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Active nanomaterials for biomedical applications

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Active nanomaterials for biomedical applications

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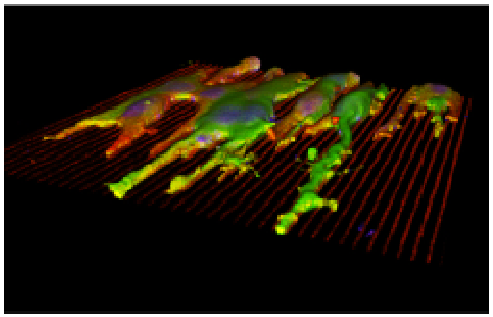
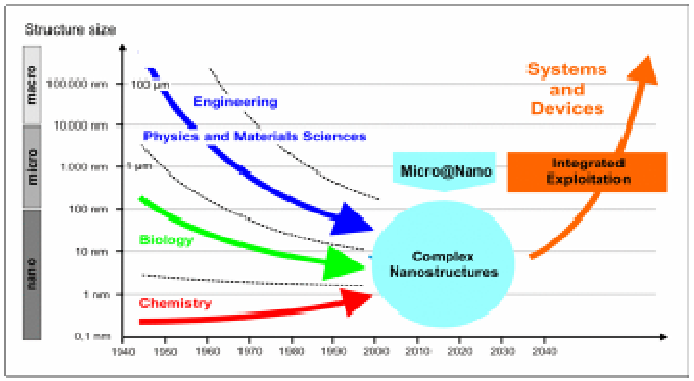
OUR GROUP

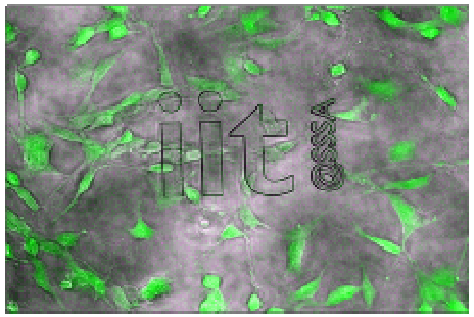


SMART BIO-INTERFACES

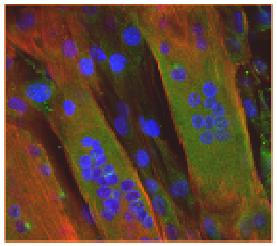
Istituto Italiano di Tecnologia

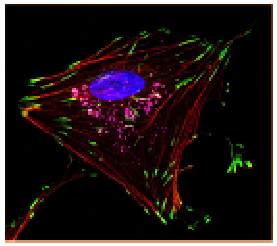
Center for Micro-BioRobotics

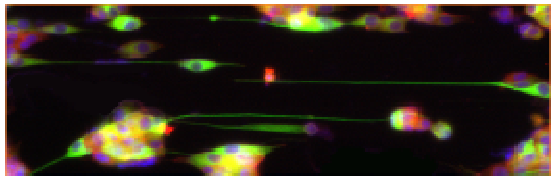




Cells







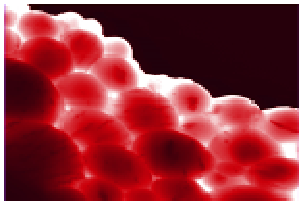
Inside the cells

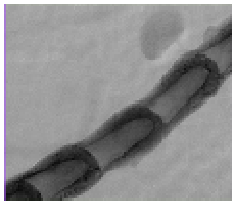
Drug delivery and cell stimulation

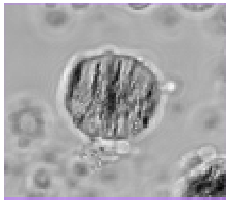
Outside the cells

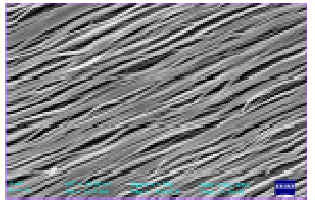
Tissue regeneration and biorobotics

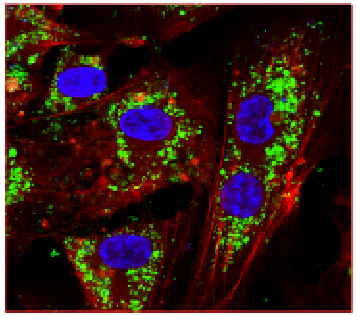
Smart nanomaterials

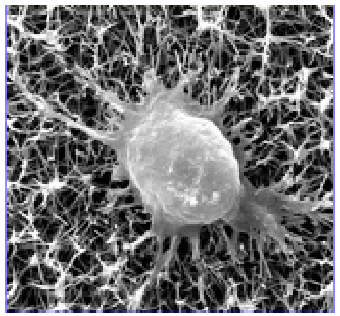


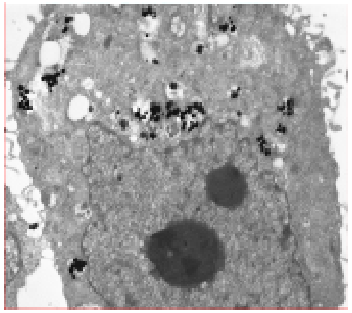


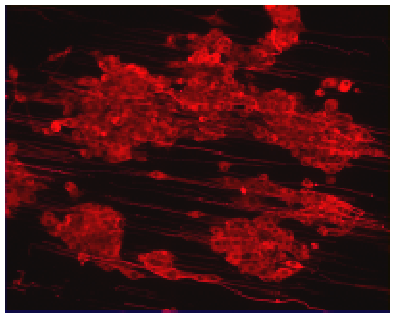


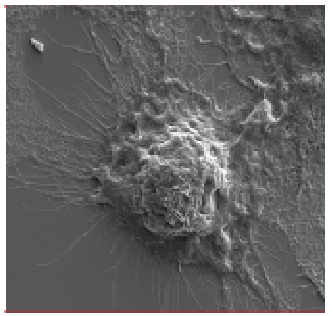




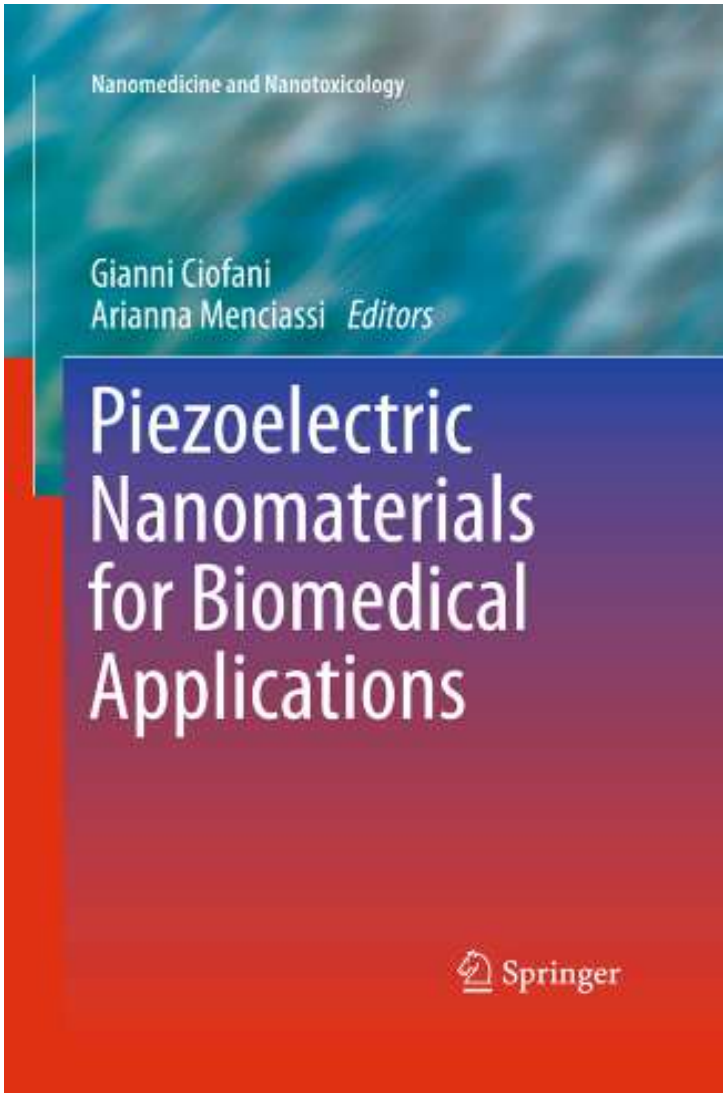








PIEZOELECTRICITY IN NANOMEDICINE



ARTICLE

Enhancement of Neurite Outgrowth in Neuronal-Like Cells following Boron Nitride Nanotube-Mediated Stimulation

Gianni Ciofani,[*,†] Serena Danti,[‡] Delfo D'Alessandro,[‡,§] Leonardo Ricotti,[⊥] Stefania Moscato,[§] Giovanni Bertoni,[¶] Andrea Falqui,[¶] Stefano Berrettini,[‡] Mario Petrini,[∥] Virgilio Mattoli,[†] and Arianna Menciassi[†,⊥]

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ACS Nano, 4(10): 6267–6277 (2010)

ARTICLE

Piezoelectric Nanoparticle-Assisted Wireless Neuronal Stimulation

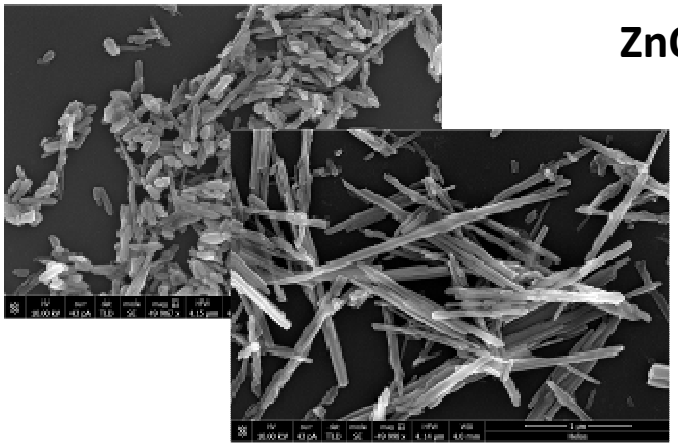
Attilio Marino,[*,†,‡] Satoshi Arai,[§] Yanyan Hou,[§] Edoardo Sinibaldi,[†] Mario Pellegrino,[⊥] Young-Tae Chang,[∥,#] Barbara Mazzolai,[†] Virgilio Mattoli,[†] Madoka Suzuki,[*,§,▽] and Gianni Ciofani[*,†]

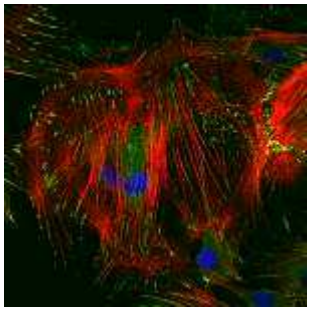
[†]Center for Micro-BioRobotics, Istituto Italiano di Tecnologia, Viale Rinaldo Piaggio 34, 56025 Pontedera (Pisa), Italy, [‡]The Biorobotics Institute, Scuola Superiore Sant'Anna, Viale Rinaldo Piaggio 34, 56025 Pontedera (Pisa), Italy, [§]WASEDA Bioscience Research Institute in Singapore (WABIOS), Biopolis Way 11, #05-02 Helios, 138667 Singapore, [⊥]Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, University of Pisa, Via Savi 10, 56126 Pisa, Italy, [∥]Department of Chemistry, National University of Singapore, MedChem Program of Life Sciences Institute, National University of Singapore, 3 Science Drive 3, 117543 Singapore, [#]Laboratory of Bioimaging Probe Development, Singapore Bioimaging Consortium, Agency for Science, Technology and Research (A*STAR), Biopolis, 138667 Singapore, and [▽]Organization for University Research Initiatives, Waseda University, #304, Block 120-4, 513 Waseda-Tsurumaki-Cho, Shinjuku-Ku, 162-0041 Tokyo, Japan

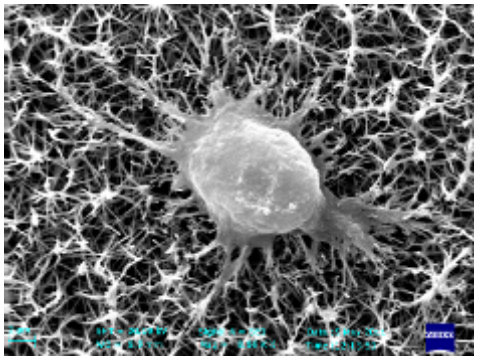
ACS Nano, 9(7): 7678-7689 (2015)

Piezoelectric nanomaterials

ZnO nanorods

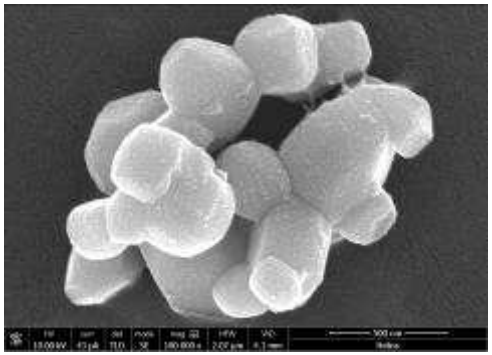


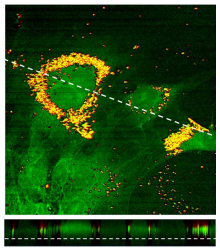




Ciofani G., Genchi G.G. and Mattoli V. ZnO nanowire arrays as substrates for cell proliferation and differentiation. ***Mat Sci Eng C*** *32: 341-347 (2012)*

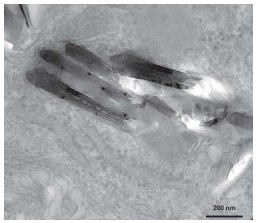
Barium titanate nanoparticles



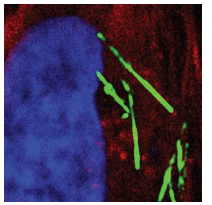


Rocca A., […], Ciofani G. Barium titanate nanoparticles and hypergravity stimulation improve differentiation of mesenchymal stem cells into osteoblasts. ***Int. J. Nanomed.*** *10: 433-445 (2015)*

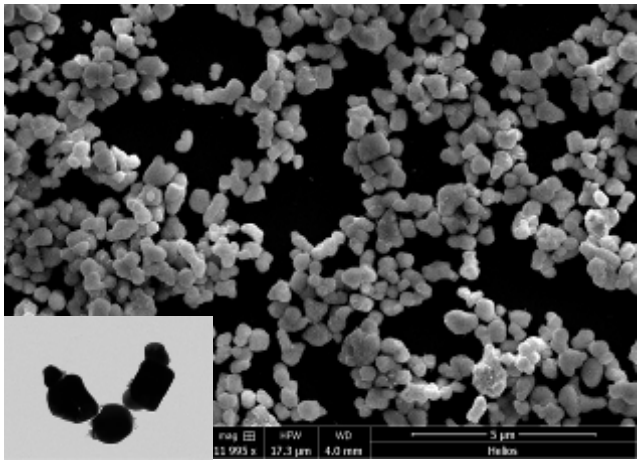
Boron nitride nanotubes

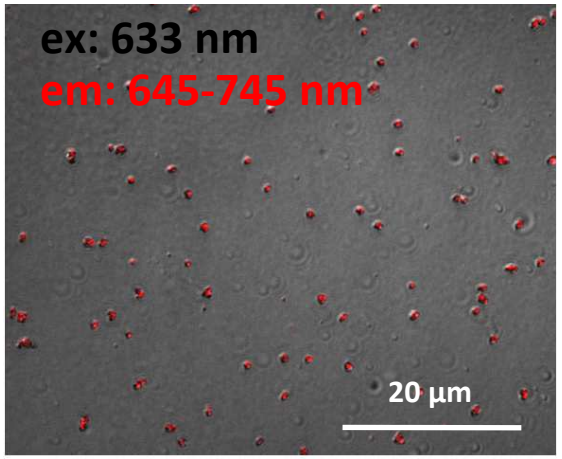


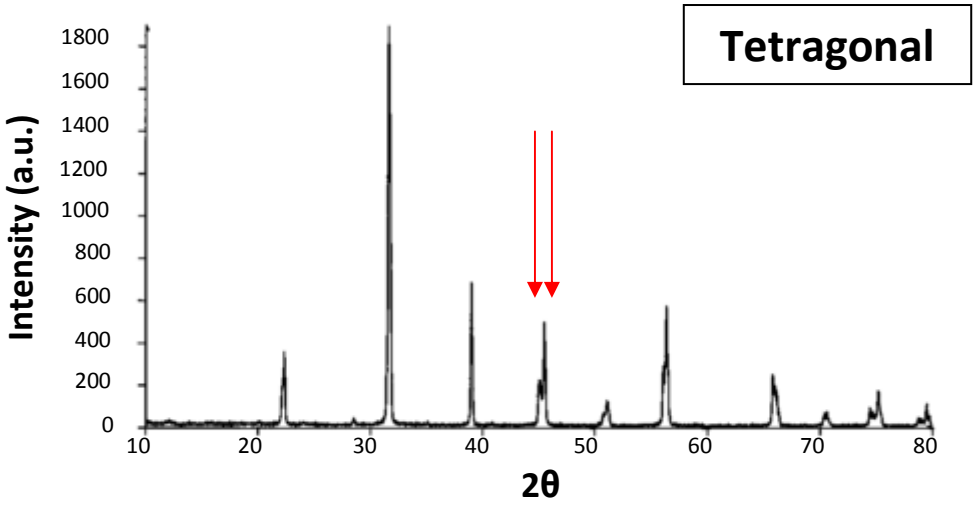
Ciofani G., […], Mattoli V. Cytocompatibility evaluation of gum Arabic-coated ultra-pure boron nitride nanotubes on human cells. ***Nanomed. UK*** *9: 773-788 (2014)*

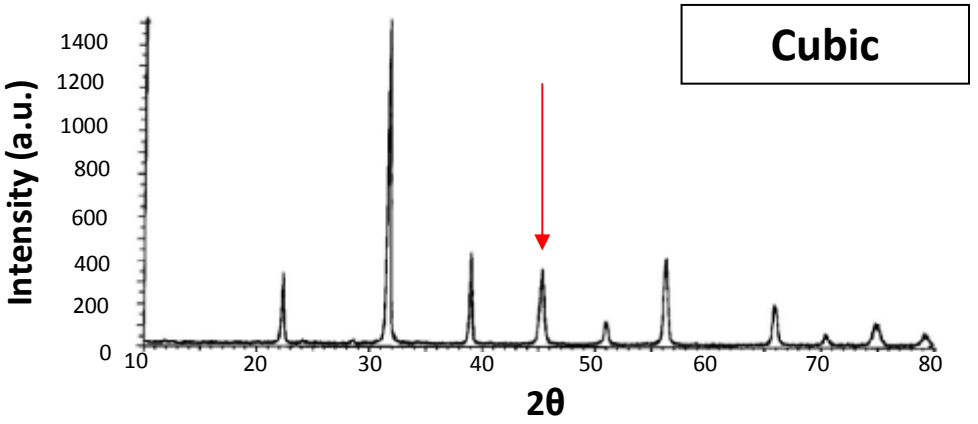


Barium Titanate Nanoparticles



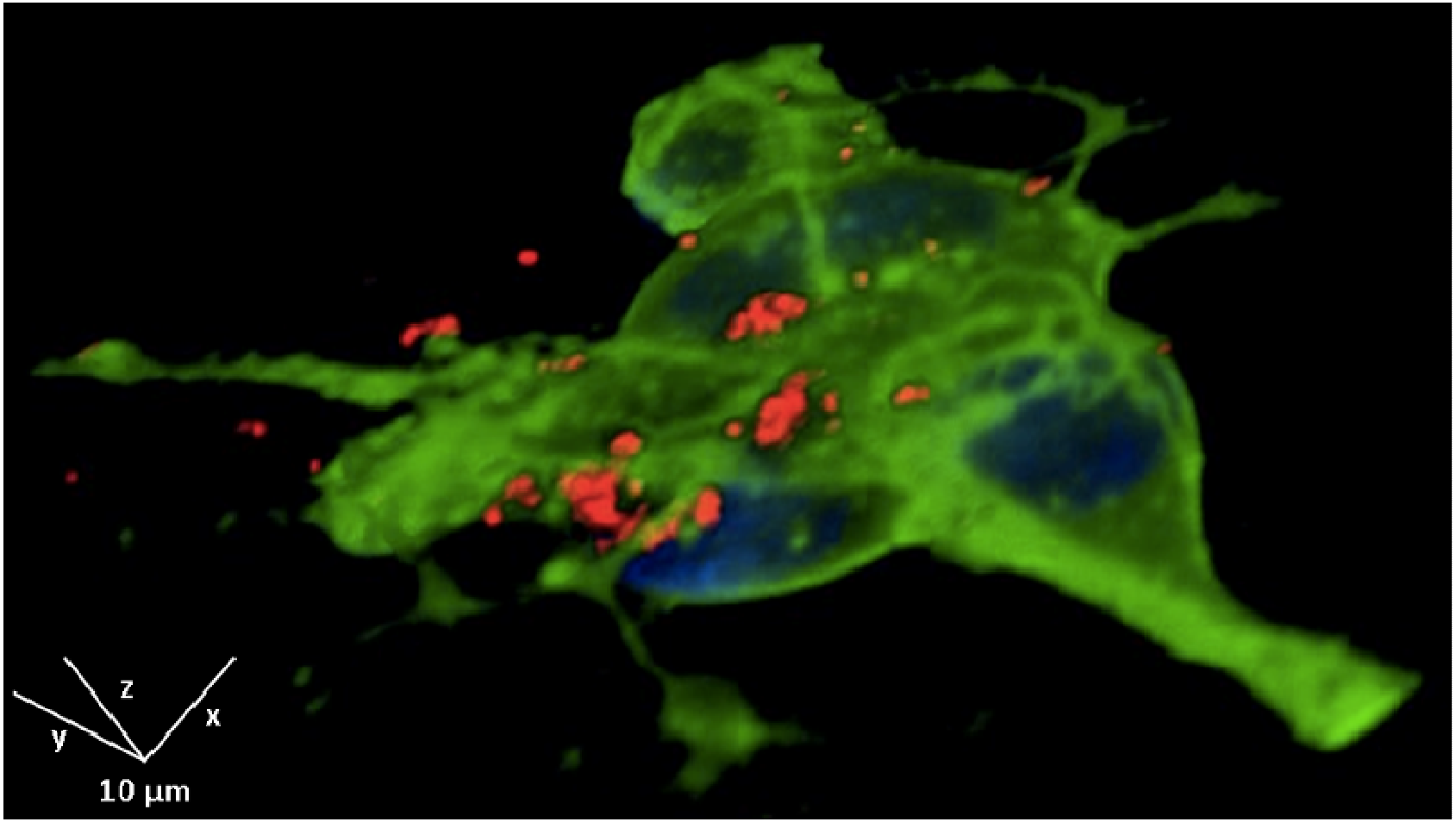




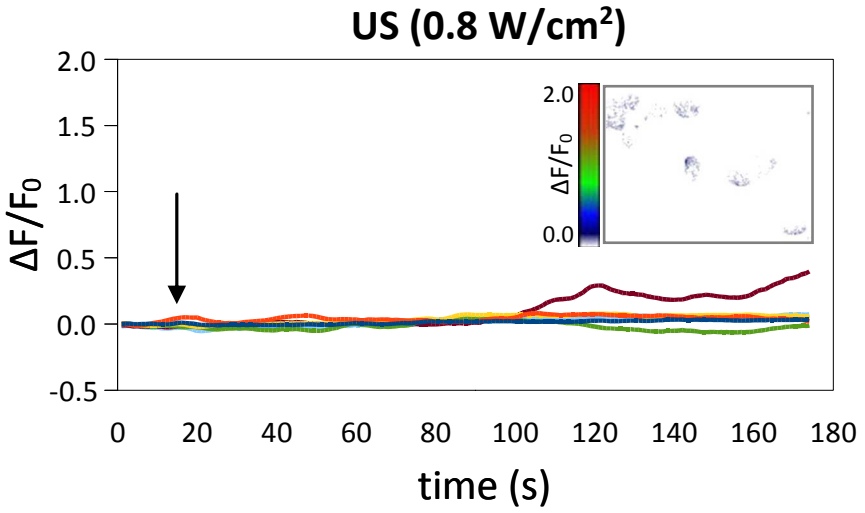


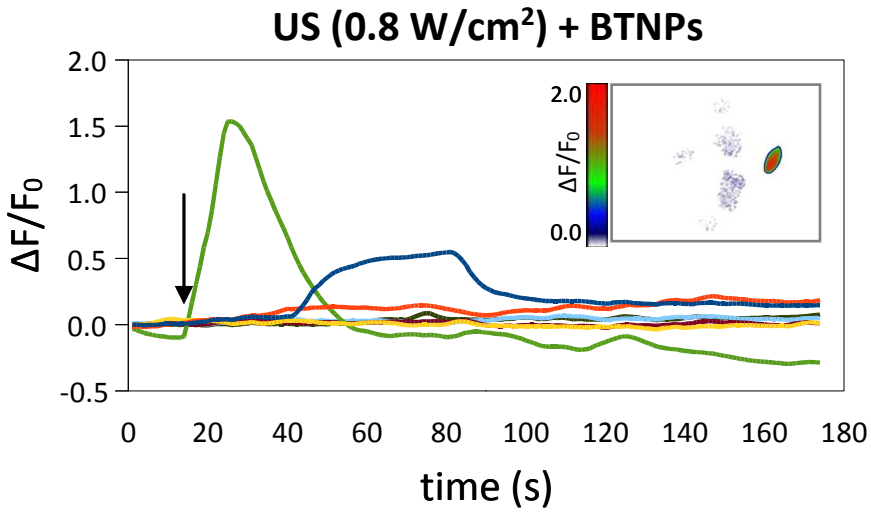
G. Ciofani, […], V. Mattoli, Effects of barium titanate nanoparticles on proliferation and differentiation of mesenchymal stem cells. ***Coll. Surf. B: Biointerfaces*** *102: 312-320 (2013)*

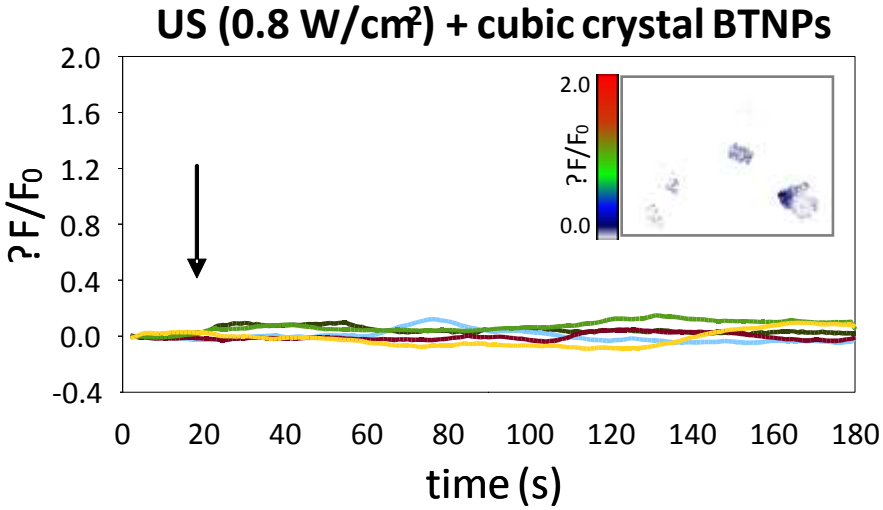
Barium Titanate Nanoparticles



BTNP-MEDIATED STIMULATION



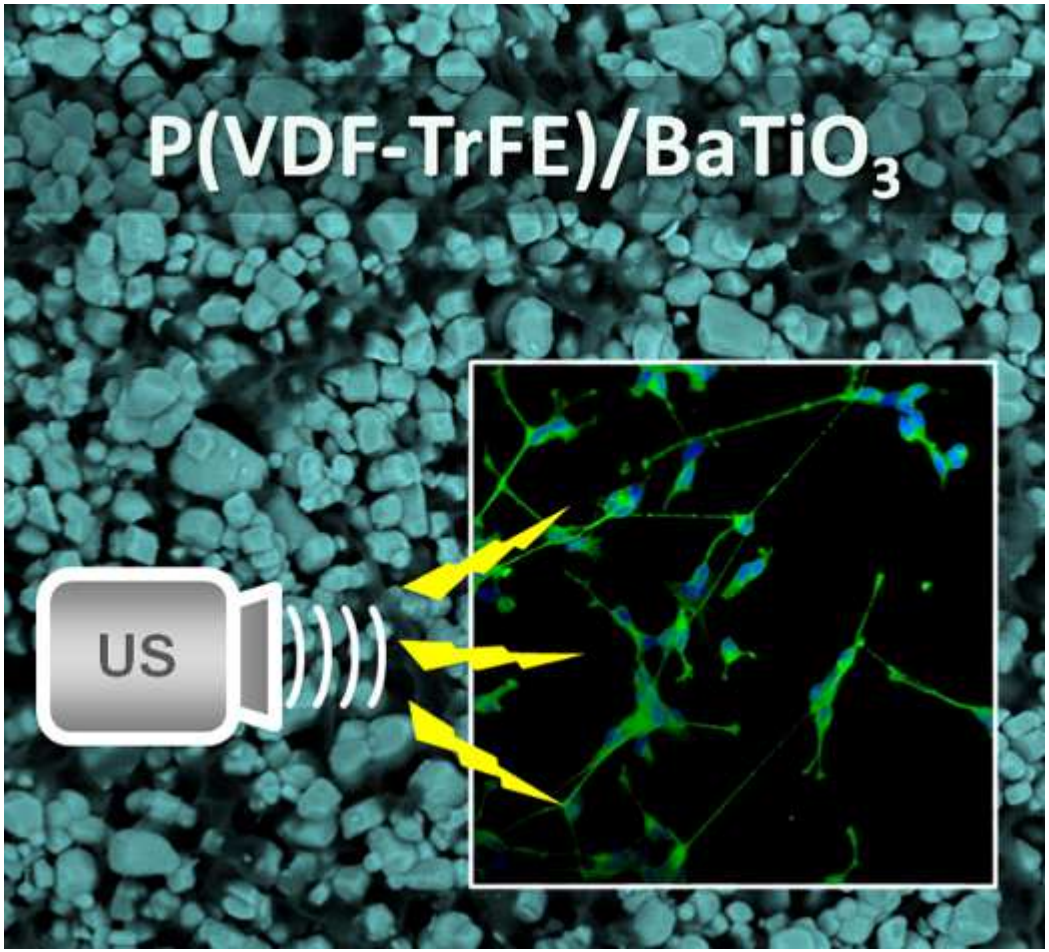




$$\varphi_R \equiv -\frac{R(se_{rr} + 2e_{r\theta})}{s\varepsilon_{rr}}\left(\frac{p_{US}}{s\gamma + 2\alpha}\right)$$

*Marino A., […], **Ciofani G**. Piezoelectric nanoparticle-assisted wireless neuronal stimulation. **ACS Nano**, 9(7): 7678-7689 (2015)*

P(VDF-TrFE)/BaTiO3 nanoparticle composite films



Genchi G.G. […], ***Ciofani G****. P(VDF-TrFE)/BaTiO3 nanoparticle composite films mediate piezoelectric stimulation and promote differentiation of SH-SY5Y neuroblastoma cells.* ***Advanced Healthcare Materials****, 10.1002/adhm.201600245*

Sample preparation and characterization: Electron Microscopy

1) Powder dissolution/dispersion in methylethylketone:

   200 mg/ml P(VDF-TrFE, 70/30)

   40% P(VDF-TrFE) and 60% BTNPs (w/w)

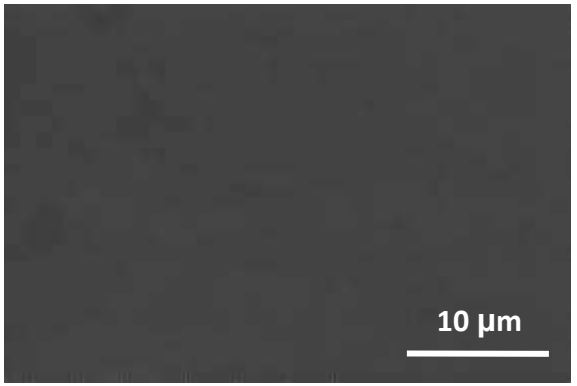
2) Sonication at 8 W for 10 min

3) Casting

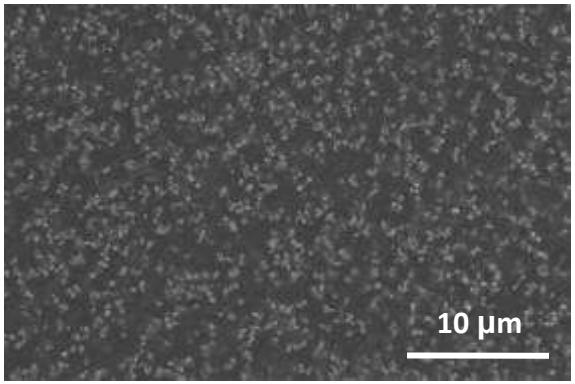
4) Annealing at 40°C

5) Under vacuum for 12 h

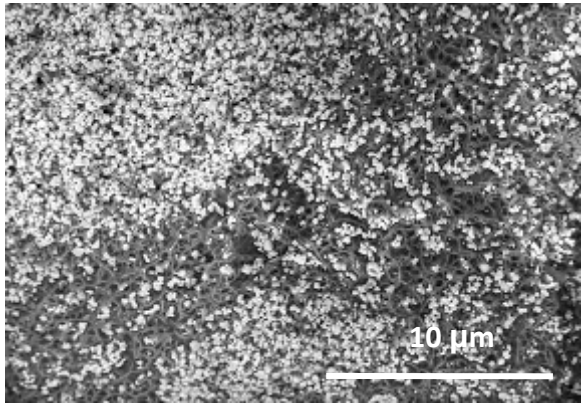
P(VDF-TrFE)



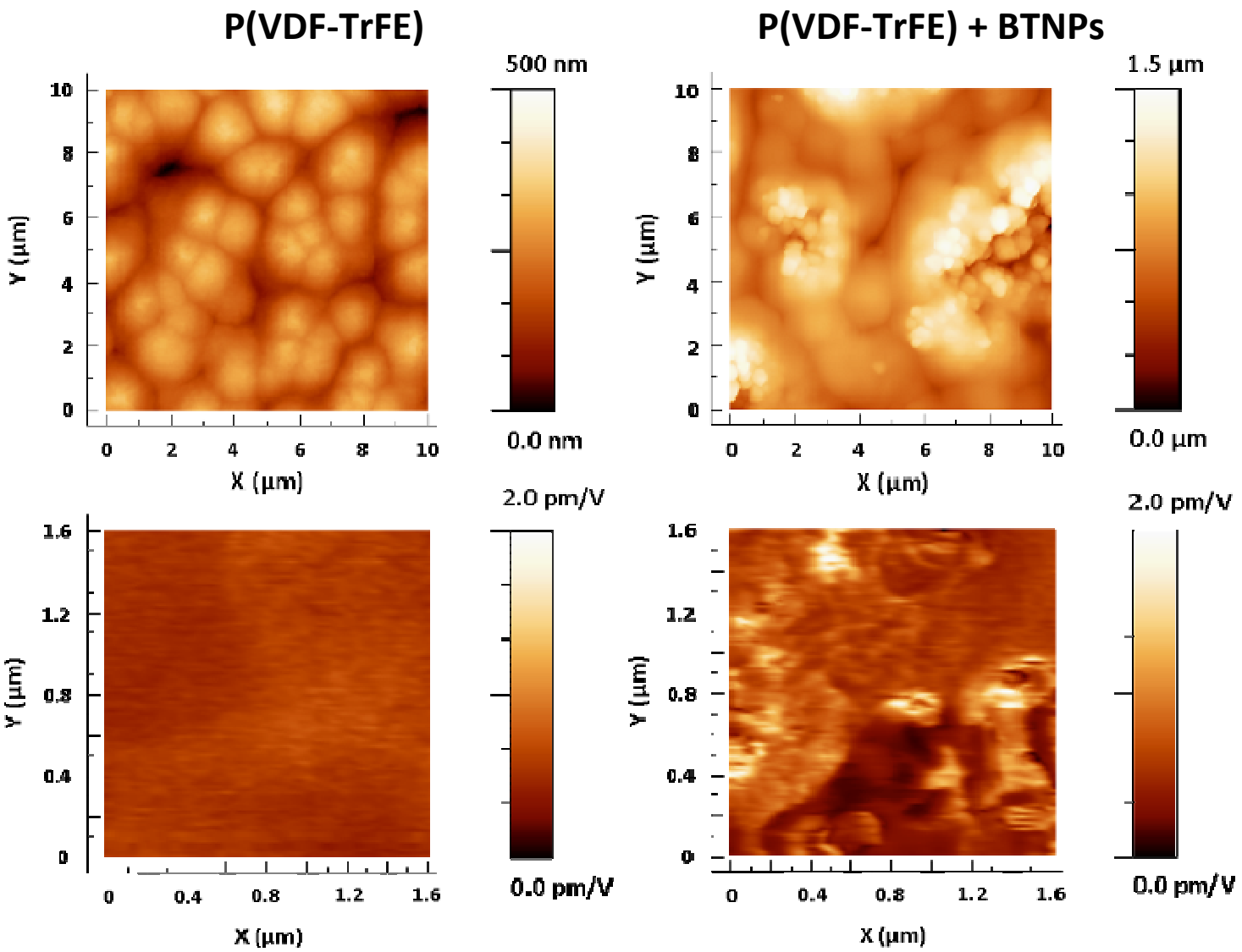
P(VDF-TrFE) + BTNPs



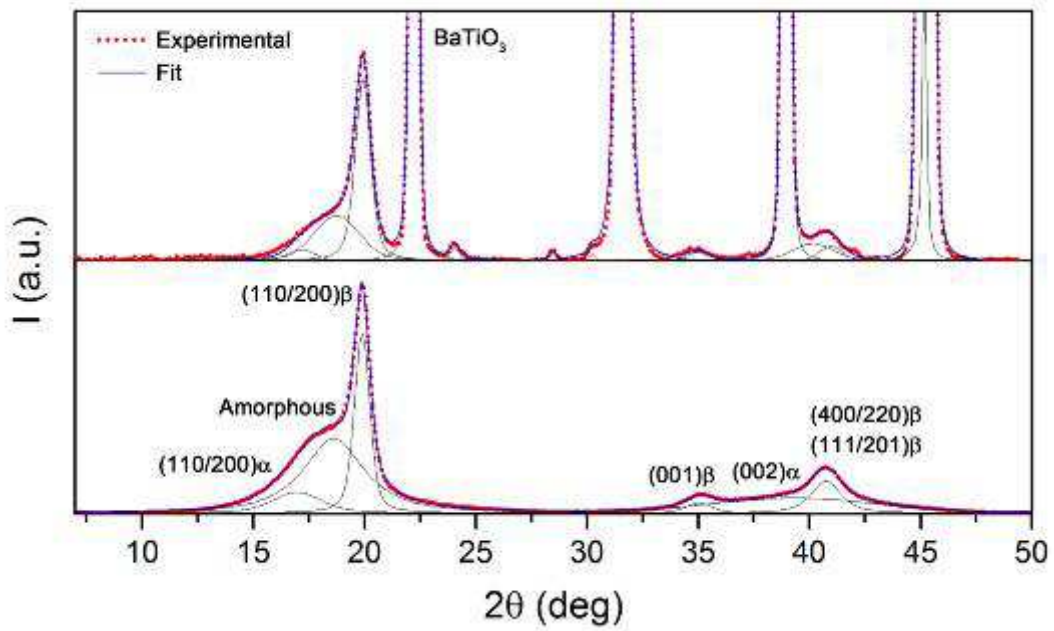
P(VDF-TrFE) + BTNPs (cryosection)



Sample preparation and characterization: AFM & PFM

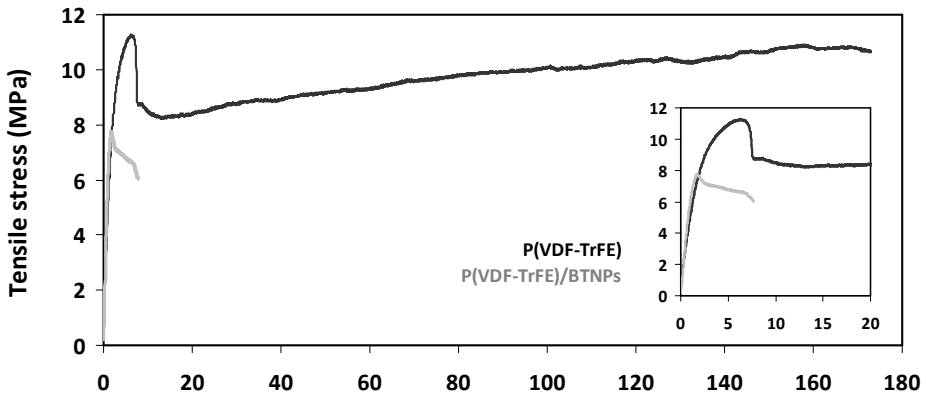


X-Ray Diffraction



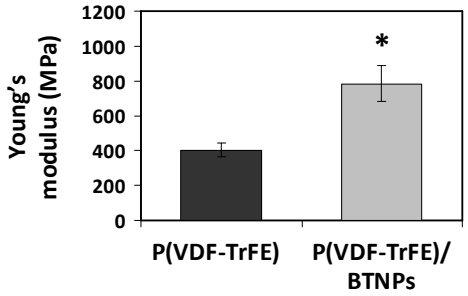
X-ray diffraction		P(VDF-TrFE)	P(VDF-TrFE) + BTNPs
Crystallinity (%)	α phase	27.1	15.8
	β phase	32.3	52.6
	total	59.4	68.4

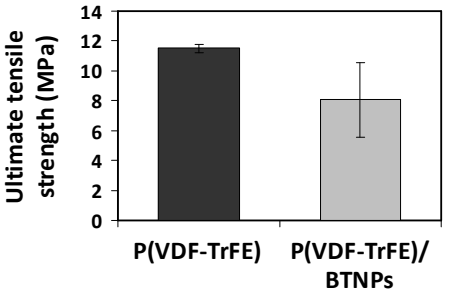
EXTENSIMETRY

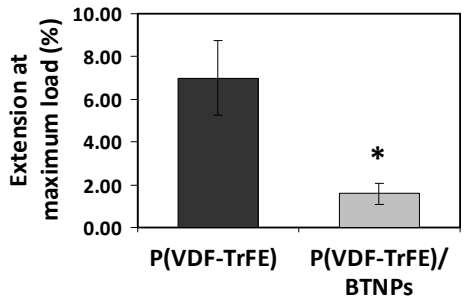


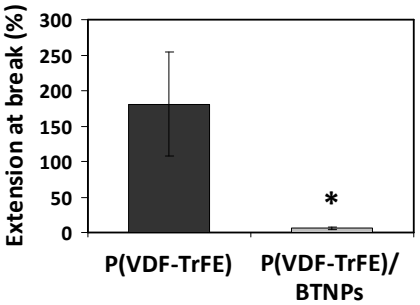
$$E_C = E_{PT}\left[1 + \frac{2V_{BT}^{\frac{2}{3}}}{\left(mV_{BT}^{\frac{1}{3}} + 1\right)/(m-1) - V_{BT}^{\frac{2}{3}}}\right]$$

Cube-within-cube model by Ogorkiewicz and Weidmann

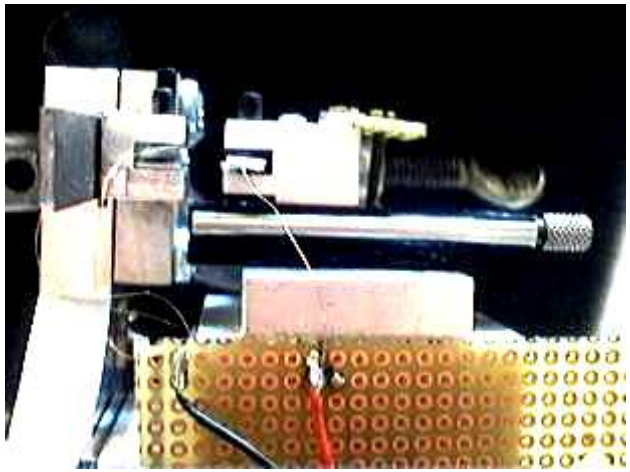








Piezoresponse characterization



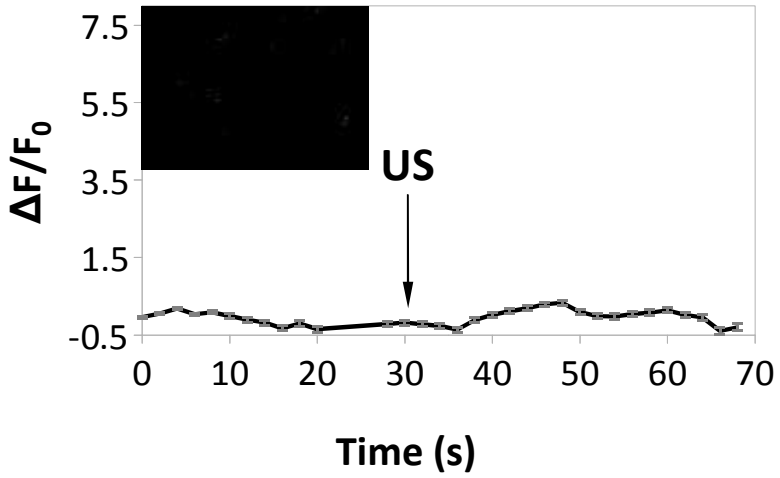
res./sample	PTFE (non piezo)	P(VDF-TrFE)	P(VDF-TrFE) + BTNPs
V_{out1} [mV_{RMS}]	4.0	6.1	15.75
Q	22.7	18.6	22.5
ε_r	2.1	12	25.7
ε_S	2.03	11.12	23.7
$d_{31,1}$ [pm/V]	1.1	11.8	53.5
$g_{31,1}$ [mV/N]	0.059	0.11	0.24

Ca^{2+} imaging

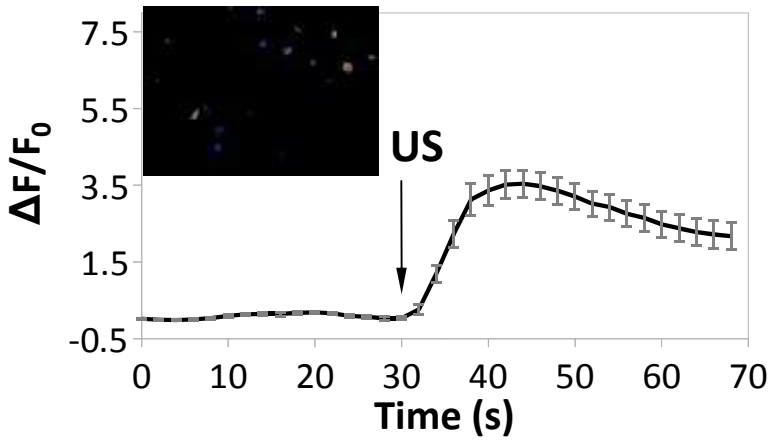
Acute ultrasound stimulation:

1 W/cm², 100 Hz Burst Rate

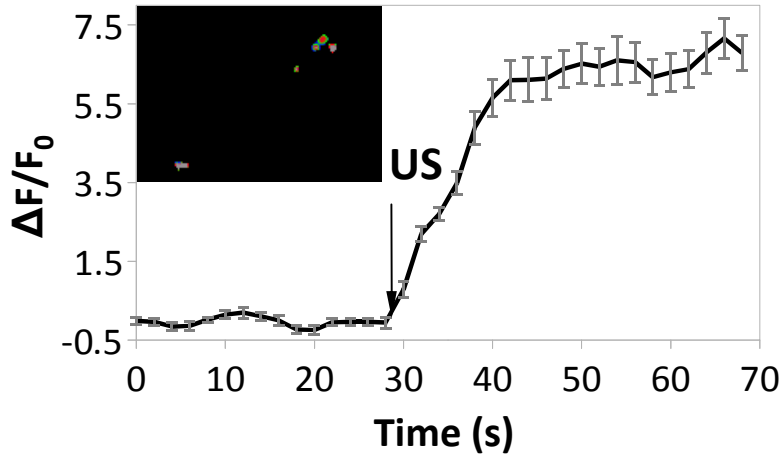
Ctrl



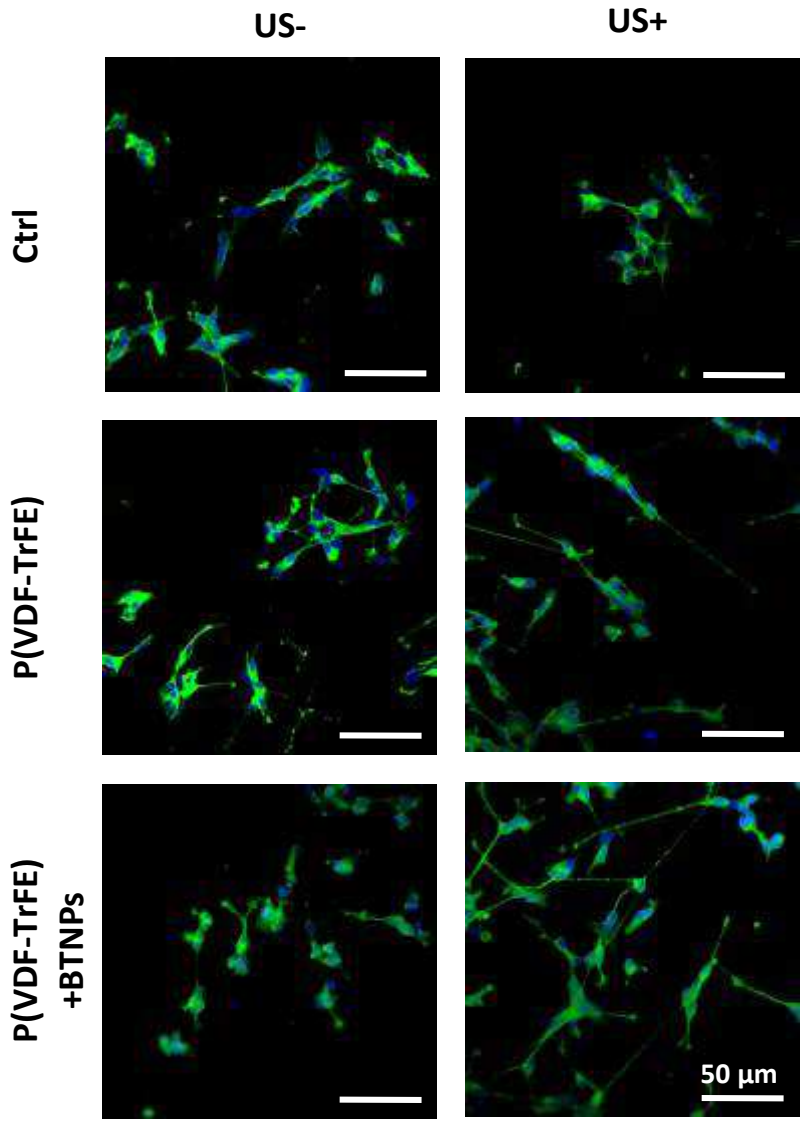
P(VDF-TrFE)



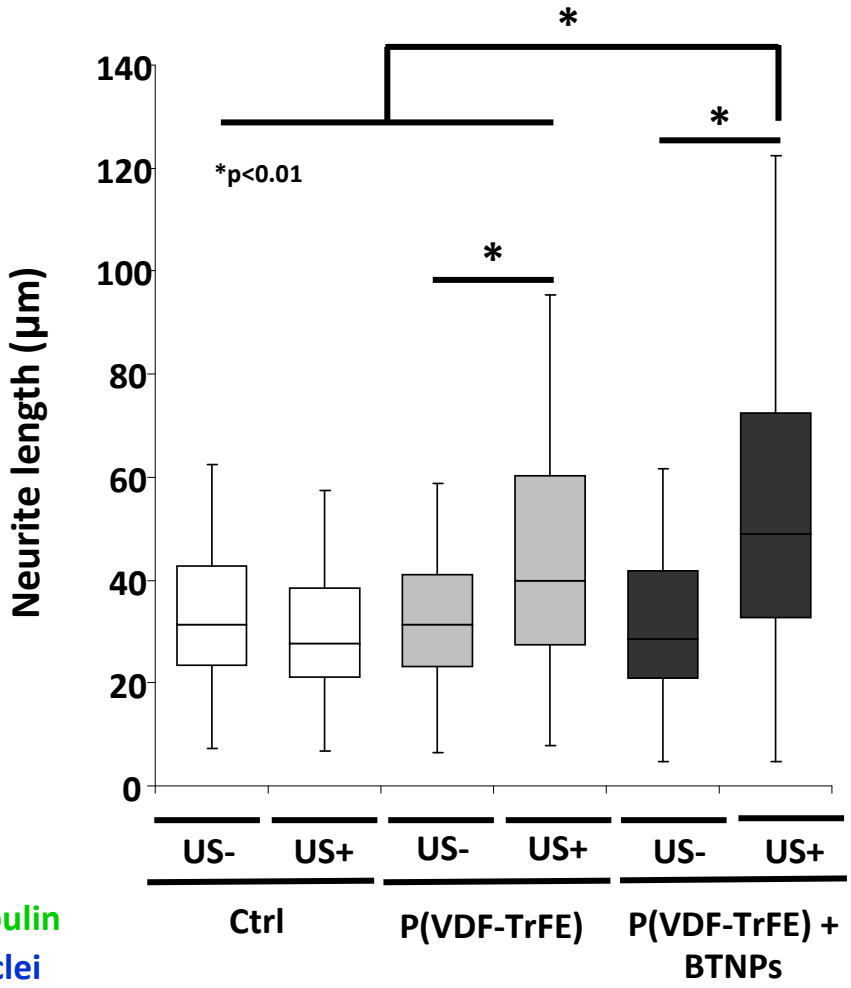
P(VDF-TrFE) + BTNPs



Neurite emission and analysis

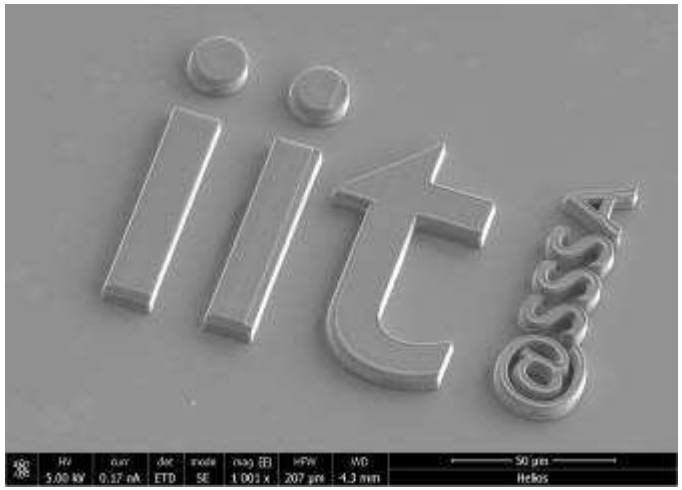


Chronic ultrasound stimulation: 1 W/cm², 100 Hz
Burst Rate, 2X/day, 6 dd

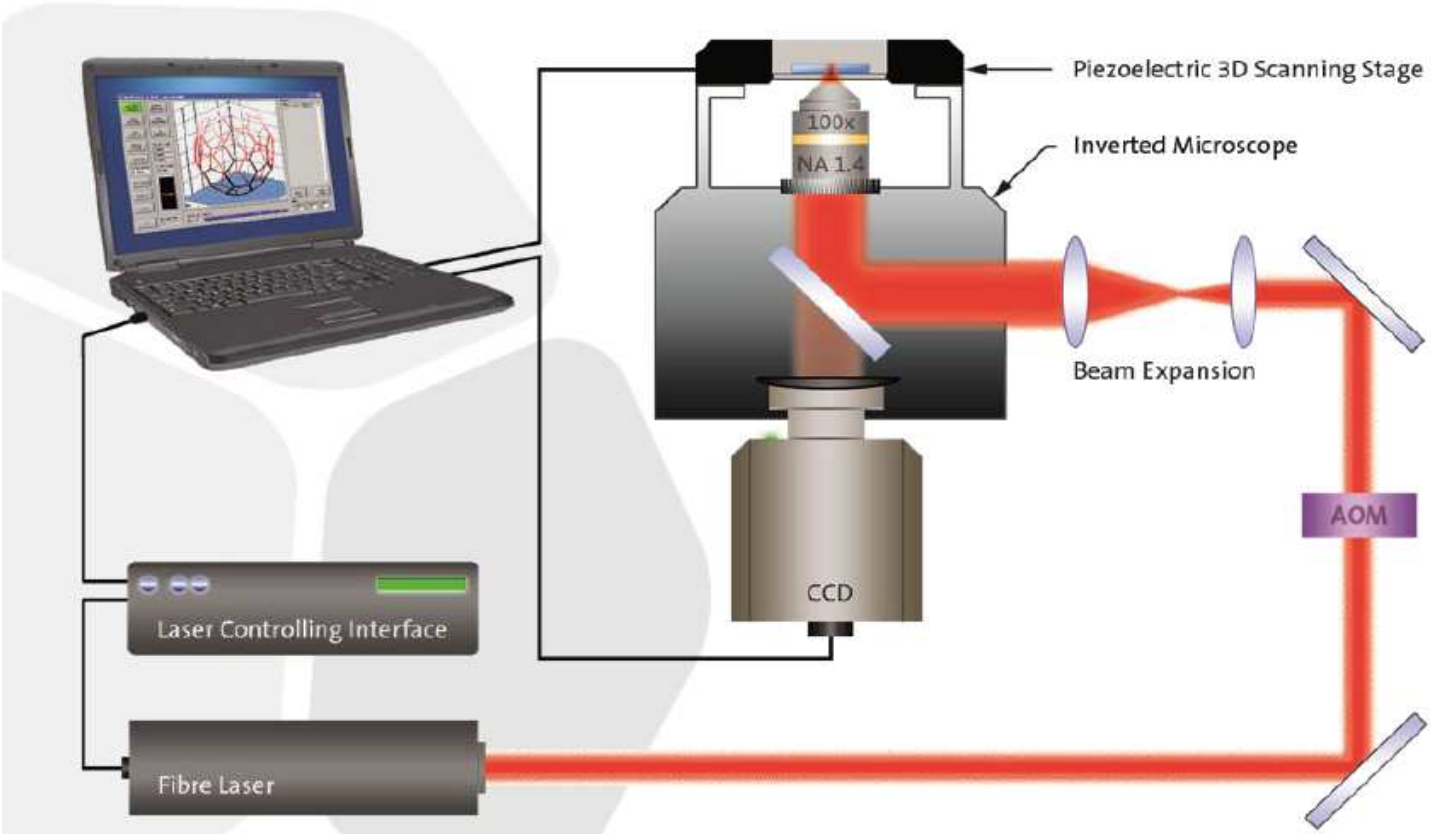


DIRECT LASER WRITING

- 3D Laser Lithography
- Resolution < 100 nm
- Two-photon polymerization (laser 780 nm, power > 60 mW)
- Dedicated resist



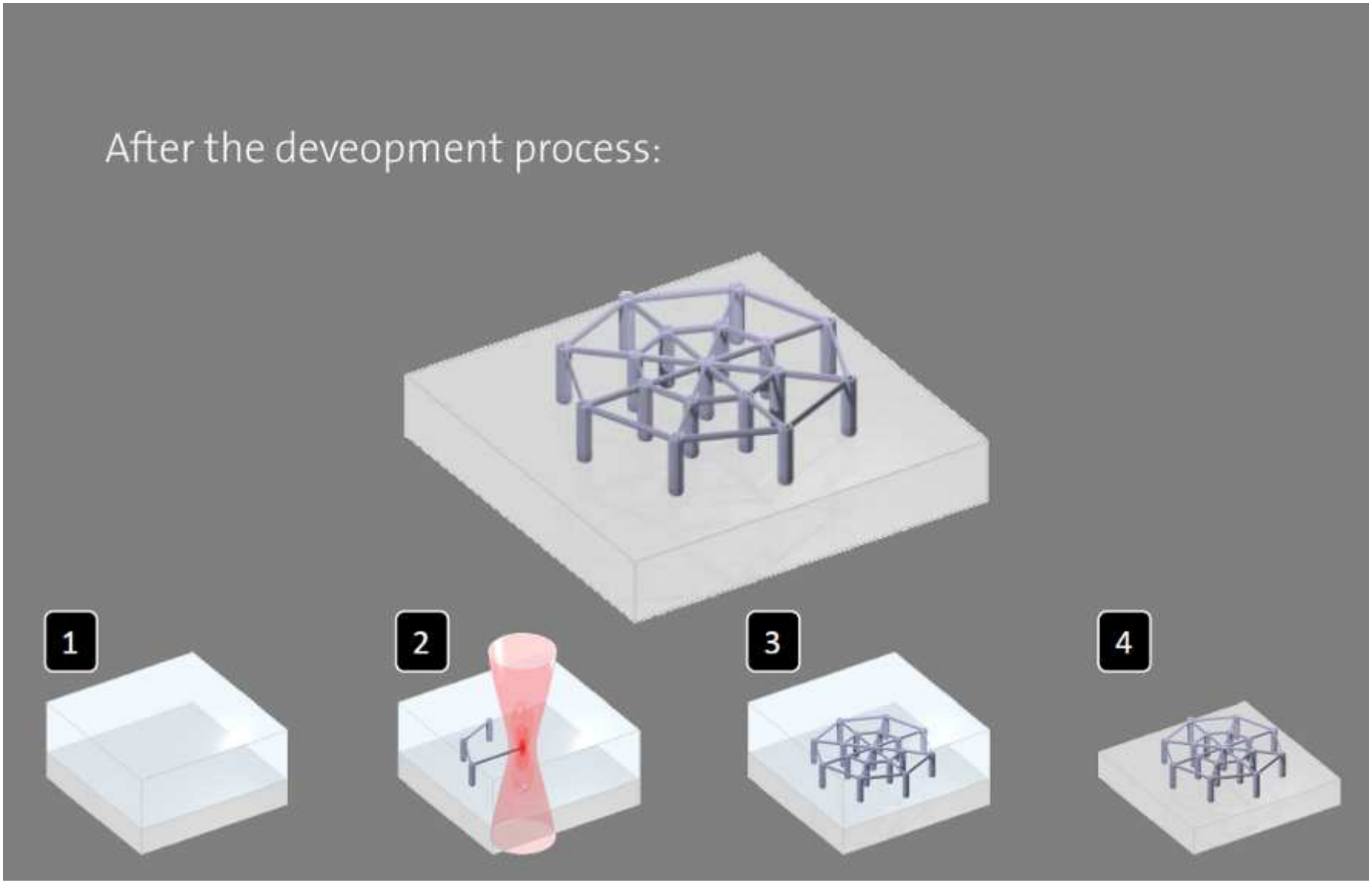
DIRECT LASER WRITING



Light source:

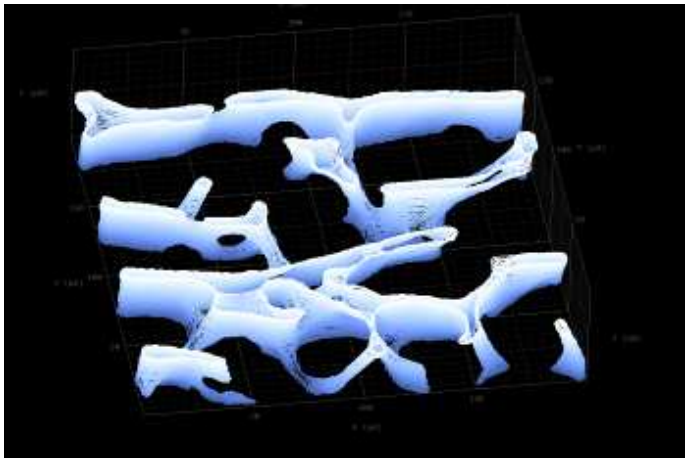
- Er-doped fiber laser @ λ = 780 nm
- Pulse duration < 150 fs / repetition rate: 100 MHz
- Power > 60 mW

DIRECT LASER WRITING: THE PROCESS

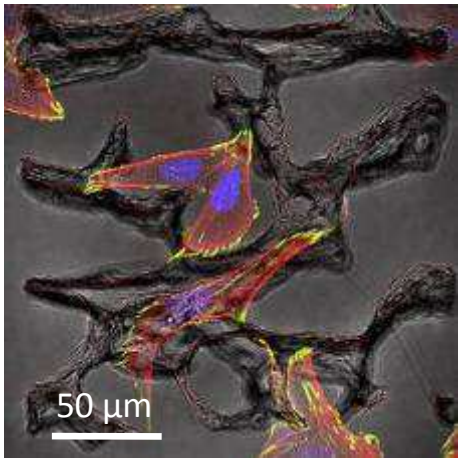


THE OSTEOPRINT

3D model of trabecular bone

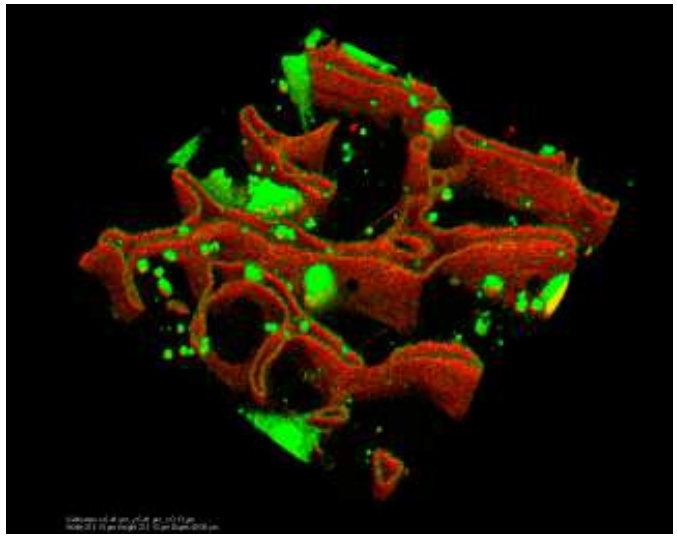


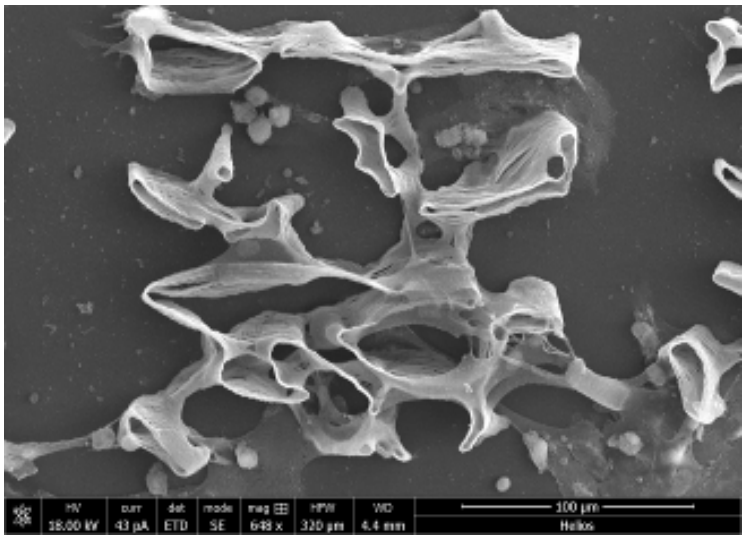
Adhesion of SaOS-2 cells



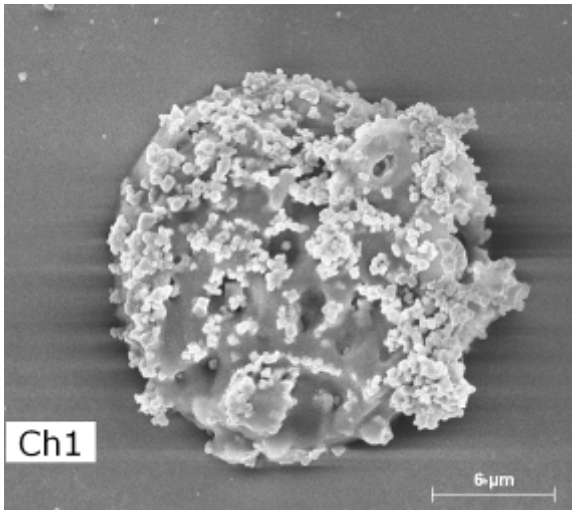
Marino A., […], Ciofani G. The Osteoprint: A two-photon polymerized 3D structure for the enhancement of bone-like cell differentiation. Acta Biomaterialia, 10(10): 4303-4313 (2014)

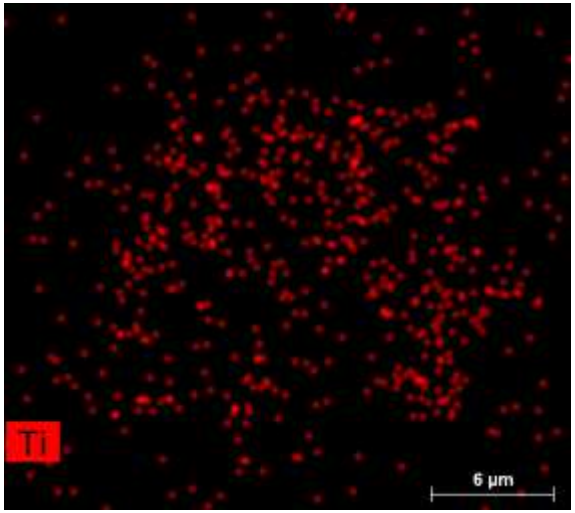
Differentiation of SaOS-2 cells (confocal & SEM)

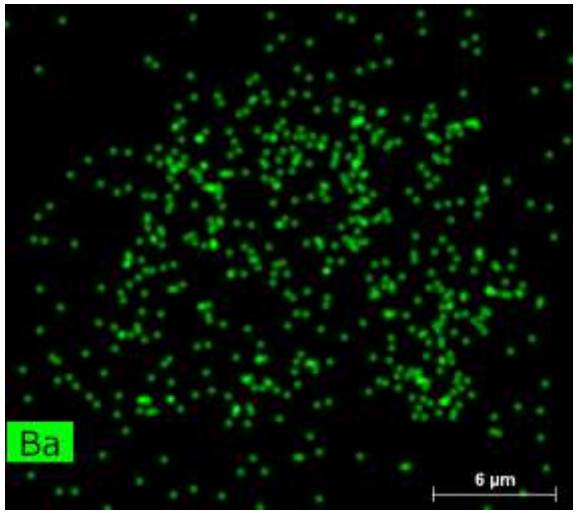


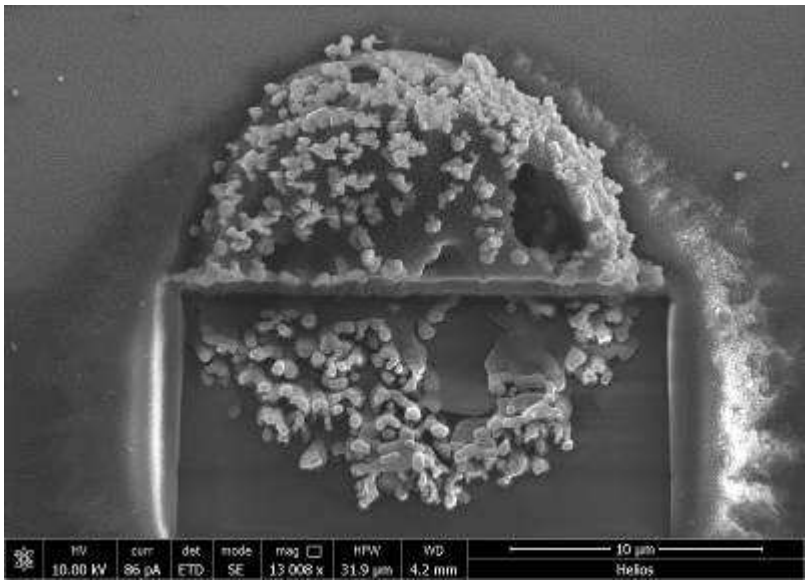


BTNP-DOPED RESIST



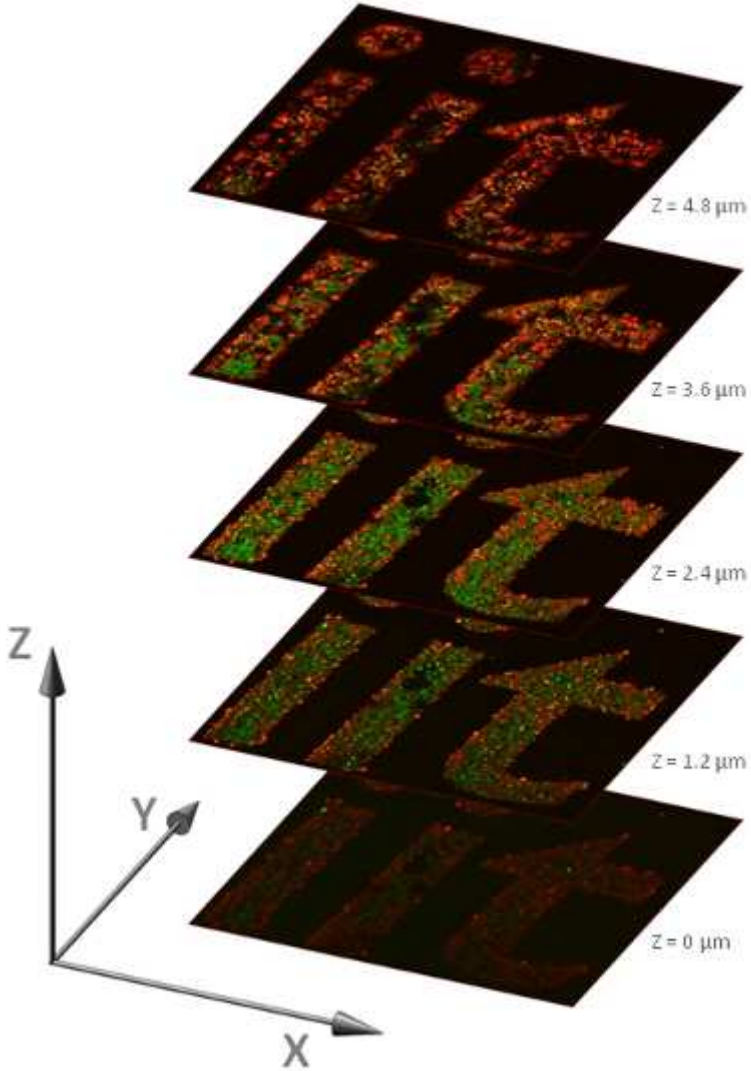


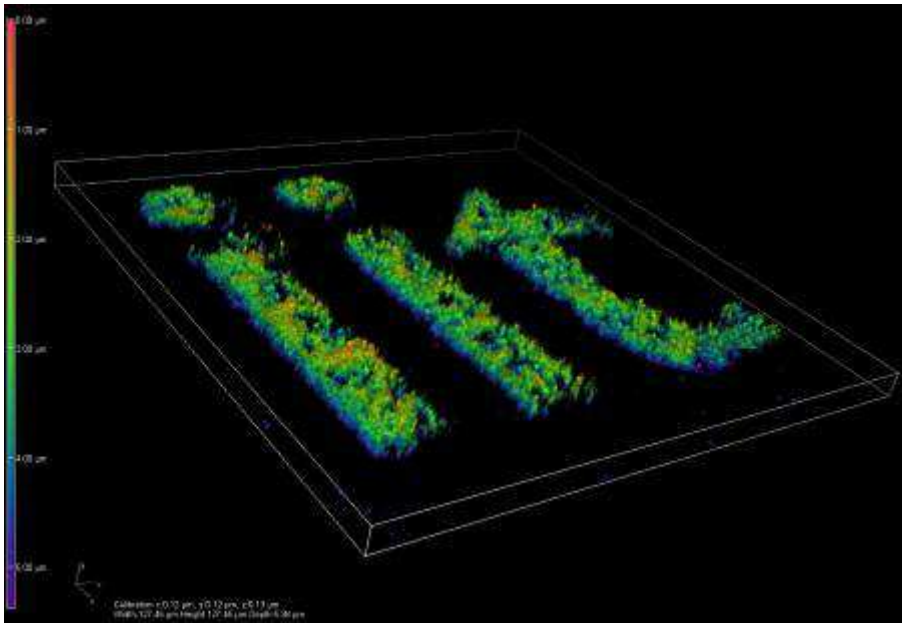




- BTNP mixed with ormocomp
- Sonication
- 2pp process
- SEM/FIB/EDX analysis: BTNP uniformely dispersed in the structures

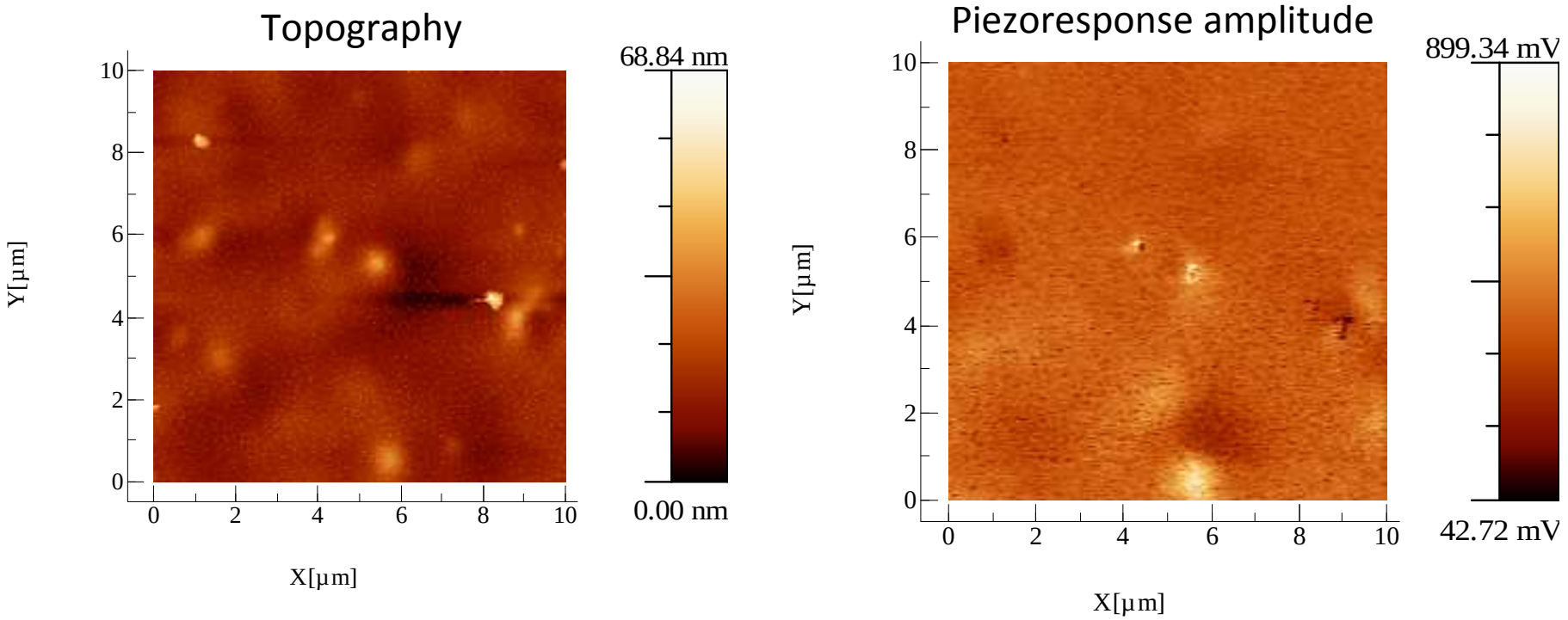
BTNP-DOPED STRUCTURES





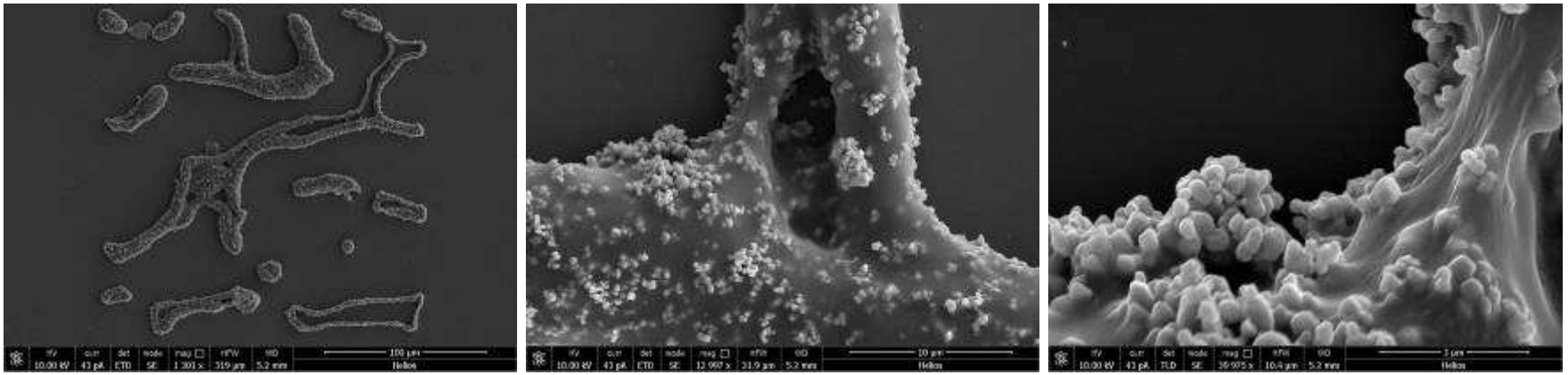
- 2pp of complex structures
- BTNP uniformely dispersed in the 3D scaffolds
- SHG signal detection

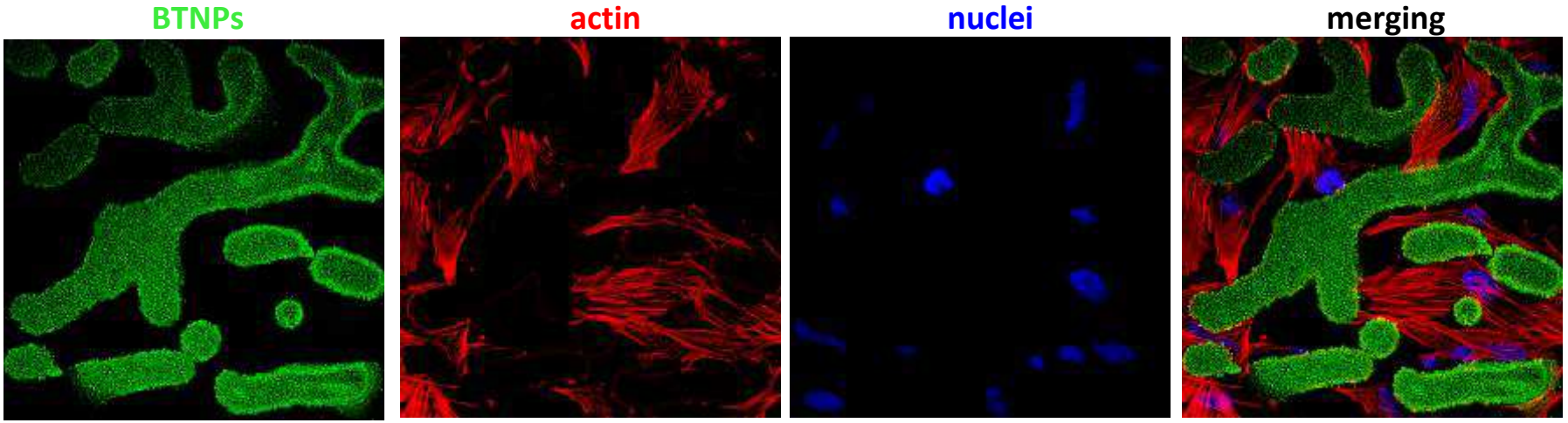
Piezoelectric characterization: AFM & PFM



$$d_{33} = 0.6\ pm/V$$

BTNP-DOPED "OSTEOPRINTS"

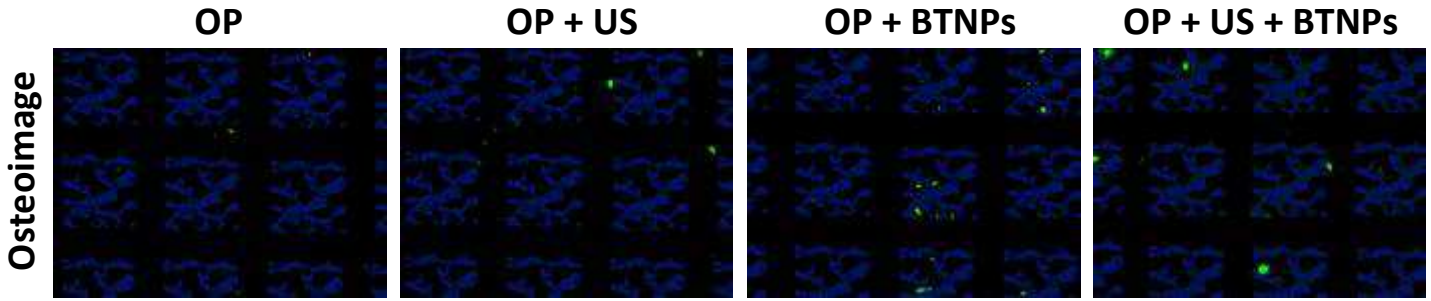


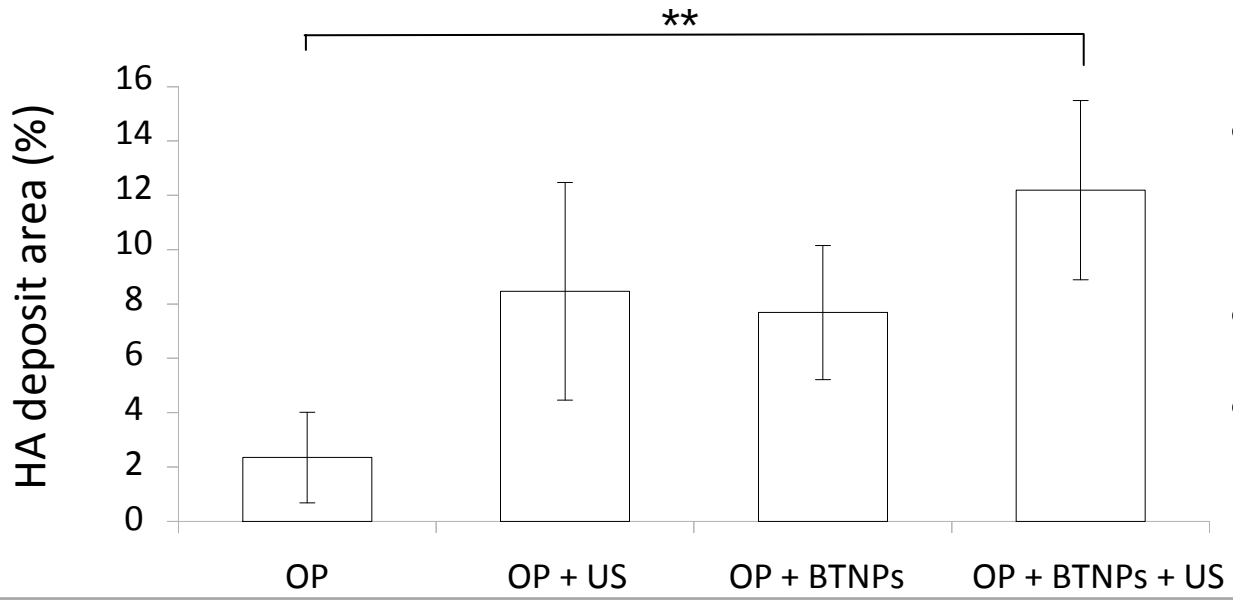


Marino A., […], Ciofani G. Two-photon lithography of 3D nanocomposite piezoelectric scaffolds for cell stimulation. ACS Applied Materials and Interfaces, 7(46): 25574-25579 (2015)

PIEZOELECTRIC STIMULATION

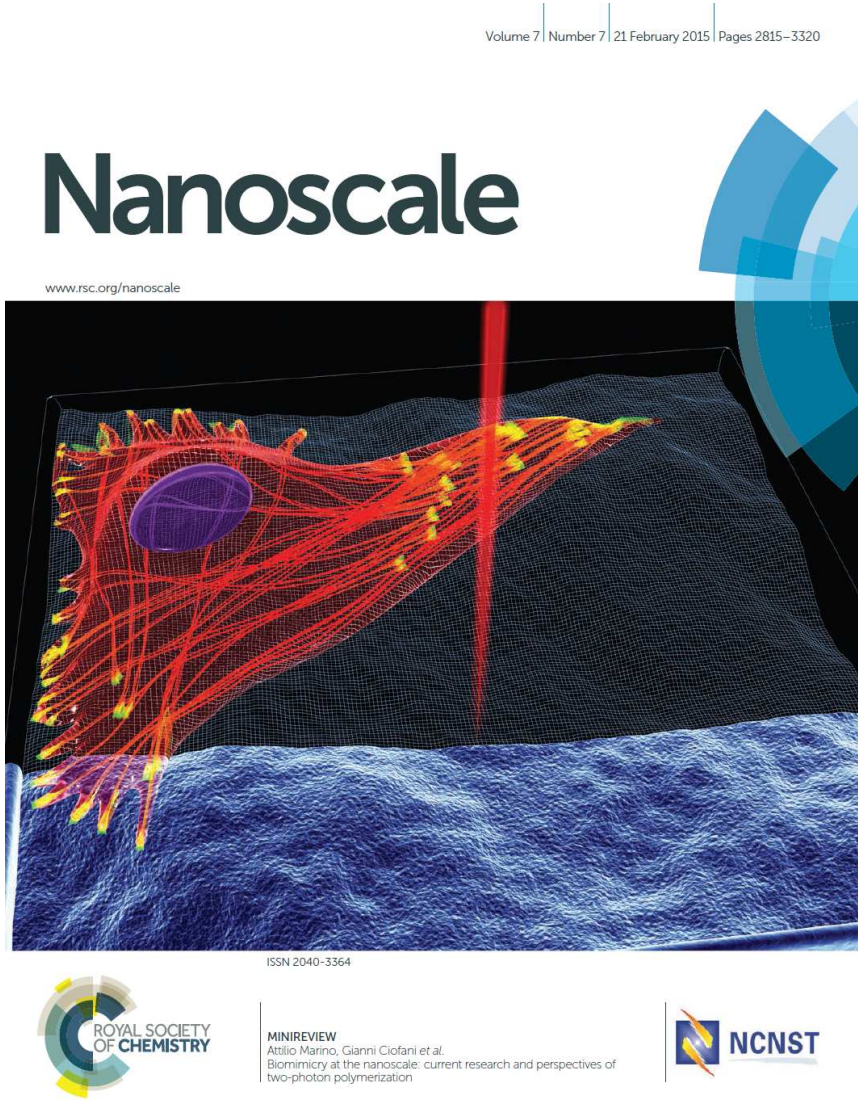
- Human Saos-2 cell testing
- Stimulation with US for 5 days (30 s, 3 times *per* day, 0.8 W/cm^2)





- Evaluation of the mineralization
- Osteoimage staining
- Quantification of HA deposits

CONCLUSIONS



- 2D/3D micro/nanofabrication
- High resolution
- Nanostructured surfaces
- Biomimetic substrates
- Tuning of physical properties

Marino A., […], Ciofani G. Biomimicry at the nanoscale: Current research and perspectives of two-photon polymerization. Nanoscale, 7(7): 2841–2850 (2015)

Thank you for your attention!