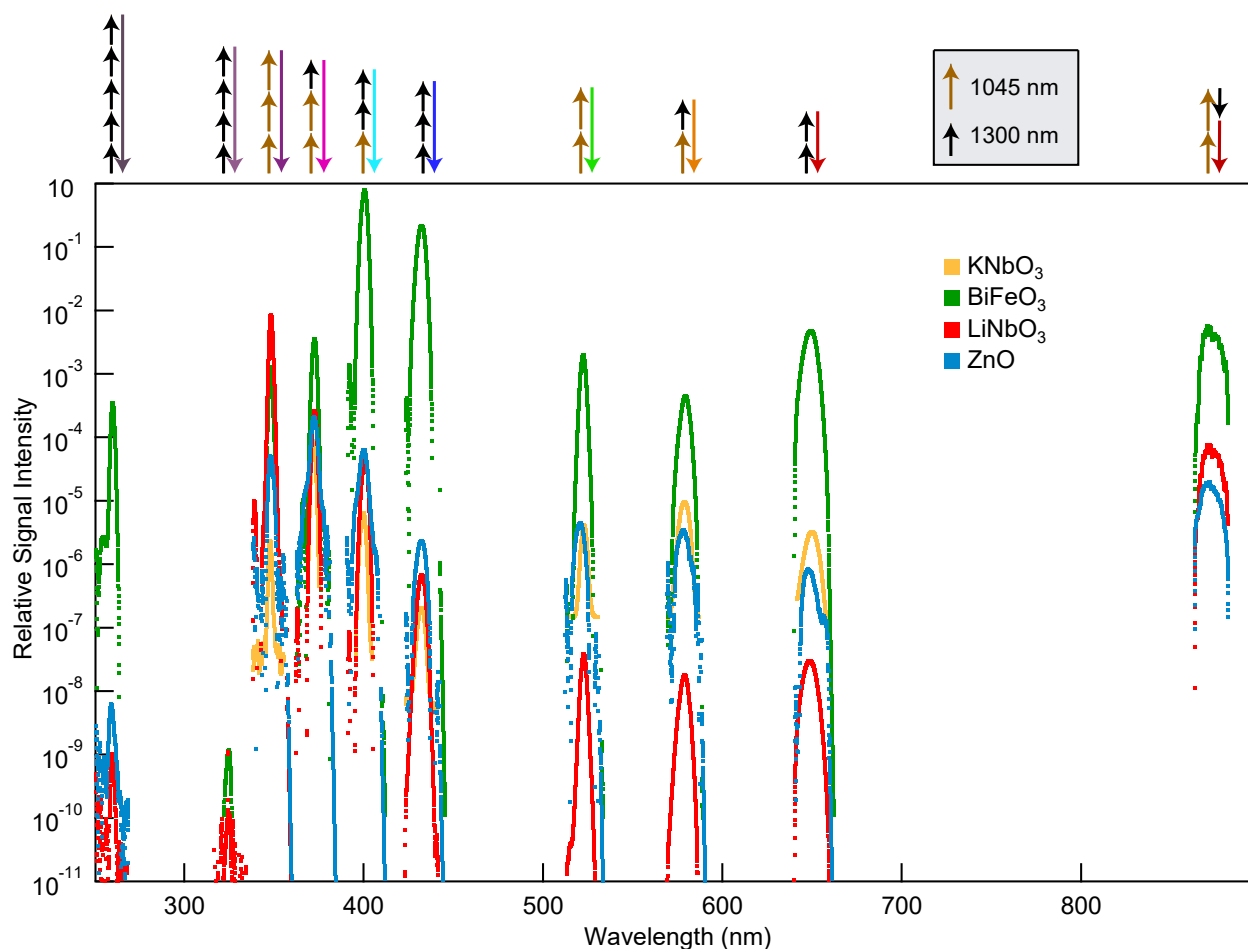


Figure 3: Excitation- and detection-corrected spectral response of HNPs of different metal oxide materials upon 1045 and 1300 nm excitation. The focal intensity corresponds to 1.8 TW/cm² for both excitation beams. All traces are normalized to the highest signal obtained (BiFeO₃ 4WM at 401 nm).

FHG, which is systematically considerably smaller) from four different HNP materials.

Besides the effect of sample-dependent properties on conversion efficiency, emissions are expected to scale with the excitation intensity according to the order of the nonlinear interaction at their origin. The intensity dependence of the harmonic progression stemming from 1300 nm is reported in the left panel of Fig. 4 up to a maximum intensity of 1 TW/cm². The nominal curves (I^n , with $n = 2, 3, 4, 5$) are plotted as continuous lines, the values for the exponent n obtained from fitting the data are reported in parentheses. Ostensibly, the experimental amplitudes are in agreement with the prediction of perturbative nonlinear response throughout the whole range we explored. The perturbative relationship with the excitation

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3 intensity, together with the wavelength and interaction-order flexibility of the approach, is
4 further exemplified by the comparison in the bottom plot of Fig. 4. In this case, we selected
5 two distinct mixing processes leading to emission at 648 nm. This wavelength was obtained
6 on the same KNbO₃ object either by 3WM or 4WM, as $\lambda_{3WM} = \frac{1}{\frac{1}{\lambda_1} - \frac{1}{\lambda_2}}$ ($\lambda_1 = 400$ nm ;
7 $\lambda_2 = 1045$ nm) or $\lambda_{4WM} = \frac{1}{\frac{2}{\lambda_1} - \frac{1}{\lambda_2}}$ ($\lambda_1 = 800$ nm; $\lambda_2 = 1045$ nm), respectively. In this com-
8 parison, the 1045 nm intensity was kept fixed, while the 400 and 800 nm intensities, which
9 can be read on the horizontal axes labelled I_{400} and I_{800} , were adjusted to yield a similar
10 output at 648 nm. 4WM requires 10 TW/cm² 800 nm excitation to generate similar signal
11 than 3WM with 0.8 TW/cm² 400 nm excitation. The dependence on the intensity of the
12 laser at λ_1 scales with the number of photons involved, being linear for I_{400} and quadratic
13 for I_{800} , respectively.
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27 Discussion

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30 Our work highlights the extremely rich optical response that can be obtained by the com-
31 bination of dual output femtosecond MHz lasers as light sources in scanning microscopy
32 using nonlinear objects as probes. The response observed can be readily associated with
33 processes relying on both the even and the odd orders of the nonlinear susceptibility per-
34 turbative development. Although several of these signals have been previously observed
35 separately, the possibility to exert all of them *simultaneously* on sub-micron objects with
36 no pre-selection in terms of size, morphology, and specific chemical composition (here we
37 used 4 different noncentrosymmetric metal oxide nanomaterials) emphasizes the versatility
38 of the approach. In particular, efficient *in situ* frequency conversion can lead to enabling
39 approaches for bio-imaging and for devising novel photo-interaction schemes.³⁰
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50 With this kind of applications in mind, we investigated whether the multi-order nonlinear
51 response is preserved when the particles are embedded in a biological environment and not
52 simply dispersed on a substrate in dry form. In the top-left panel of Fig. 5, we present a bright
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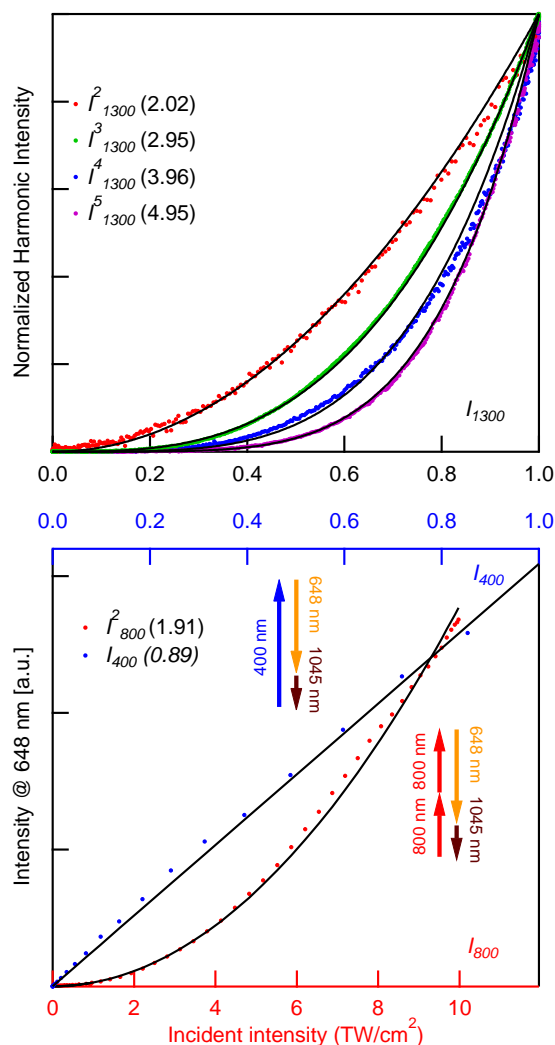


Figure 4: *Top*: Power dependence of the harmonic series obtained from a BiFeO₃ HNP upon excitation at 1300 nm. Traces are normalized to their maximum value. Dots: experimental data points. Lines: nominal traces I_{1300}^n , $n = 1, \dots, 5$. The values of the exponent n obtained by fitting the function I_{1300}^n to the data points are reported in parentheses. *Bottom*: 648 nm emission from a KNbO₃ HNP either by a $\chi^{(2)}$ (400 and 1045 nm excitation, blue) or a $\chi^{(3)}$ (800 and 1045 nm excitation, red) process. The top axis indicates the intensity at 400 nm (I_{400}) and the bottom one at 800 nm (I_{800}), respectively. Dots: experimental data points. Lines: nominal traces I_{400} and I_{800}^2 . The values of the exponent n obtained by fitting the function $I_{400,800}^n$ to the data points are reported in parentheses. All horizontal axes report the intensity of the excitation pulses in TW/cm².

field microscopy image, where one can distinguish two human cancer cells (DU145 androgen-independent prostate cancer) and numerous KNbO₃ HNP aggregates attached to the cell membranes or to the substrate. The corresponding set of multiphoton images acquired by

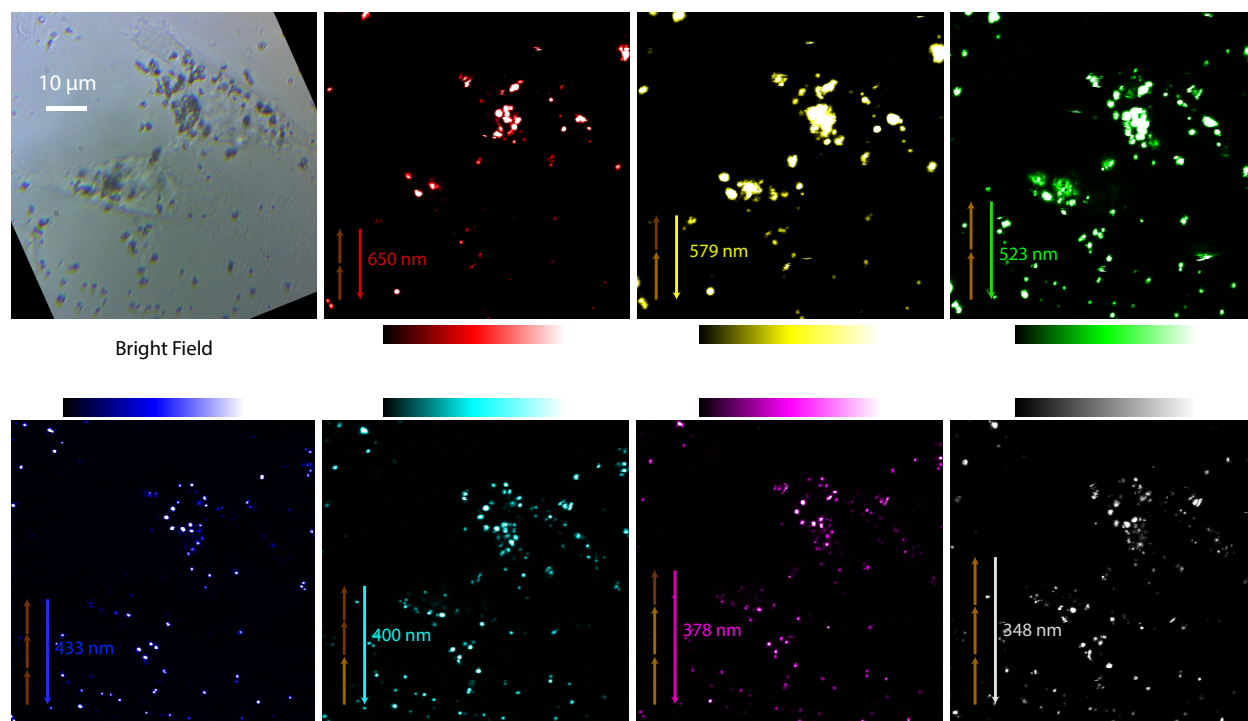


Figure 5: Laser scanning microscopy images of KNbO_3 HNPs in contact with human prostate cancer cells upon 1300 and 1045 nm excitation. The 1045 and 1300 nm contribution to the different nonlinear combinations are now plotted as light and dark brown arrows, respectively. *Top panels*: bright field image and 3WM processes (leftmost panel). *Bottom panels*: 4WM processes. The colormap hues are based on the actual wavelengths for visible emissions.

raster-scanning (60 μs dwell time) the 1300 and 1045 nm laser outputs collinearly focused onto the sample through a $\text{NA} = 0.75$ air objective is presented in all successive panels. Images are sorted from the longest to the shortest wavelength detected. The panels in the top row correspond to three $\chi^{(2)}$ processes (SHG and 3WM), the ones in the bottom row to four $\chi^{(3)}$ ones (THG and 4WM). Most of the particles are visible in all images, although their relative intensities might vary because of the reasons discussed in the context of Fig. 3 (see also Fig. S.I. 3). The visible improvement in spatial resolution of the $\chi^{(3)}$ series is associated with the higher nonlinearity order, as the effective point spread function (PSF) is the product of the excitation PSFs involved in the interaction.

In previous works, we have shown how the simultaneous detection of SHG and THG from HNPs used as labelling probes for tracking individual cells can greatly improve image-selectivity¹⁴ especially in highly optically congested environments with strong endogenous

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3 sources (collagen and lipids for SHG and THG, respectively).³¹ Alternatively, the efficient
4 *in situ* generation of new wavelengths can be used to deploy nonlinear photo-triggering ap-
5 proaches by fully exploiting the nonlinear conversion efficiencies of nanoparticles as opposed
6 to the comparatively smaller nonlinear absorption cross-sections of molecules and drugs.^{32,33}
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8 The generation of light in the SWIR region, apart from its interest in optoelectronics, can
9 be used in combination with imaging approaches critically requiring low-scattering of the
10 emitted signal for the image formation process, such as nonlinear light-sheet microscopy.³⁴
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12 Phase-coherent schemes based on two-color interactions have been recently demonstrated for
13 increasing spatial resolution both for scanning³⁵ and wide-field approaches.³⁶
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21 Finally, the analysis of time-resolved traces as reported in Fig. 1 paves the way to re-
22 fined multi-order pulse characterization methods. In the context of multiphoton microscopy,
23 the use of nanometric objects for femtosecond pulse diagnostics have been already explored
24 bridging to the nanoscale approaches such as SHG autocorrelation and FROG.^{37–41} The si-
25 multaneous access to multiple nonlinear combinations (and frequencies) demonstrated here
26 can be exploited to avoid temporal ambiguity in the time axis orientation²⁰ and to gain
27 spectral and temporal resolution due to the higher nonlinearities involved. In Fig S.I. 5, we
28 report a series of simulated spectrograms obtained by changing the ϕ values of the excitation
29 pulses. The shapes of the 3WM and 4WM traces in the Δt /wavelength space change in an
30 non-uniform fashion highlighting the sensitivity to the phase of the two laser outputs. Such
31 an approach could be prospectively used to infer spatially-resolved information about the
32 optical properties of the sample where the particles are embedded. Indeed, the fraction of
33 ballistic photons from the two beams reaching the HNP are expected to be modulated dif-
34 ferently due to wavelength-dependent differences in the scattering and absorption properties
35 of the local environment. This subtle differences can be read-out with nonlinear sensitivity
36 providing information on the local optical properties. In fact, spectrally-resolved scattering
37 is often analysed using photon transport equation for tissue diagnostics.⁴² However this ap-
38 proach is valid for macroscopic propagation lengths. With the approach outlined here, one
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3 could spectrally resolve scattering phenomena on length-scales considerably smaller than
4 those associated with the diffusive approximation, but longer than those typical for stan-
5 dard microscopy thanks to the extended propagation allowed by excitation in the SWIR
6 region.⁴³ We expect that this length-scale is suited to explore tissue micro-architecture for
7 correlating, for example, the relationship between the extracellular matrix and the cancer
8 onset in a tissue.
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17 Conclusions

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20 We have shown that metal-oxide particles with no prior strict morphology- or size-selection
21 readily generates a multi-order phase-coherent response spanning from DUV to SWIR upon
22 tunable two-color excitation at MHz repetition rate. The full response, which features sev-
23 eral direct harmonic emissions (up to $\chi^{(5)}$) and frequency mixing signals, is well reproduced
24 spectrally and temporally by an analytical expression derived within the perturbative devel-
25 opment of nonlinear optics. We have also demonstrated that the response is conserved when
26 the particles are embedded in biological media and the excitation beams are raster-scanned,
27 two aspects essential for developing diagnostics and sensing schemes taking full advantage
28 of the nonlinear sensitivity of the optical read-out.^{44,45}
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41 Supplementary Information

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43 Supporting information describing the set-up, nanoparticle characterization, and further
44 details on data analysis and modelling is available free of charge via the internet at <http://pubs.acs.org>.
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