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Emerging Applications of Ferroelectric Nanoparticles in Materials Technologies, Biology and Medicine

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1. Introduction

Consider an insulating system with non-zero spontaneous polarization P_s (dielectric dipole moment per unit volume). If an applied external electric field E that is greater than the so-called coercive field E_c can reverse P_s then our system is a ferroelectric system. Ferroelectricity has a long and exciting history described in [1,2]. In the beginning of its historical development (the Rochelle salt period) ferroelectricity was considered an academic curiosity with no practical applications. There was little theoretical interest due to the quality of the ferroelectric materials (very fragile and water-soluble) existing at that time. The discovery of ferroelectricity in robust ceramic materials (barium titanate) during World War II launched a new era of rapid progress in the field. The structural simplicity of barium titanate stimulated numerous theoretical works, while its physical properties were utilized in many devices. Since that time, ferroelectric response has been found in a wide range of materials, including inorganic, organic, and biological species. According to [3] there are 72 families of ferroelectrics presented in Landolt–Börnstein-Vol.III/36 (LB III/36). Forty-nine of these families are inorganic crystals (19 families of oxides + 30 families of crystals other than oxides), and 23 families are organic crystals, liquid crystals, and polymers.

The enormously broad range of materials exhibiting ferroelectricity and the variety of their physical properties result in numerous applications of bulk ferroelectrics [4]. Table 1 shows the connections between different physical effects exhibited by bulk ferroelectrics and their applications.

Recent advances in nanotechnologies, especially in nanoinstrumentation (for example, scanning probe microscopy [5]) and materials nanofabrication [6], allowed the direct probing of ferroelectricity at the nanoscale. The new and unexplored world of nanoscale ferroelectrics (nanoparticles of different shapes and sizes, nanofilms, nanopatterned structures, etc.) raised fundamental questions and stimulated very active research in both academic and industrial sectors [7]. As a result, a new era of nanoscale ferroelectrics was launched. Novel effects, associated with reduced dimensions and found in nanoscaleferroelectrics, highlighted exciting possibilities for new applications reviewed recently in [8]. Almost all of the attention for the mentioned review [8] was devoted to the *thin film* nanoscale device structures (which can be easily integrated with a Si chip) with focus on ultrafast switching, electrocaloric coolers for computers, phase-array radar, three-dimensional trenched capacitors for dynamic random access memories, room temperature magnetic field detectors, and miniature X-ray and neutron sources. So far, we have not found a coherent review summarizing the actual and possible applications of ferroelectric *nanoparticles*. Our book chapter is an attempt to describe and analyze the state of the field of applications of ferroelectric nanoparticles with focus on materials technologies, medicine, and biology.

Physical effect/property	Applications
Ferroelectric hysteresis	Nonvolatile computer information storage
High relative permittivities (several thousands)	Capacitors
Direct piezoelectric effect	Sensors (microphones, accelerometers, hydrophones, etc.)
Converse piezoelectric effect	Actuators, ultrasonic generators, resonators, filters
Pyroelectric effect	Uncooled infra-red detectors
Electro-optic effects	Laser Q-switches, optical shutters and integrated optical (photonic) devices
Nonlinear optical effects	Laser frequency doubling, optical mixing, including four-wave mixing and holographic information storage
Coupling between stress and birefringence	Radar signal processing
Positive temperature coefficient of resistance (PTCR)	Electric-motor overload-protection devices and self-stabilizing ceramic heating elements

Table 1. Applications of bulk ferroelectrics

2. Methods of ferroelectric nanoparticles production: Nano-powders and nano-colloids

The existing methods that produce ferroelectric nanoparticles are numerous and can be classified as physical, chemical, and biological (Fig. 1). The primary goal of each method is to control size, shape, morphology, and crystallinity of nanoparticles to produce a desirable effect. This task represents a real challenge, and, as a result, there are no well-defined boundaries between physical, chemical, or biological methods. Moreover, in many cases, a combination of at least two methods (for example, physical and chemical methods, i.e. a physical-chemical approach) is required in order to fabricate good quality particles (small sizes, narrow size distribution, ferroelectric phase).
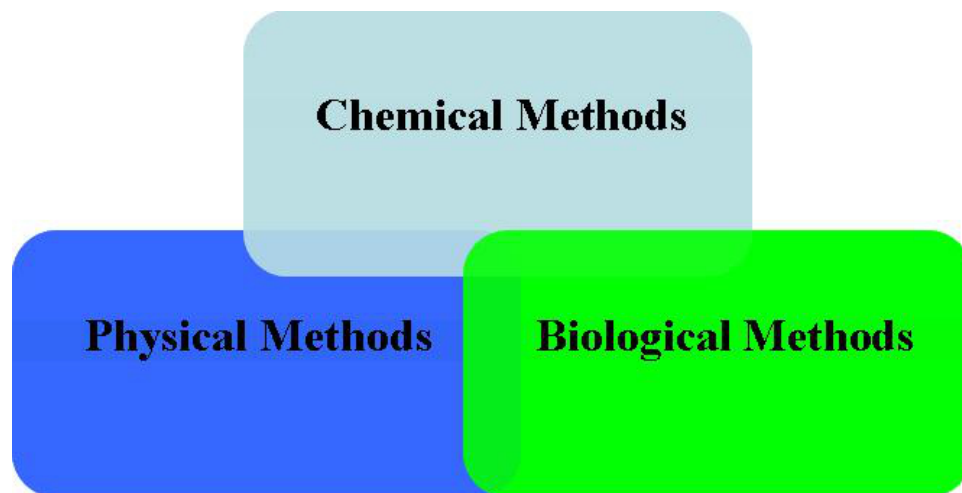
Chemical Methods

Physical Methods

Biological Methods

Figure 1. Methods used to fabricate ferroelectric nanoparticles

2.1. Chemical methods

The most widely used chemical methods for the synthesis of ferroelectric nanoparticles are: 1) solid-state reaction; 2) sol-gel technique; 3) solvothermal method; 4) hydrothermal method; and 5) molten salt method.

Table 2 shows selected examples of these methods applied to synthesis of ferroelectric nanoparticles of $BaTiO_3$. As can be seen from Table 2, the ultra-fine ferroelectric nanoparticles (<10 nm) in almost all cases except [16] are synthesized in a cubic phase which is not ferroelectric. The tetragonal phase (with ferroelectric response) is possible for relatively large particles (~50-70 nm). This fact can be critical for certain types of applications, and will be discussed later.

Shape of nanoparticles; Ref.	Synthesis method; Raw materials	Relevant parameters (size, morphology, crystallinity, spontaneous polarization etc.); Measurement and characterization methods	Possible applications & comments
Nanotubes; [10]	Wet chemical route at low temperature (50°C); H_2TiO_3 nanotubes; ethanol/water mixture with 25% ethanol by volume; $Ba(OH)_2 \cdot 8H_2O$	Uniform $BaTiO_3$ nanotubes, a *cubic phase*, average diameter = 10 nm and wall thickness = 3 nm at room temperature; Powder X-ray diffraction (XRD), field-emission scanning electron microscopy (FE-SEM), transmission electron microscopy (TEM), Raman spectroscopy, and X-ray photoelectron spectroscopy	Promising microwave-absorbing materials
Nanocrystals; [11]	Sol-gel technique; Barium titanium ethyl hexano-isopropoxide, $BaTi(O_2CC_7H_{15})$ $(OCH(CH_3)_2)_5$; a mixture of diphenyl ether, $(C_5H_5)_2O$; stabilizing agent oleic acid, $CH_3(CH_2)_7CHdCH(CH_2)_7$-$CO_2H$, at 140 °C, under argon or nitrogen	Monodisperse nanoparticles with diameters ranging from 6 to 12 nm, *cubic phase;* XRD,TEM	Multilayer ceramic capacitors
Dense polycrystalline aggregates (~80 nm) of nanocrystals (~30 nm); [12]	Solid-state reaction as a function of temperature (400–8000C), time (1–24 hr); Nanocrystalline TiO_2, ultrafine $BaCO_3$ and submicrometer $BaCO_3$ were intensively mixed in an aqueous suspension for 24 hr using polyethylene jars and zirconia media. The polymer (ammonium polyacrylate) was required for the formation of a monolayer on the particle surface	Nanoparticle size is 70 nm. Specific surface area up to ~15m²/g, *tetragonal phase;* TG and DTA analysis, XRD, SEM	Multilayer ceramic capacitors
Polyhedral with hexagonal outline in shape; [13]	Molten salt method; Hydroxide octahydrate $(Ba(OH)_2 \cdot 8H_2O)$, titanium dioxide (TiO_2), and the eutectic salts (NaCl–KCl), 600-900 °C	50 nm, *cubic phase;* XRD, Fourier transform infrared spectrometry, UV–Vis diffuse reflectance spectra, and field emission SEM	Nanoparticles are well dispersed

Shape of nanoparticles; Ref.	Synthesis method; Raw materials	Relevant parameters (size, morphology, crystallinity, spontaneous polarization etc.); Measurement and characterization methods	Possible applications & comments
Single crystalline nanoparticles; [14]	Solvothermal method; $Ba(CH_3COO)_2$ and $Ti(OC_4H_9)_4$; the autoclave was maintained at 200 °C for 12 hr	5-20 nm, *cubic phase*; XRD, TEM, SAED, FTIR	Dense bulk nanocomposites
Nanoparticles; [15]	Hydrothermal method; $(Ba,Sr)(OiPr)_2$, $Ti(OiPr)$, EtOH, 330–400 °C, 16-30 MPa	15-50 nm, *cubic or tetragonal phase*; XRD, TEM	Dense bulk nanocomposites
Nanopowders; [9]	Combined wet-chemical and rapid calcination process; $BaCO_3$–TiO_2 precursors	125 nm, *tetragonal phase*, remnant polarization $P_r = 1.64$ $\mu C/cm^2$, the coercive field, $E_c = 4.91$ kV/cm; (cigar-like loop);surface area 7.96 m^2/g XRD, TEM, TGA, SMPS, SAED,dielectric spectroscopy	Multilayer ceramic capacitor
Nanocrystals; [16]	One-step solvothermal route; Tetra-n-butyl titanate, Barium hydroxide octahydrate, solvent (Diethylene glycol), surfactant (Polyvinyl Pyrrolidone)	5 nm, *tetragonal phase*; XRD, TEM, HRTEM, Raman spectroscopy	Multilayer ceramic capacitor

Table 2. Chemical methods

2.2. Physical methods

Dry and wet mechanical grindings are methods of choice for inexpensive nanoparticle preparation. For technological applications, wet grinding is preferable because it allows more options to control the size of the nanoparticles. During the last few years, substantial progress was made in the field of ferroelectric nanoparticle preparation by means of wet mechanical grinding [17]. Generally, three components are needed: raw material to grind (micron-sized powders of $BaTiO_3$); surfactant (which covers the particle surface and prevents their aggregation and overheating during grinding; oleic acid is a good choice for $BaTiO_3$); and fluid carrier (both raw material and surfactant are mixed with fluid carrier; heptane is widely used to grind $BaTiO_3$). An extensive list of references, as well as recent achievements in the field, are discussed in the review [18]. Table 3 shows how particle sizes depend upon grinding time [19].

As is seen from Table 3, wet mechanical grinding can produce 9 nm nanoparticles, and such small particles are still in ferroelectric phase. It is important to remember that $BaTiO_3$ nanoparticles of the same sizes synthesized by the majority of chemical methods are not ferro-

electric – the method used to fabricate nanoparticles really does matter. The ability to produce ferroelectric nanoparticles of very small sizes is a defining characteristic of this physical method (see [18] for more references).

Grinding time, hrs	3	7	10	16	20	24
Average particle diameter, nm	26	14.9	11.6	9.5	9.2	9

Table 3. BaTiO$_3$ particle sizes as a function of grinding time (liquid carrier – heptane; two-station PM200 planetary ball mill from Retsch)

The net dipole moment of ferroelectric nanoparticles allows them to be harvested by using an inhomogeneous electric field. The harvesting concept proposed in [20] is based on the fact that dipoles experience a translational force only when exposed to a field gradient. For a given linear field gradient and assuming a single ferroelectric domain, the net translational force on a dipole scales proportionally with the particle size. The Brownian motion effects also become progressively more pronounced at smaller particle sizes and so the required field strength for successful separation scales nonlinearly as the particle size is reduced.

Both gas-phase and liquid-phase harvesting methods were proposed and tested successfully, and single ferroelectric monodomain nanoparticles as small as 9 nm from mechanically ground nanoparticles were selectively harvested [20]. In contrast to many reports on the lack of ferroelectricity for nanoparticles below 10 nm (see Table 2), the harvested nanoparticles do maintain ferroelectricity. The ferroelectric response of such tiny nanoparticles was attributed to the existence of an induced surface strain as a result of the grinding process [20]. The lack of a mechanically induced strain in similarly sized but chemically produced nanoparticles accounts for the absence of ferroelectricity in these materials. The concept of stress-induced ferroelectricity was verified in further experiments, which are reviewed in [18]. It was found [21] that the spontaneous polarization of the nanoparticles is four to five times larger than the spontaneous polarization of the bulk raw materials. To obtain this result the following two conditions must be satisfied: (1) a nonpolar solvent for the nanoparticle suspension and (2) nonaggregated nanoparticles. Under these conditions, for 9 nm nanoparticles, the values of 100–120 μC/cm^2 and 8.9 10^{-23}C cm have been measured for the spontaneous polarization and dipole moment, respectively. The aggregation of ferroelectric nanoparticles masks the ferroelectric response due to the partial compensation of the dipole moments of the individual particles. Finally, we can conclude that recent advances in the production of uniform, monodomain, highly ferroelectric nanoparticles indicate that this field has reached its maturity. The particles can now be reliably prepared to certain specifications and characteristics [18].

2.3. Physical-chemical methods

In order to prepare ferroelectric nanoparticles with controllable sizes and shapes a combination of chemical methods with external physical factors (for example, a chemical reaction in the presence of electromagnetic fields or mechanical milling) is needed. Table 4 shows several examples of these physical-chemical methods for the case of BaTiO$_3$.

As can be seen from Table 4, chemical reactions under the presence of an external driver (microwave, ultrasonic, milling, heat, pressure) are able to produce very fine particles (~5-10 nm) with tetragonal structures.

Shape of nanoparticles; Ref.	Synthesis method; Raw materials	Relevant parameters (size, morphology, crystallinity, spontaneous polarization etc.); Measurement and characterization methods	Possible applications & comments
Truncated nanocubes; [22]	Microwave (2.45 GHz, output power ~ 800W) hydrothermal; High-purity reagents barium nitrate (Sigma Aldrich, purity ≥99.99%), titanium isoproxide (Sigma Aldrich, purity ≥97%), nitric acid (ACS reagent 70%), ammonium hydroxide (Sigma Aldrich), and glycine (Sigma-Aldrich, purity ≥99%)	Cross section 70 ± 9 nm in [100] projection; *tetragonal structure*; remnant polarization is 15.5 $\mu C/cm^2$; saturation polarization is 19.3 $\mu C/cm^2$; XRD, high resolution TEM, impedance spectroscopy	Charge storage devices
Nearly spherical nanoparticles; [23]	Sol–gel-hydrothermal method under an oxygen (partial pressure is ~60 bar); $TiCl_4$; HCl; $BaCl_2 \cdot 2H_2O$; deionized water, stirring and N_2 bubbling, NaOH	Sizes range from 50 to 75nm; transition of $BaTiO_3$ from *cubic* to a *pseudotetragonal phase* with the increase ofthe reaction temperature from 80 to 220 °C; remnant polarization $P_r = 2.2$ C/cm^2; the coercive field, $E_c = 3.2$ kV/cm (cigar-like loop); XRD, TEM, Raman and dielectric spectroscopy; energy-dispersive X-ray spectroscopy; AFM	Oxygen atmosphere decreases sizes of the nanoparticles (for example , at 200 °C sizes decrease from 72.54 nm to 49.54 nm)
Nanocrystals; [24, 25]	Direct synthesis from solution (DSS) – mechanochemical synthesis; Anhydrous $Ba(OH)_2$ and tetrabutyl titanate [$Ti (OC_4H_9)_4$] Mechanical milling at the rate of 200 rpm, room temperature	7 nm, *tetragonal structure*; XRD, TEM, Raman spectroscopy	Chemical reaction during milling
Large aggregates of 5–10 nm small nanocrystals; [26]	Sonochemical synthesis; $BaCl_2$; $TiCl_4$; NaOH	100 nm aggregates, *cubic phase*; XRD, TEM, DLS, SAED	Multilayer ceramic capacitors

Shape of nanoparticles; Ref.	Synthesis method; Raw materials	Relevant parameters (size, morphology, crystallinity, spontaneous polarization etc.); Measurement and characterization methods	Possible applications & comments
Single nanocrystals; [27]	RF-Plasma chemical vapor deposition (CVD); iso-propoxide (Ti(OiPr)$_4$, bis-dipivaloylmethanate (Ba(DPM)$_2$	12.2-15.4 nm; XRD, TEM, SAED, EDX	Multilayer ceramic capacitors
Nanofibers; [28, 29, 30]	Electrospinning, sol-gel; barium acetate, PVP, titanium isopropoxide, ethanol, acetic acid	80-190 nm in diameter, 0.1 mm in length; XRD, TEM, SAED	Piezo, microwave material, sensors, capacitors
Nanopowders; [31]	Flame spray pyrolysis; barium carbonate and titanium tetra-*iso*-propoxide, citric acid	70 nm, *tetragonal structure*; XRD, TEM, SEM	Multilayer ceramic capacitors

Table 4. Physical-chemical methods

Another interesting subject is the possible application of ceramic nanofibers produced by the method of electrospinning. These possible applications include: nanofiber-based supports for catalysts, nanofiber-based photocatalysts, nanofiber-based membrane for filtration, nanofiber-based sensors, nanofiber-based photoelectrodes for photovoltaic cells, nanofiber-based electrodes for lithium batteries, nanofiber-based electrode-supports for fuel cells, and materials for implants [28, 29, 30].

2.4. Biological methods

The proper combination of chemical and physical methods (Table 4) allows the production of very small ferroelectric nanoparticles (5-10 nm). However, toxic chemicals and/or high temperatures/pressures are needed in most cases. These requirements substantially limit the possible biomedical applications of ferroelectric nanoparticles. Biological methods were proposed as eco-friendly "green" alternatives to existing chemical and physical methods. The biosynthesis of different types of nanoparticles was reviewed recently in a few papers [32, 33, 34, 35], but biological methods that produce specifically ferroelectric nanomaterials are not very numerous. For example, the first review [32] lists nearly a hundred variations for the synthesis of nanoparticles by microorganisms, and only a few of them produce ferroelectric nanoparticles. The biological methods applied to synthesize the nanoparticles of the most widely known ferroelectric BaTiO$_3$ are summarized in Table 5 (papers published before 2008 were discussed in [36]). The references listed in this table show that most of the biological methods mentioned employ some chemical or physical steps as well.

Shape of nanoparticles; Ref.	Synthesis method; Raw materials	Relevant parameters (size, morphology, crystallinity, spontaneous polarization etc.); Measurement and characterization methods	Comments
Aggregates (~500 nm) of nanocrystals (~ 50 nm); [37]	The peptides BT1 and BT2 induce the room-temperature *precipitation* of $BaTiO_3$; Aqueous precursor solution composed of barium acetate ($Ba(OOCCH_3)_2$) potassium bis(oxalato) oxotitanate(IV) ($K_2[TiO(C_2O_4)_2]2H_2O$); pH 6.8	50-100 nm; *tetragonal phase* remnant polarization $P_r \sim$ 2-3 C/cm^2; the coercive field, E_c = 5-6 kV/cm (cigar-like loop); SEM, TEM, SAED and XRD analysis, dielectric measurements	Rapid room-temperature synthesis of ferroelectric (tetragonal) $BaTiO_3$ within 2 hr
Quasi-spherical nanoparticles; [38]	*Lactobacillus* - assisted biosynthesis; $BaCO_3$ and TiO_2 solid state synthesis $BaTiO_3$; Slush of micron-sized $BaTiO_3$ particles+ Lactic acid Bacillus spore tablets	20-80 nm, *single-phase tetragonal structure*; XRD, TEM	Extracellular synthesis
Spherical nanoparticles; [39]	*(Fusarium oxysporum)* fungus-assisted biosynthesis of $BaTiO_3$ nanoparticles; $(CH_3COO)_2Ba$ and K_2TiF_6 + fungal micelles of *Fusarium oxysporum*	4-5 nm, *tetragonal structure*; XRD, DCS, TEM, SAED, XPS, SPM	Extracellular synthesis
Spherical nanoparticles; [40]	Peptide nanorings used as templates; $BaTi(O_2CC_7-H_{15})[OCH(CH_3)_2]_5$	6-12 nm, *tetragonal structure*; AFM, TEM, XRD, EFM, Raman	4 days
Spherical nanoparticles; [41]	*(Saccharomyces cerevisiae)* baker's yeast-assisted biosynthesis of $BaTiO_3$ nanoparticles; $BaCO_3$ and TiO_2 solid state synthesis $BaTiO_3$, Slurry of large $BaTiO_3$ + yeast culture	8-21 nm, *single-phase hexagonal structure*; XRD, TEM	Extracellular synthesis
Spherical nanoparticles; [42]	Kinetically controlled vapor diffusion Single source, bimetallic alkoxide with the vapor diffusion of a hydrolytic catalyst (H_2O)	6-8 nm, *cubic phase*; XRD, TEM	~250 g.

Table 5. Biological methods

One can note from Table 5 that these biological methods can be roughly grouped into two categories: the synthesis of ferroelectric nanoparticles using a number of seed chemicals and some type of biological or bio-inspired system, and the creation of nanoparticles using large particles of ready ferroelectric material and some type of biological system. Most of the methods that are currently available fall into the first category; the methods in the second category have appeared only very recently.

The earliest discoveries of nanoparticle synthesis by microorganisms (fungus, *Lactobacillus* and yeast) involve metal, alloy, and metal oxide nanoparticles. With a lag of one to two years, this research was followed by attempts at ferroelectric nanoparticle synthesis by the same living systems [32]. Fungus (*Fusarium oxysporum*, commonly found in soil) has been shown to synthesize extracellularly ferroelectric nanoparticles of barium titanate (4-5 nm of average size) [39, 43] at room temperature, producing small ferroelectric nanoparticles on a scale that has been previously inaccessible. This method falls into the first category, since fungus produces barium titanate from more than one seed chemical. *Lactobacillus* (bacteria commonly used to curdle milk and produce buttermilk) has been shown to synthesize ferroelectric nanoparticles (with sizes ranging from 20 to 80 nm) from the slush of large barium titanate particles [38]. Baker's yeast (*Saccharomyces cerevisiae*) has also been attempted as a biosynthesis agent; the barium titanate nanoparticles received were on average ~10nm [41]. Both the yeast- and lactobacillus-mediated production of barium titanate nanoparticles fall into the second category: they start with large particles of ready barium titanate in water and produce small (under 100 nm) nanoparticles extracellularly.

Peptide nanorings provide another interesting biomimetic route to the template-mediated synthesis of $BaTiO_3$ and $SrTiO_3$ nanoparticles [40]. Developed in 2006, it was the very first method of obtaining ferroelectric barium titanate nanoparticles at room temperature (many previous room-temperature methods had trouble growing barium titanate not in the cubic phase).

In this category of biological methods, one has to mention bioinspired methods of dispersing nanoparticles and producing stable colloids. Take for examplethe production of stable nanoparticle suspensions using microbial-derived surfactants [44] where usual garden variety surfactants are replaced with bio-derived materials that are significantly smaller in size and that help prevent aggregation of multiple nanoparticles during sol-gel synthesis. This process relies on some physical/chemical steps, just like the majority of other biological methods of ferroelectric nanoparticle production that have been developed to date.

These bio-inspired methods show great promise because they produce relatively small ferroelectric nanoparticles at room (or low) temperature compared to conventional physical and chemical methods, many of which require lengthy processes, use of high temperatures, harsh chemicals, etc.

3. Applications of ferroelectric nanoparticles in materials technologies

3.1. Multilayered capacitors and nanocomposites

As was previously mentioned in the introduction, the era of applied ferroelectricity was launched after the first reliable ferroelectric material – ceramic $BaTiO_3$ – was discovered [1]. The very high dielectric constants (~1000) of bulk ferroelectric materials were applied in the manufacturing of discrete and multilayered ceramic capacitors. Advances in the production of ferroelectric nanoparticles broadened this application to a large extent. Currently, nanosized $BaTiO_3$ powders are successfully used for manufacturing miniaturized and highly volume-efficient multilayer ceramic capacitors (MLCCs, for more details see review [45]).

Typical MLCCs utilize pellets of nanopowders sintered at high temperatures, producing structures with high rigidity that can impose certain limitations. Nanocomposites made of flexible polymers and ferroelectric nanoparticles overcome the restrictions caused by rigidity of sintered structures. Polymeric materials doped with ferroelectric nanoparticles are of considerable interest as a solution for processable high permittivity materials for various electronic applications: volume efficient multilayer capacitors, high-energy-density capacitors, embedded capacitors, and gate insulators in organic field effect transistors [46].

Both components (polymer and ferroelectric nanoparticle) of such nanocomposites are essential. The polymeric material brings flexibility and the ability to cover a large surface area, while nanoparticles share high values of dielectric permittivity with the matrix-enhancing effective dielectric permittivity of the composite. It's not easy to achieve homogeneous dispersion of ferroelectric nanoparticles in a polymeric matrix because of the high surface energy of nanoparticles, which usually leads to aggregation and phase separation, resulting in poor processability of the films and a high defect density. In order to make high-quality nanocomposites (good solution processability, low leakage current, high permittivity, and high dielectric strength), surface modification of nanoparticles is needed. The surface modification of nanoparticles decreases attractive forces between them, thus preventing aggregation. In addition, the proper design of a surface agent can increase interactions between the nanoparticles and the polymeric matrix. As a result, a quite homogeneous distribution of the nanoparticles in the polymeric matrix can be achieved. However, there are several obstacles that prevent nanocomposites "polymer/ferroelectric nanoparticle" from mass commercialization. The most common are poor temperature stability of dielectric constants and large dielectric losses. The proper design of both the nanoparticles (material size, shape, surface modification) and the polymer matrix can overcome these problems. For example, Table 6 shows short descriptions of the relatively successful (in terms of material performance) nanocomposites "polymer/$BaTiO_3$". All of them are optically transparent, have high dielectric permittivity (25-30), and moderate losses (loss tangent is in the range 0.01-0.05 for different materials).

Composition (polymer/ nanoparticle)	Particle surface functionalization	Dielectric permitti-vity of nanocom-posite	Particle size &breakdown electric field	Ref.
Barium titanate / poly(vinylidene fluoride-co-hexafluoro propylene), volume concentration < 80%	Phosphonic acid surface-modified $BaTiO_3$ nanoparticles	35	30-50 nm >164 V/µm	[46]
Barium titanate/polyimide ($BaTiO_3$/PI); volume concentration < 40%	Core-shell structure; polyamic acid (PAA) was used to cover particle	20	70-100 nm 67 MV/m	[47]
Poly(vinylidene fluoride)/ Barium titanate (PVDF/ $BaTiO_3$); volume concentration 10%- 30%	Surface hydroxylated $BaTiO_3$	18-25	85-100 nm	[48]
Barium titanate/polyimide ($BaTiO_3$/PI); volume concentration < 50%	$BaTiO_3$ nanoparticles were prepared by the alkoxide route	30	30-50 nm 50-80 nm	[49]
Barium titanate/poly(methyl methacrylate) ($BaTiO_3$/PMMA); volume concentration 53%	$BaTiO_3$ nanoparticles were modified with a silane coupling agent (3-methacryloxypropyltrimethoxysilane)	36	16-21 nm	[50]
Barium titanate/polyimide ($BaTiO_3$/PI); volume concentration 59%	$BaTiO_3$ nanoparticles are surface modified by phthalimide with the aid of a silane coupling agent as a scaffold	37	20 nm	[51]

Table 6. Nanocomposites of polymer/ferroelectric nanoparticles

3.2. Ferroelectric nanoparticles and liquid crystals: Display and non-display applications

It is an established fact that modern technologies require novel and highly advanced materials. During the last decade, nanochemistry has developed a dozen conceptually different pathways of synthesis to satisfy the constantly growing demand for new materials [52]. However, chemical methods are elaborate, time consuming, and expensive. Although they are generally accepted as universal, nanochemistry methods do not work perfectly in certain cases. For example, it's very difficult (but not impossible) to produce 5-10 nm ferroelectric nanoparticles with tetragonal structures through chemical methods (see Table 2). In many cases, the chemical methods used to produce novel materials can be efficiently supplemented or even replaced with non-synthetic ones. The addition of ferroelectric nanoparticles to different materials (polymers; see Table 6, liquids, liquid crystals etc.) is a good example of a non-synthetic method used to develop materials with improved properties. This subsection will discuss how ferroelectric nanoparticles can modify properties of liquid crystals – materials that found numerous applications in the display industry, photonics, optical processing, and the biotech industry.

The concept of ferroelectric colloids in liquid crystals was created by Yu. Reznikov and co-authors [53] – liquid crystal material was doped with stabilized ferroelectric nanoparticles of low concentration (~0.3 %). Ferroelectric nanoparticles share their intrinsic properties with the liquid crystals matrix due to the alignment within the liquid crystal and interactions between mesogenic molecules. The low concentration of nanoparticles and their stabilization with surfactant (oleic acid) provided the stability of such systems. This classic paper reported on the main features of such colloids: (1) a lower threshold voltage by a factor of 1.7; (2) an enhanced dielectric anisotropy by a factor of 2; (3) a linear electro-optical response (the sensitivity to the sign of an applied electric field). It should be pointed out that pure nematics are not sensitive to the sign of an electric field – this property is intrinsic to ferroelectric liquid crystals rather than to nematics. The first experimental results stimulated a very active global interest in the field. More than 100 papers were published during the last decade, and, in the last few years, several review papers summarized the most important results [18, 54, 55]. The review paper [54] published this year by the founder of this field is of special interest since it comprehensively discusses the past, the present, and the future of the liquid crystal colloids.

Ferroelectric nanoparticles embedded into a liquid crystal host strongly interact with the surrounding mesogenic molecules, due to the strong permanent electric field of this particle. These interactions can affect the basic physical parameters of liquid crystals: birefringence, dielectric permittivity, elastic constants, viscosity, electrical and thermal conductivity, temperatures of phase transitions, etc. There are two basic mechanisms responsible for the observed effects: (1) the increase of the orientation coupling between mesogenic molecules; and (2) the direct contribution of the permanent polarization of the particle [54]. Experimental data suggests that the first scenario (the increase of the orientation coupling between mesogenic molecules) is more likely to happen in the case of single component liquid crystals [54]. The second mechanism (associated with the direct contribution of the permanent polarization of the ferroelectric nanoparticle to the physical properties of liquid crystals) is the primary factor in the case of multi-component liquid crystal mixtures [54].

So far most of the reported experimental data describes the properties of multi-component nematics: liquid crystals doped with ferroelectric nanoparticles. The electric field generated by ferroelectric nanoparticles can cause micro- and/or nano-separation of such mixturesandaffect the macroscopic properties of the liquid crystal colloid. As a result, in some cases, the data found for single component liquid crystals (5CB) is different from the data obtained for multi-component mixtures. Nevertheless, an analysis of the existing literature [18] shows that most of the published experimental data report that ferroelectric nanoparticles embedded in liquid crystals at low concentrations: (1) enhance dielectric permittivity, dielectric anisotropy, and optical birefringence; (2) lower the switching voltage U_{th} for the Freedericksz transition; (3) increase the orientational order parameter S and the isotropic–nematic transition temperature T_{NI}; and (4) reduce the switching times needed to reorient liquid crystals by an external electric field. It should be pointed out that in all of these cases, wet grinding was used to prepare the ferroelectric nanoparticles. Few papers claim results opposite to the ones (1)-(4) listed above; however, nanoparticles used to make a liquid crystal colloid in

this case were not ferroelectric [18]. The important conclusion to take from these findings is that a strong ferroelectric response of ferroelectric nanoparticles is a key factor leading to all "positive" effects (1)-(4).

The stability of liquid crystal colloids is the most challenging problem that prevents the transition of liquid crystal colloids of ferroelectric nanoparticles from the academic sector to the industrial domain. During the last few years, the general focus of the research has shifted toward this problem, and the proper surface functionalization of nanoparticles is now being considered as one of the most important factors affecting the stability of liquid crystal colloids. The shape and size of nanoparticles are also of the utmost importance – it was found that 10-20 nm ferroelectric nanoparticles affect the properties of a liquid crystal host much morethan the same but larger nanoparticles(~100 nm).

In summary, ferroelectric nanoparticles can modify the intrinsic properties of liquid crystal materials without time-consuming and expensive chemical synthesis. Experimental data on the enhancement of electro-optical, optical, and nonlinear-optical responses of such materials shows the strong potential of ferroelectric nanoparticles for improving the "practical" properties of liquid crystals, especially for those materials where the method of chemical synthesis has reached its limit. Such modified materials are very attractive and suitable for use in switchable lenses, displays, and beam steering, as well as other light-controlling devices (spatial light modulators, tunable filters etc.) [18].

4. Ferroelectric nanoparticles in biology

In the last decade, ferroelectric nanoparticle areas of application veered toward biology and medicine. The first challenge to address when introducing nanoparticles to biological and medical systems is how to make them stable in media that is bio-compatible, namely in aqueous solutions. If the ferroelectric nanoparticles are not coated with a stabilizing agent, the intrinsic properties of such nanoparticles very often lead to unwanted effects such as aggregation and precipitation, as well as the leaching of some ions (leading to change in particle properties) in aqueous solutions. There has been a tremendous amount of effort in the last twenty years to create many species of ferroelectric nanoparticles with different surface coatings [56and references within]. For example, such stabilizing agents as polyacrylic acid, polymethacrylic acid, polyaspartic acid, (aminomethyl) phosphonic acid and poly-l-lysine were tried on barium titanate nanoparticles. A large variety of possible coatings yields different surface properties of said nanoparticles – different thickness and charge of the surface layer, different strength of stabilizing agent adhesion, different resulting particle size – all of it leading to very different interactions with biological objects such as cells and cellular components. Such water-soluble ferroelectric nanoparticles can be further functionalized with fluorescent markers or antibodies [57], and they have been recently observed within a number of mammalian cells [58, 59, 60] in vitro. The majority of ferroelectric nanoparticles that have been successfully functionalized are in the middle of nano size range (~100 nm or more), and the surface functionaliza-

tion very frequently adds a thick surface layer, resulting in particles that are a few hundred nanometers in size. This poses a challenge which a few researchers are attempting to overcome through bio-inspired surfactants [44]. The surface functionalization of nanoparticles can be crucial for a desired effect in a biosystem – the response is often cell-specific, and biocompatibilty has to be experimentally tested for each new combination of nanoparticle and cell [61]. For example, a recent study [62] indicates that larger (over 200 nm) barium titanate nanoparticles have been successfully used with and without surface modification and they cause no toxic response in endothelial cell cultures.

Current efforts in this area concentrate on carrying these findings through to the systems of cells and tissue in vivo [63, 64]. Such biocompatible nanoparticles can be used in a variety of ways: as imaging agents [58, 59, 60, 64, 65], biocompatible nanoprobes [62, 66, 67, 68], cell proliferation agents [65], etc. Ferroelectric nanoparticles are currently being widely explored for applications in the area of medical imaging, e.g. for enhancing contrast in second harmonic generating methods for imaging deep tissue in vitro and in vivo [64, 69] for such important applications as screening for genetic diseases or cancer[70].

5. Ferroelectric nanoparticles applications in medicine and medical engineering

As mentioned above, ferroelectric nanoparticles have become widely used in material science and engineering applications, but biological and medical applications of these fascinating nanoparticles has only begun to be explored in the last decade. It has been recently discovered that they can be used for cell imaging or the detection of malignancies in lung cancer studies, or they can be functionalized to induce cell proliferation. Ferroelectric materials have a non-centrosymmetric crystalline structure, and are thus capable of generating a second harmonic of light [67]. This distinctive feature of ferroelectrics is the basis for a growing number of applications of ferroelectric nanoparticles as imaging/diagnostic agents and nanoprobes in optical imaging [64].

Optical imaging and detection methods are the most widespread among biological and medical communities. For example, second harmonic generation imaging has been successfully used for detection of *osteogenesis imperfecta* in biopsies of human skin [71] and lung cancer [72]. To improve contrast, many of the imaging methods rely on imaging probes, such as fluorescent markers or quantum dots [73]. This is the case for the SHG imaging technique: the SHG signal from biological cell components is often weak, so novel nanoprobes have been introduced to enhance contrast. SHG probes are photo-stable, and do not bleach or blink unlike conventional fluorescent probes. By definition, second harmonic generating nanoprobes (such as ferroelectric nanoparticles) are capable of converting two photons of light into one photon of half the incident wavelength [74]. This second-harmonic light can be detected using methods of nonlinear optical microscopy. Nonlinear optical properties of ferroelectric nanomaterials can be used for optical phase conjugation [75] and nonlinear microscopy [62, 76] – these properties have allowed them to spread to the area of medical sensors.

This also gives the ferroelectric SHG particle an edge in cell and tissue imaging in vivo. For example, recent advances in this area include imaging a tail of a living mouse with the aid of barium titanate nanoparticles [69].

The intrinsic large values of the dielectric permittivities of ferroelectric nanoparticles suggest their use to enhance the dielectric contrast of materials, such as polymers [77 and references within] and biological tissue [70]. These unique properties of ferroelectric nanoparticles lead to their novel use as contrast-enhancing agents for microwave tomography, which is a method of non-invasive assessment and diagnostics of soft tissues (such as detecting malignancies)[70].Recently, ferroelectric electro spun nanofibers also emerged in various biomedical areas including medical prostheses, tissue engineering, wound dressing, and drug delivery [28,29,30].

In conclusion, ferroelectric materials found a wide variety of biomedical applications in the last decade – and the list is constantly growing [78]. The ferroelectric material (e.g. barium titanate) used in medical implants has been known to accelerate osteogenesis [79], and the same material in nanoparticle form works both as an SHG probe to detect Osteogenesis Imperfecta [71] and, through microwave tomography, to detect lung cancer [70]. We expect more applications will become possible if other effects, such as piezoelectricity, ferroelectric hysteresis or stress-birefringence coupling, are exploited with biology and medicine in mind.

6. Conclusions

A review of recently published research papers allows us to conclude that the unique properties of ferroelectric nanoparticles offer an enormous range of applications, especially in material technologies, biology, and medicine. However, since such a conclusion has become an academic cliché, we would like to make just a few realistic and optimistic comments on the subject.

Discussing any application, we have to be more specific and distinguish between potential applications and actual (i.e. mass commercialized) ones. So far, the "applied" field of ferroelectric nanoparticles is at the stage of high potential for commercialization rather than real mass-commercialization. However, after the very first proof-of-concept research studies were completed just recently, a serious shift toward real applications was initiated. The research community realized that the controllable preparation of nanoparticles (size, shape), their proper surface functionalization, and the homogeneous dispersion into host material (liquid crystals, polymers, biological species) are among the most critical steps on the way to mass-commercialization. Many applications (especially bio-medical) require a large-scale preparation of mono-dispersed, very fine (5-10 nm) ferroelectric nanoparticles in the tetragonal phase – and only recently has substantial progress been made in this direction (see section 2). However, such ultra-fine nanoparticles were mostly tested in material technologies (ferroelectric liquid crystal colloids), while bio-medical methods utilized relatively large ferroelectric nanoparticles (~50-100 nm) (sections 4-5). The bioconjugation of 5-10 nm ferroelec-

tric nanoparticles can extend the area of biomedical application even more, since these nanoparticles can be used as both passive and active nanoprobes.

The applied science of ferroelectric nanoparticles is in the beginning of its development. Many fundamental and applied problems still need to be solved before the potential applications will be converted into actual ones. Nevertheless, despite the fact that the emerging problems in applying nanoparticles in material technologies and biomedicine are still numerous [80], we can conclude that a good balance between purely academic and purely applied foci of research is the key toward mass commercialization of ferroelectric nanoparticles in all applied fields mentioned above.

Acknowledgements

List of abbreviations

AFM atomic force microscopy

DCS differential scanning calorimetry

DLS dynamic light scattering

DTA differential thermal analysis

EDX energy dispersive X-rayspectroscopy

EFM electrostatic force microscopy

FE-SEM field-emission scanning electron microscopy

FTIR Fourier transform infrared spectroscopy

HRTEM high resolution transmission electron microscopy

MLCC multilayer ceramic capacitors

PAA polyamic acid

PTCR positive temperature coefficient of resistance

PMMA poly(methyl methacrylate)

PVDF poly(vinylidene fluoride)

SAED selected area electron diffraction

SEM scanning electron microscopy

SHG probe second harmonic generating probe

SMPS scanning mobility particle size

SPM scanning probe microscopy

TEM transmission electron microscopy

TG or TGA thermo gravimetric analysis

XPSX-ray photoelectron spectroscopy

XRDX-ray diffraction

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References

[1] Haertling, G.H. Ferroelectric ceramics: history and technology. *Journal of the American Ceramic Society*82, 797-818 (1999).

[2] Cross, L.E. & Newnham, R.E. in *High-Technology Ceramics—Past, Present,and Future* 289–305 (American Ceramic Society, Westerville, OH, 1987).

[3] Mitsui, T. in Springer Handbook of Condensed Matter and Materials Data (ed. Warlimont, W.M.a.H.) 903 – 938 (Springer, Berlin, 2006).

[4] Whatmore, R. in Springer Handbook of Electronic and Photonic Materials (ed. Capper, S.K.a.P.) 597 – 623 (Springer, Berlin, 2006).

[5] Kalinin, S.V. et al. Nanoscale Electromechanics of Ferroelectric and Biological Systems: A New Dimension in Scanning Probe Microscopy. *Annual Review of Materials Research*37, 189-238 (2007).

[6] Gruverman, A. & Kholkin, A. Nanoscale ferroelectrics: processing, characterization and future trends. *Reports on Progress in Physics*69, 2443-74 (2006).

[7] Ahn, C.H., Rabe, K.M. & Triscone, J.M. Ferroelectricity at the nanoscale: local polari‐ zation in oxide thin films and heterostructures. *Science*303, 488-91 (2004).

[8] Scott, J.F. Applications of modern ferroelectrics. *Science*315, 954-9 (2007).

[9] Sarkar, D. Synthesis and Properties of BaTiO$_3$ Nanopowders. *Journal of the American Ceramic Society*94, 106-110 (2011).

[10] Zhu, Y.-F., Zhang, L., Natsuki, T., Fu, Y.-Q. & Ni, Q.-Q. Facile Synthesis of BaTiO$_3$ Nanotubes and Their Microwave Absorption Properties. *ACS Applied Materials & In‐ terfaces*4, 2101-2106 (2012).

[11] O'Brien, S., Brus, L. & Murray, C.B. Synthesis of Monodisperse Nanoparticles of Bari‐ um Titanate: Toward a Generalized Strategy of Oxide Nanoparticle Synthesis. *Jour‐ nal of the American Chemical Society*123, 12085-12086 (2001).

[12] Buscaglia, M.T., Bassoli, M., Buscaglia, V. & Vormberg, R. Solid-State Synthesis of Nanocrystalline BaTiO$_3$: Reaction Kinetics and Powder Properties. *Journal of the American Ceramic Society*91, 2862-2869 (2008).

[13] Zhang, Y., Wang, L. & Xue, D. Molten salt route of well dispersive barium titanate nanoparticles. *Powder Technology*217, 629-633 (2012).

[14] Wei, X. et al. Synthesis of Highly Dispersed Barium Titanate Nanoparticles by a Nov‐ el Solvothermal Method. *Journal of the American Ceramic Society*91, 315-318 (2008).

[15] Hayashi, H. & Hakuta, Y. Hydrothermal Synthesis of Metal Oxide Nanoparticles in Supercritical Water. *Materials*3, 3794-3817 (2010).

[16] Zhang, H. et al. Fabrication of Monodispersed 5-nm BaTiO$_3$ Nanocrystals with Nar‐ row Size Distribution via One-Step Solvothermal Route. *Journal of the American Ce‐ ramic Society*94, 3220-3222 (2011).

[17] Atkuri, H. et al. Preparation of ferroelectric nanoparticles for their use in liquid crys‐ talline colloids. *Journal of Optics A: Pure and Applied Optics*11, 024006 (2009).

[18] Garbovskiy, Y. & Glushchenko, A. in Solid State Physics (ed. Camley, R.E.) 1 – 74 (2010).

[19] Cook, G. et al. Nanoparticle doped organic-inorganic hybridphotorefractives. *Optics Express*16, 4015-4022 (2008).

[20] Cook, G. et al. Harvesting single ferroelectric domain stressed nanoparticles for opti‐ cal and ferroic applications. *Journal of Applied Physics*108, 064309-4 (2010).

[21] Basun, S.A., Cook, G., Reshetnyak, V.Y., Glushchenko, A.V. & Evans, D.R. Dipole moment and spontaneous polarization of ferroelectric nanoparticles in a nonpolar fluid suspension. *Physical Review B*84, 024105 (2011).

[22] Swaminathan, V. et al. Microwave synthesis of noncentrosymmetric BaTiO$_3$ truncat‐ ed nanocubes for charge storage applications. *ACS Appl Mater Interfaces*2, 3037-42 (2010).

[23] Fuentes, S. et al. Synthesis and characterization of $BaTiO_3$ nanoparticles in oxygenatmosphere. 505, 568–572 (2010).

[24] Qi, J.Q. et al. Direct synthesis of ultrafine tetragonal $BaTiO_3$ nanoparticles at room temperature. *Nanoscale Research Letters*6, 466 (2011).

[25] Kong, L.B., Zhang, T.S., Ma, J. & Boey, F. Progress in synthesis of ferroelectricceramicmaterialsviahigh-energymechanochemicaltechnique. 53, 207–322 (2008).

[26] Dang, F. et al. Aneweffect of ultrasonication on the formation of $BaTiO_3$ nanoparticles. 17, 310–314 (2010).

[27] Suzuki, K. & Kijima, K. Well-crystallized barium titanate nanoparticles prepared by plasma chemical vapor deposition. 58, 1650–1654 (2004).

[28] Ramaseshan, R., Sundarrajan, S., Jose, R. & Ramakrishna, S. Nanostructured ceramics by electrospinning. *Journal of Applied Physics*102, 111101-17 (2007).

[29] He, Y. et al. Humidity sensing properties of $BaTiO_3$ nanofiber prepared via electrospinning. *Sensors and Actuators B: Chemical*146, 98-102 (2010).

[30] Dai, Y., Liu, W., Formo, E., Sun, Y. & Xia, Y. Ceramic nanofibers fabricated by electrospinning and their applications in catalysis, environmental science, and energy technology. *Polymers for Advanced Technologies*22, 326-338 (2011).

[31] Jung, D.S., Hong, S.K., Cho, J.S. & Kang, Y.C. Nano-sizedbariumtitanatepowders with tetragonalcrystalstructureprepared by flamespraypyrolysis. 28, 109–115 (2008).

[32] Li, X., Xu, H., Chen, Z.-S. & Chen, G. Biosynthesis of Nanoparticles by Microorganisms and Their Applications. *Journal of Nanomaterials*2011 (2011).

[33] Chen, C.-L. & Rosi, N.L. Peptide-Based Methods for the Preparation of Nanostructured Inorganic Materials. *Angewandte Chemie International Edition*49, 1924-1942 (2010).

[34] Briggs, B.D. & Knecht, M.R. Nanotechnology Meets Biology: Peptide-based Methods for the Fabrication of Functional Materials. *The Journal of Physical Chemistry Letters*3, 405-418 (2012).

[35] Dhillon, G.S., Brar, S.K., Kaur, S. & Verma, M. Green approach for nanoparticle biosynthesis by fungi: current trends and applications. *Critical Reviews in Biotechnology*32, 49-73 (2011).

[36] Beier, C.W., Cuevas, M.A. & Brutchey, R.L. Room-Temperature Synthetic Pathways to Barium Titanate Nanocrystals. *Small*4, 2102-2106 (2008).

[37] Ahmad, G. et al. Rapid Bioenabled Formation of Ferroelectric $BaTiO_3$ at Room Temperature from an Aqueous Salt Solution at Near Neutral pH. *Journal of the American Chemical Society*130, 4-5 (2007).

[38] Jha, A.K. & Prasad, K. Ferroelectric $BaTiO_3$ nanoparticles: Biosynthesis and characterization. *Colloids and Surfaces B: Biointerfaces*75, 330-334 (2010).

[39] Bansal, V., Poddar, P., Ahmad, A. & Sastry, M. Room-Temperature Biosynthesis of Ferroelectric Barium Titanate Nanoparticles. *Journal of the American Chemical Society*128, 11958-11963 (2006).

[40] Nuraje, N. et al. Room Temperature Synthesis of Ferroelectric Barium Titanate Nanoparticles Using Peptide Nanorings as Templates. *Advanced Materials*18, 807-811 (2006).

[41] Jha, A.K. & Prasad, K. Synthesis of $BaTiO_3$ nanoparticles: A new sustainable green approach. *Integrated Ferroelectrics*117, 49-54 (2010).

[42] Ould-Ely, T. et al. Large-scale engineered synthesis of $BaTiO_3$ nanoparticles using low-temperature bioinspired principles. *Nature Protocols*6, 97-104 (2011).

[43] Bansal, V., Bharde, A., Ramanathan, R. & Bhargava, S.K. Inorganic materials using 'unusual' microorganisms. *Advances in Colloid and Interface Science*.

[44] Kamiya, H. et al. Preparation of Highly Dispersed Ultrafine Barium Titanate Powder by Using Microbial-Derived Surfactant. *Journal of the American Ceramic Society*86, 2011-2018 (2012).

[45] Pithan, C., Hennings, D. & Waser, R. Progress in the Synthesis of Nanocrystalline $BaTiO_3$ Powders for MLCC. *International Journal of Applied Ceramic Technology*2, 1-14 (2005).

[46] Kim, P. et al. High Energy Density Nanocomposites Based on Surface-Modified $BaTiO_3$ and a Ferroelectric Polymer. *ACS Nano*3, 2581-2592 (2009).

[47] Dang, Z.-M. et al. Fabrication and Dielectric Characterization of Advanced $BaTiO_3$/ Polyimide Nanocomposite Films with High Thermal Stability. *Advanced Functional Materials*18, 1509-1517 (2008).

[48] Zhou, T. et al. Improving Dielectric Properties of $BaTiO_3$/Ferroelectric Polymer Composites by Employing Surface Hydroxylated $BaTiO_3$ Nanoparticles. *ACS Applied Materials & Interfaces*3, 2184-2188 (2011).

[49] Fan, B.-H., Zha, J.-W., Wang, D.-R., Zhao, J. & Dang, Z.-M. Experimental study and theoretical prediction of dielectric permittivity in $BaTiO_3$/polyimide nanocomposite films. *Applied Physics Letters*100, 092903-4 (2012).

[50] Nagao, D., Kinoshita, T., Watanabe, A. & Konno, M. Fabrication of highly refractive, transparent $BaTiO_3$/poly(methyl methacrylate) composite films with high permittivities. *Polymer International*60, 1180-1184 (2011).

[51] Abe, K., Nagao, D., Watanabe, A. & Konno, M. Fabrication of highly refractive barium-titanate-incorporated polyimide nanocomposite films with high permittivity and thermal stability. *Polymer International*, n/a-n/a (2012).

[52] Balzani, V. Nanochemistry: A Chemical Approach to Nanomaterials. Geoffrey A. Ozin and André C. Arsenault. *Small*2, 678-679 (2006).

[53] Reznikov, Y. et al. Ferroelectric nematic suspension. *Applied Physics Letters*82, 1917-1919 (2003).

[54] Reznikov, Y. in Liquid Crystals Beyond Displays: Chemistry, Physics, and Applications (ed. Li, Q.) 403-426 (John Wiley & Sons, Inc., 2012).

[55] Liang, H.-H. & Lee, J.-Y. Enhanced Electro-Optical Properties of Liquid Crystals Devices by Doping with Ferroelectric Nanoparticles. *Ferroelectrics - Material Aspects*, 193-210 (2011).

[56] Ciofani, G. et al. Preparation of stable dispersion of barium titanate nanoparticles: Potential applications in biomedicine. *Colloids and Surfaces B: Biointerfaces*76, 535–543 (2010).

[57] Hsieh, C.-L., Grange, R., Pu, Y. & Psaltis, D. Bioconjugation of barium titanate nanocrystals with immunoglobulin G antibody for second harmonic radiation imaging probes. *Biomaterials*31, 2272–2277 (2010).

[58] Hsieh, C.-L., Grange, R., Pu, Y. & Psaltis, D. (eds. Campagnola, P.J., Stelzer, E.H.K. & von Bally, G.) 73670D-6 (SPIE, Munich, Germany, 2009).

[59] Hsieh, C.-L., Grange, R., Pu, Y. & Psaltis, D. Three-dimensional harmonic holographic microcopy using nanoparticles as probes for cell imaging. *Optics Express*17, 2880-2891 (2009).

[60] Grange, R., Hsieh, C.L., Pu, Y. & Psaltis, D. in European Conference on Lasers and Electro-Optics 2009 and the European Quantum Electronics Conference. CLEO Europe - EQEC 2009. 1-1 (2009).

[61] Ciofani, G. et al. in Piezoelectric Nanomaterials for Biomedical Applications 213-238 (Springer Berlin Heidelberg, 2012).

[62] Yust, B.G., Razavi, N., Pedraza, F. & Sardar, D.K. (eds. Cartwright, A.N. & Nicolau, D.V.) 82310H-6 (SPIE, San Francisco, California, USA, 2012).

[63] Zipfel, W.R. et al. Live tissue intrinsic emission microscopy using multiphoton-excited native fluorescence and second harmonic generation. *Proceedings of the National Academy of Sciences*100, 7075-7080 (2003).

[64] Pantazis, P., Maloney, J., Wu, D. & Fraser, S.E. Second harmonic generating (SHG) nanoprobes for in vivo imaging. *Proceedings of the National Academy of Sciences*107, 14535-14540 (2010).

[65] Ciofani, G., Ricotti, L. & Mattoli, V. Preparation, characterization and in vitro testing of poly(lactic-co-glycolic) acid/barium titanate nanoparticle composites for enhanced cellular proliferation. *Biomedical Microdevices*13, 255-266 (2011).

[66] Pantazis, P., Pu, Y., Psaltis, D. & Fraser, S. (eds. Periasamy, A. & So, P.T.C.) 71831P-5 (SPIE, San Jose, CA, USA, 2009).

[67] Horiuchi, N. Imaging: Second-harmonic nanoprobes. *Nature Photonics*5, 7-7 (2011).

[68] Hsieh, C.-L., Grange, R., Pu, Y. & Psaltis, D. (eds. Mohseni, H. & Razeghi, M.) 77590T-6 (SPIE, San Diego, California, USA, 2010).

[69] Hsieh, C.-L., Lanvin, T., Grange, R., Pu, Y. & Psaltis, D. in Conference on Lasers and Electro-Optics (CLEO), 2011 1-2 (2011).

[70] Semenov, S., Pham, N. & Egot-Lemaire, S. in World Congress on Medical Physics and Biomedical Engineering (eds. Dössel, O. & Schlegel, W.C.) 311-313 (Springer Berlin Heidelberg, Munich, Germany, 2009).

[71] Adur, J. et al. (eds. Periasamy, A., Konig, K. & So, P.T.C.) 82263P-7 (SPIE, San Francisco, California, USA, 2012).

[72] Wang, C.-C. et al. Differentiation of normal and cancerous lung tissues by multiphoton imaging. *Journal of Biomedical Optics*14, 044034-4 (2009).

[73] Chan, W.C.W. in Advances in Experimental Medicine and Biology 208 (Springer Science+Business Media, LLC, 2007).

[74] Dempsey, W.P., Fraser, S.E. & Pantazis, P. SHG nanoprobes: Advancing harmonic imaging in biology. *BioEssays*34, 351-360 (2012).

[75] Yust, B.G., Sardar, D.K. & Tsin, A. (eds. Cartwright, A.N. & Nicolau, D.V.) 79080G-7 (SPIE, San Francisco, California, USA, 2011).

[76] Ganeev, R.A., Suzuki, M., Baba, M., Ichihara, M. & Kuroda, H. Low- and high-order nonlinear optical properties of $BaTiO_3$ and $SrTiO_3$ nanoparticles. *Journal of the Optical Society of America B*25, 325-333 (2008).

[77] Lai, K.T., Nair, B.G. & Semenov, S. Optical and microwave studies of ferroelectric nanoparticles for application in biomedical imaging. *Microwave and Optical Technology Letters*54, 11-13 (2012).

[78] Ciofani, G. et al. 987-990 (KINTEX, Korea, 2010).

[79] Furuya, K., Morita, Y., Tanaka, K., Katayama, T. & Nakamachi, E. (eds. Martin-Palma, R.J. & Lakhtakia, A.) 79750U-6 (SPIE, San Diego, California, USA, 2011).

[80] Florence, A.T. "Targeting" nanoparticles: The constraints of physical laws and physical barriers. (2012).