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Review Article

# Janus Particles Recent and Novel Approach in Drug Delivery: An Overview. Y.R. Indalkar<sup>a,\*</sup>, S.S. Gaikwad<sup>a</sup>, A. T. Ubale<sup>a</sup> *<sup>a</sup>College of Pharmacy, Medha, Satara, Maharashtra, India.*

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# **Abstract**

Janus particles are microscopic particles composed of two different sides. It is an analogue to the surfactant molecule, which has a hydrophilic head group and hydrophobic tail. Janus particle shows fundamental as well as commercial application in drug delivery system. Janus partials have collectively considerable attention in drug delivery system due to their self-organization into complex and well-defined assemblies and advanced surface-active properties with a segregated corona over particles with a uniform wettability. More recently its applications are in Pickering emulsions, electro spinning, and up scaled micro fluidic devices. Along with it has commercial application in areas such as painting, ceramics, and Photonic materials. In this article we highlight several aspects of Janus particles regarding their general properties, synthesis and its application in future opportunity.

**Keywords:** *Janus particles, drug delivery, surface-active, Self-assembly.*

#### **1. Introduction** [1-4]

 A few years ago, Janus particals comes by suggestion of de Gennes. These are special class of colloidal particles with different chemical makeups on their two hemispheres that is hydrophilic and hydrophobic. Originally, the term Janus particle was coined by C. Casagrande *et al.* in 1988 to describe spherical glass particles with one of the hemispheres hydrophilic and the other hydrophobic. In that work, the amphiphilic beads were synthesized by protecting one hemisphere with varnish and chemically treating the other hemisphere with a silane reagent. This method resulted in a particle with equal hydrophilic and hydrophobic areas. In 1991, Pierre-Gilles de Gennes mentioned the term "Janus" particle in his [Nobel](http://en.wikipedia.org/wiki/Nobel_Prize) lecture. Janus particles are named after the two faced Roman god [Janus](http://en.wikipedia.org/wiki/Janus) because these particles may be said to have "two faces" since they possess two distinct types of properties. In Chinese philosophy, seemingly opposite forces are viewed as naturally interconnected, a concept known as Yin and Yang. Hence, Janus particles can also be viewed as Yin− Yang particles. De Gennes pushed for the advancement of Janus particles by pointing out these "Janus grains" have the unique property of densely self-assembling at liquid-liquid interfaces, while allowing material transport to occur through the gaps between the solid [amphiphilic](http://en.wikipedia.org/wiki/Amphiphile) particles. Although the term "Janus particles" was not yet used, Lee and coworkers reported the first particles matching this description in 1985. They introduced asymmetric [polystyrene](http://en.wikipedia.org/wiki/Polystyrene) / [polymethylmethacrylate](http://en.wikipedia.org/wiki/Poly%28methyl_methacrylate%29) lattices from seede[d emulsion](http://en.wikipedia.org/wiki/Emulsion) polymerization.

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One year later, Casagrande and Veyssie reported the synthesis of glass beads that were made hydrophobic on only one hemisphere using octadecyl trichlorosilane, while the other hemisphere was protected with a cellulose varnish. The glass beads were studied for their potential to stabilize emulsification processes. Recently, Binks and Flechter investigated the [wettability](http://en.wikipedia.org/wiki/Wetting) of Janus beads at the interface between oil and water and conclude that Janus particles are both surface-active and amphiphilic, whereas [homogeneous](http://en.wikipedia.org/wiki/Homogeneous) particles are only surface-active. Colloidal particles are fundamental to nature and technology. In terms dimension they present in small molecules form (A°), which can only be approached by modern tools of electron microscopy, and big objects (100 mm). They are pushed around by the random collisions from thermal movement of liquid molecules surrounding them (Brownian motion).Its Chemical composition can incorporate both inorganic and organic species upon design. Janus particles can be divided into three categories as polymeric, inorganic, and polymeric–inorganic, and each kind of Janus particles can be present in various forms like spherical, dumbbell, half raspberry, cylindrical, disk, or any of a variety of other shapes. Janus particals are considered in two types as Janus ellipsoids and Janus dumbbells Out of Janus ellipsoids can be kinetically trapped in a metastable state due to the presence of secondary energy minimum while jaus dumbbells possess only a primary energy minimum, showing that these particles prefer to be in a single orientation. Their potential applications even at that time as surfactants and membrane applications, a "skin" that can "breathe". Such particles are expected to adsorb to interfaces and foam surfaces even more strongly than particles whose chemical makeup is isotropic. Beyond this applications Janus particles

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can also assist chemical catalysis, boosting catalytic activity. They find applications in drug delivery as a variety of drugs can be loaded and subsequently released either simultaneously to achieve synergy between them or in controlled sequence if demand changes with time , in display technology, used by the controlled orientational switch between the dark and bright sides, by external magnetic or electric fields. In the field of polymer-filled composites, its applications to assemble stress networks and tailored pathways of electrical conductivity. In the field of template-directed synthesis, the unique structures formed from their self-assembly can serve as templates by growing chemicals conformally around these exotic structures and removing them afterward. Article includes review of progress in development of synthetic methods to form Janus particles along with its application

# Synthesis of Janus particles [3]

In the early days, methods to synthesize Janus particles were not much advanced than today's standards. Initially Janus particles were synthesized by fictionalization in which particle break into fragments and then giving automatic Janus character to the fragments. This generates heterogeneous particles without control over the shape, size, or purity; but remains an easy, low-cost approach for synthesis. While considering synthesis of Janus particles two important points should be addressed. First is the ability to control the geometry of the Janus particles, i.e., the relative areas of their two sides and second is the ability to produce Janus particles in large quantities. So far, various ways to synthesize Janus particles have been developed.

### Pickering emulsions [4]

This method can synthesize Janus particles with controllable geometry in a wide range of sizes and can be scaled up to synthesize particles in gramsized quantities. A schematic representation of the method is summarized in Fig. 1. At liquid-liquid interface particles whose surface energy is between that of the two liquids will adsorb onto the interface, thereby lowering the total free energy. In the case of our wax–water system, untreated hydrophilic fused silica particles adsorb to the oil-in-water emulsion interface at an elevated temperature where the wax is molten.

After the particles have fully adsorbed, the temperature is lowered to solidify the wax phase and lock the particles in place. Subsequently, chemical modification is carried out at temperatures where the oil phase is solid, thus ensuring the modification of only those faces of the particle that are not buried in wax. The use of a solidified oil phase offers several advantages. First, it freezes the particles into fixed positions during the chemical modification step, avoiding the possibility that adsorbed particles might wobble or rotate at the liquid–liquid interface. Indeed, particle rotation at the liquid–air interface has been reported by others. Second, the presence of a solid oil phase presents advantages at the stage of separation and purification of the particles. Third, when two stages of chemical modification are intended, this eliminates the need to find a liquid–liquid combination where the reactant is soluble in only one liquid. In experiment, scanning electron microscopy (SEM) images reveal that most of the particles adsorb at the emulsion droplet surfaces, whereas only few particles are found inside the wax droplet (as viewed after the wax droplet is broken). The excess of particles dispersed in water are filtered and rinsed away. The Janus geometry is confirmed by visualizing particles that contain fluorescent dye attached to one hemisphere. This method has several advantages first; the reaction can easily be scaled up to synthesize large quantities of Janus particles, since large amounts of interfaces can be created during emulsification. Second, the Janus geometry can be thermodynamically controlled by the contact angle between the particle surface and the liquids used in the emulsion. Compared to alternative methods where the surface coverage of modified chemical makeup is controlled kinetically, this is easier to achieve, and the monodispersity of surface coverage is better from batch to batch. Also, a wide range of Janus geometries can be achieved by simply tuning the amount of surfactants added during the synthesis. Third, the chemistry that can be applied to this method is versatile. Besides the amphiphilic Janus particles mentioned here, also bipolar Janus particles, with opposite charges on each side, can be produced via this method.



Fig. 1. Pickering emulsions: Method of synthesis of JANUS particle.

#### Block copolymers [5]

A schematic representation of the method is summarized in Fig. 2. Block copolymer method was first described by Erhardt *et al.* in 2001.This method produce block polymers with well-defined geometries and compositions across a large variety of substrates. They produced a triblock polymer from [polymethylacrylate,](http://en.wikipedia.org/wiki/Polymethylacrylate) polystyrene and low[molecular-weight](http://en.wikipedia.org/wiki/Molecular_weight) [polybutadiene.](http://en.wikipedia.org/wiki/Polybutadiene) The polystyrene and polymethylacrylate formed alternating layers in between which polybutadiene sat in nanosized spheres. The blocks were then [cross-linked](http://en.wikipedia.org/wiki/Cross-linked) and dissolved in [THF,](http://en.wikipedia.org/wiki/Tetrahydrofuran) and after several washing steps, yielded spherical Janus particles with polystyrene on one face and polymethylacrylate on the other, with a polybutadiene core. The production of Janus [spheres,](http://en.wikipedia.org/wiki/Spheres) [cylinders,](http://en.wikipedia.org/wiki/Cylinder_%28geometry%29) sheets, and [ribbons](http://en.wikipedia.org/wiki/Ribbons) is possible using this method by adjustment of the starting material's [molecular weights](http://en.wikipedia.org/wiki/Molecular_weight) and degree of crosslinking.



Fig. 2: Synthesis of Janus nanoparticles using the block copolymer self-assembly method.

# Competitive adsorption [7]

The core aspect of competitive absorption involves two substrates that phase-separate due to one or more opposite physical or chemical proprieties. When these substrates are mixed with a nanoparticle, typically gold, they maintain their separation and form two faces. A good example of this technique has been demonstrated by Vilain *et al.*, where [phosphinine-](http://en.wikipedia.org/wiki/Phosphinine)coated gold nanoparticles were exposed to long-chain thiols, resulting in substitution of the phosphinine ligands in a phaseseparated manner to produce Janus nanoparticles. Phase separation was proven by showing the [thiols](http://en.wikipedia.org/wiki/Thiols) formed one locally pure domain on the nanoparticle using [FT-IR.](http://en.wikipedia.org/wiki/FT-IR) Jakobs *et al.* demonstrated a major issue with the competitive adsorption method when they attempted to synthesize amphiphilic gold Janus nanoparticles using the competitive adsorption of hydrophobic and hydrophilic [thiols.](http://en.wikipedia.org/wiki/Thiols) The synthesis demonstrated was quiet simple and only involved two steps. First gold nanoparticles capped with tetra-n-oct[ylammonium](http://en.wikipedia.org/wiki/Ammonium) [bromide](http://en.wikipedia.org/wiki/Bromide) were produced. Then the capping agent was removed followed by the addition of various ratios of hydrophilic disulfide functionalized [ethylene oxide](http://en.wikipedia.org/wiki/Ethylene_oxide) and hydrophobic disulfide functionalized oligo(p-phenylenevinylene). They then attempted to prove that phase separation

on the particle surface occurred by comparing the [contact angles](http://en.wikipedia.org/wiki/Contact_angle) of water on the surface of a [monolayer](http://en.wikipedia.org/wiki/Monolayer) of the Janus particles with nanoparticles made with only the hydrophobic or hydrophobic ligands. Instead the results of this experiment showed that while there was some phase separation, it was not complete. This result highlights that the ligand choice is extremely important and any changes may result in incomplete phase separation.

# Phase separation [6]

A schematic representation of the method is summarized in Fig. 3.This method involves the mixing of two or more incompatible substances which then separate into their own domains while still part of a single nanoparticle. These methods can involve the production of Janus nanoparticles of two [inorganic,](http://en.wikipedia.org/wiki/Inorganic) as well as two [organic,](http://en.wikipedia.org/wiki/Organic_compound) substances. In typical organic phase separation methods use cojetting of polymers to produce Janus nanoparticles. This technique is exemplified by the work of Yoshid *et al.* to produce Janus nanoparticles where one hemisphere has affinity for human [cells,](http://en.wikipedia.org/wiki/Cells_%28biology%29)  while the other hemisphere has no affinity for human cells. This was achieved by cojetting polyacrylamide/poly (acrylic acid) copolymers which have no affinity for human cells with [biotinylated](http://en.wikipedia.org/wiki/Biotinylation) polyacrylamide/poly (acrylic acid) copolymers, which when exposed to [streptavidin-](http://en.wikipedia.org/wiki/Streptavidin)modified antibodies, obtain an affinity for human cells. While in inorganic phase separation methods are diverse and vary greatly depending on the application. The most common method uses the growth of [a crystal](http://en.wikipedia.org/wiki/Crystal_structure) of one inorganic substance on or from other inorganic nanoparticles. A unique method has been developed by Gu *et al.*, where [iron](http://en.wikipedia.org/wiki/Iron)[-platinum](http://en.wikipedia.org/wiki/Platinum) nanoparticles were coated with [sulfur](http://en.wikipedia.org/wiki/Sulfur) reacted with [cadmium](http://en.wikipedia.org/wiki/Cadmium) acetylacetonate, trioct[ylphosphineoxide,](http://en.wikipedia.org/wiki/Phosphine)  and hexadecane-1,2[-diol](http://en.wikipedia.org/wiki/Diol) at 100°C to produce nanoparticles with an iron-platinum core and an [amorphous](http://en.wikipedia.org/wiki/Amorphous) cadmium-sulfur shell. The mixture was then heated to 280°C, resulting in a [phase transition](http://en.wikipedia.org/wiki/Phase_transition) and a partial eruption of the Fe-Pt from the core, creating a pure Fe-Pt sphere attached to the CdScoated nanoparticles. A new method of synthesizing inorganic Janus nanoparticles by phase separation has recently been developed by Zhao and Gao. In this method, they explored the use of the common homogeneous nanoparticles synthetic method of flame synthesis. They found when a [methanol](http://en.wikipedia.org/wiki/Methanol) solution containing [ferric](http://en.wikipedia.org/wiki/Ferric) triacetylacetonate and [tetraethylorthosilicate](http://en.wikipedia.org/wiki/Tetraethylorthosilicate) was burned, the iron and silicon components formed an intermixed solid, which undergoes phase separation when heated to approximately 1100°C to produce [magnetite-](http://en.wikipedia.org/wiki/Maghemite)[silica](http://en.wikipedia.org/wiki/Silicon_dioxide) Janus nanoparticles. Additionally, they found it was possible to modify the silica after producing the Janus nanoparticles, making it hydrophobic by reacting it with [oleylamine.](http://en.wikipedia.org/wiki/Oleylamine)



Fig. 3. Phase separation method of producing Janus nanoparticles.

Applications [7,8,9] Self-assembly

Janus particles' two or more distinct faces give them special properties in solution. In particular, they have been observed to [self-assemble](http://en.wikipedia.org/wiki/Self-assembly) in a specific way in [aqueous](http://en.wikipedia.org/wiki/Aqueous) or organic solutions. In the case of spherical Janus [micelles](http://en.wikipedia.org/wiki/Micelles) having hemispheres of polystyrene (PS) and poly (methyl methacrylate) (PMMA), [aggregation](http://en.wikipedia.org/wiki/Particle_aggregation) into clusters has been observed in various organic solvents, such as [tetrahydrofuran.](http://en.wikipedia.org/wiki/Tetrahydrofuran) Similarly, Janus discs composed of sides of PS and poly (tert-butyl methacrylate) (PtBMA) can undergo back-to-back stacking into superstructures when in an organic solution. Interestingly, these particular Janus particles form aggregates in organic solvents considering that both sides of these particles are soluble in the organic solvent. It appears that the slight selectivity of the solvent is able to induce self-assembly of the particles into discrete clusters of Janus particles. This type of aggregation does not occur for either standard block copolymers nor for homogeneous particles and thus is a feature specific to Janus particles. Additionally, the behavior of Janus particle in aqueous [solutions](http://en.wikipedia.org/wiki/Solutions) is also very interesting. In an aqueous solution, two kinds of [biphasic](http://en.wikipedia.org/wiki/Biphasic) particles can be distinguished. The first type is particles which are truly amphiphilic and possess one hydrophobic and one hydrophilic side. The second type has two water-soluble, yet chemically distinct, sides. To illustrate the first case, extensive studies have been carried out with spherical Janus particles composed of one hemisphere of water-soluble PMAA and another side of water-insoluble polystyrene. In these studies, the Janus particles were found to aggregate on two [hierarchical](http://en.wikipedia.org/wiki/Hierarchical) levels. The first type of selfassembled aggregates look like small clusters, similar to what is found for the case of Janus particles in an organic solution. The second type is noticeably larger than the first and has been termed 'super micelles'. Unfortunately, the structure of the super micelles is unknown so far; however, they may be similar to [multilamellar vesicles.](http://en.wikipedia.org/wiki/Liposome) For the second case of Janus particles which contain two distinct, but still water-soluble sides, the work of Granick's group provides some insight. Their research deals with the clustering of dipolar [\(zwitterionic\)](http://en.wikipedia.org/wiki/Zwitterionic), micronsized Janus particles, whose two sides are both fully water soluble. Zwitterionic Janus particles are interesting because they do not

behave like classical [dipoles,](http://en.wikipedia.org/wiki/Dipoles) since their size is much larger than the distance at which electrostatic attractions are strongly felt. The study of zwitterionic Janus particles once again demonstrates their ability to form defined clusters. However, this particular type of Janus particle prefers to aggregate into larger clusters since this is more energetically favorable because each cluster carries a [macroscopic](http://en.wikipedia.org/wiki/Macroscopic) dipole which allows the aggregation of already-formed clusters into larger assemblies. Compared to aggregates formed through [van der](http://en.wikipedia.org/wiki/Van_der_Waals_force)  [Waals](http://en.wikipedia.org/wiki/Van_der_Waals_force) interactions for homogenous particles, the shapes of the Zwitterionic Janus nanoclusters are different and the Janus clusters are less dense and more asymmetric. The structures formed by Janus amphiphilic particles are analogous to the micellar shapes adopted by standard molecular amphiphiles. This similarity can provide an approximate idea of the fundamental rules followed by even more complex molecular systems such as the phase behavior of diblock copolymers and functionality of biological membranes assembled by phospholipids. A more detailed understanding of these systems would be built upon the answers to several more delicate questions. A comprehensive study of the phase behavior of the amphiphilic Janus particles, how they evolve from dilute solution to concentrated suspensions, might go beyond the conventional phase diagram for homogeneous colloids by revealing new behavior such as microphase separation. Inspired by the assembly behavior of surfactants, we also expect that the self-assembled structures of amphiphilic Janus particles depend on and can even be controlled by the Janus balance, the relative surface areas of the hydrophobic and charged patches. Eventually the question that needs to be answered is what new assembled structures can form when Janus amphiphilic particles of different size, surface chemistry and possibly Janus balance are mixed together, since real systems typically contain more than one component. On the application side, amphiphilic Janus particles can serve as solid surfactants that adhere to the oil– water interface, thereby stabilizing emulsions and foams. Moreover, the wormlike strings, or even the clusters, may also modify suspension rheology to produce different glass or gel dynamics and yielding behaviors, and they may be used as environmentresponsive vehicles within which to encapsulate cargo for subsequent controlled release. The idea of having solid surfactants generalizes the concept of molecular amphiphilicity that is so pervasive and useful in nature and technology.

#### Stabilizers in emulsions [9]

Application of Janus particle in stabilization of emulsion due its amphiphilic properties.In 2006, Janus nanoparticles, made from [gold](http://en.wikipedia.org/wiki/Gold%28III%29_oxide) and [iron](http://en.wikipedia.org/wiki/Iron_oxide)  [oxides,](http://en.wikipedia.org/wiki/Iron_oxide) were compared with their homogeneous counterparts by measuring the ability of the particles to reduce the interfacial tension between water and [n-hexane.](http://en.wikipedia.org/wiki/Hexane) Experimental results indicated Janus nanoparticles are considerably more surface-active than homogeneous particles of comparable size and chemical nature. Furthermore, increasing the amphiphilic character of the particles can increase

the interfacial activity. The ability of Janus nanoparticles to lower interfacial tension between water and [n-hexane](http://en.wikipedia.org/wiki/Hexane) confirmed previous theoretical predictions on their ability to stabilize [Pickering](http://en.wikipedia.org/wiki/Pickering_emulsion)  [emulsions.](http://en.wikipedia.org/wiki/Pickering_emulsion) In 2007, the amphiphilic nature of the Janus nanoparticles was examined by measuring the [adhesion](http://en.wikipedia.org/wiki/Adhesion) force between the [atomic force](http://en.wikipedia.org/wiki/Atomic_force_microscopy)  [microscopy](http://en.wikipedia.org/wiki/Atomic_force_microscopy) (AFM) tip and the particle surface. The stronger interactions between the hydrophilic [AFM](http://en.wikipedia.org/wiki/Atomic_force_microscopy) tip and the hydrophilic side of the Janus nanoparticles were reflected by a greater [adhesion](http://en.wikipedia.org/wiki/Adhesion) force. The Janus nanoparticles were drop cast onto both hydrophobic ally and hydrophilic ally modified substrates. The hydrophobic hemisphere of the Janus particles was exposed when a hydrophilic substrate surface was used, resulting in disparities in adhesion force measurements. Thus, the Janus nanoparticles adopted a confirmation that maximized the interactions with the substrate surface. The nature of amphiphilic Janus nanoparticles to orient themselves spontaneously at the interface between oil and water has been well known. This behavior allows considering amphiphilic Janus nanoparticles as analogues of molecular surfactants for the stabilization of emulsions. In 2005, spherical silica particles with amphiphilic properties were prepared by partial modification of the external surface with an alkylsilane agent. These particles form spherical assemblies encapsulating water-immiscible organic compounds in aqueous media by facing their hydrophobic alkylsilylated side to the inner organic phase and their hydrophilic side to the outer aqueous phase, thus stabilizing oil droplets in water. In 2009, [hydrophilic](http://en.wikipedia.org/wiki/Hydrophile) surface of silica particles was made partially hydrophobic by adsorbing cetyltrimethylammonium bromide. These amphiphilic nanoparticles spontaneously assembled at the water[-dichloromethane](http://en.wikipedia.org/wiki/Dichloromethane) interface. In 2010, Janus particles composed from silica and polystyrene, with the polystyrene portion loaded with nanosized [magnetite](http://en.wikipedia.org/wiki/Magnetite) particles, were used to form kinetically stable oil-in-water emulsions that can be spontaneously broken on application of an external magnetic field. Such Janus materials will find applications in magnetically controlled optical switches and other related areas. The first real applications of Janus nanoparticles were in [polymer](http://en.wikipedia.org/wiki/Polymer) synthesis. In 2008, spherical amphiphilic Janus nanoparticles, having one polystyrene and one [poly\(methyl methacrylate\)](http://en.wikipedia.org/wiki/Poly%28methyl_methacrylate%29) side, were shown to be effective as compatibilizing agents of milligram scale compatibilization of two immiscible polymer blends, polystyrene and poly(methyl methacrylate). The Janus nanoparticles oriented themselves at the interface of the two polymer phases, even under high temperature and shear conditions, allowing the formation of much smaller domains of polymethyl methacrylate) in a polystyrene phase. The performance of the Janus nanoparticles as compatibilizing agents was significantly superior to other state-of-the-art compatibilizers, such as linear bloc[k copolymers.](http://en.wikipedia.org/wiki/Copolymer)

Janus Particles as Optical Probes for Microrheology [4]

Going beyond questions of self-assembly, transport problems are also worth emphasizing. Janus particles can display anisotropic transport under certain conditions. This is usually due to the different local flow profiles or osmotic potential induced by the external field or chemical reactions. It was found that Au-coated Janus particles will diffuse perpendicular to the external electric field, due to the induced-charge electrophoresis flow close to the particle surface of different hemispheres. The effective net force pushes particles to move in the direction perpendicular to the external electric field. Another way to move Janus particles in a certain direction is by self-propulsion induced by a catalytically active surface. This may find its application in drug delivery systems, since selfmotile particles can move more efficiently than conventional Brownian particles. Another potential utilization of Janus particles is to use them as tracers to probe the local rheological properties of their environment. The contribution here is to use modulated optical nanoprobes (MOONs) whose optical properties are modulated by their rotational diffusion, thus augmenting the information about position that is obtained from conventional translational diffusion. From the rotational diffusion, a more comprehensive understanding can be obtained in many complex environments where translational and rotational diffusion are not simply proportional to one another, such as glassy materials. Indeed, when Janus particles with high enough optical contrast are viewed and magnified in an appropriate microscope, their images mimic the moon in all its phases (Fig. 4). This enables the simultaneous tracking, at the single-particle level, of two rotational degrees of freedom. Special tracking techniques have been developed to measure the orientation of two axes of a MOON particle from a single image, so that rotational dynamics can be acquired from a series of video frames. Also, the location of the center of MOON particles can be determined with modification of conventional tracking programs to give information about centerof-mass diffusion. In some cases, the translational and rotational dynamics are largely coupled as they basically convey the same rheological properties of the environment. They can, however, be decoupled in more complex systems, for example in the case of hopping of colloids on a patterned surface or for asymmetric colloidal clusters. This illustrates the richness of information that rotational diffusion of Janus probes can provide.

## Applications in biological sciences [10]

The ground breaking progress in the biological sciences has led to a drive towards custom made materials with precisely designed physical chemical properties at the nanoscale level. Inherently Janus nanoparticles play a crucial role in such applications. In 2009, a new type of bio-hybrid material composed of Janus nanoparticles with spatially controlled affinity towards human [endothelial](http://en.wikipedia.org/wiki/Endothelium) cells was reported. These nanoparticles were synthesized by selective surface modification

with one hemisphere exhibiting high binding affinity for human endothelial cells and the other hemisphere being resistant towards cell binding. The Janus nanoparticles were fabricated via electrohydrodynamic jetting of two polymer liquid solutions. When incubated with human endothelial cells, these Janus nanoparticles exhibited expected behavior, where one face binds toward human endothelial cells, while the other face was not bonding. These Janus nanoparticles not only bound to the top of the human endothelial cells, but also associated all around the perimeter of cells forming a single particle lining. The biocompatibility between the Janus nanoparticles and cells was excellent. The concept is to eventually design probes based on Janus nanoparticles to attain directional information about cell-particle interactions.

# Nanocorals [11]

In 2010, a new type of cellular probe synthesized from Janus nanoparticles called a nanocoral, combining cellular specific targeting and biomolecular sensing, was presented. Nanocoral is composed of polystyrene and gold hemispheres. The polystyrene hemisphere of the nanocoral was selectively functionalized with antibodies to target receptors of specific cells. This was demonstrated by functionalizing the polystyrene region with antibodies that specifically attached to breast cancer cells. The [gold](http://en.wikipedia.org/wiki/Gold) region of the nanocoral surface was used for detecting and imaging. Thus, the targeting and sensing mechanisms were decoupled and could be separately engineered for a particular experiment. Additionally, the polystyrene region may also be used as a carrier for drugs and other chemicals by surface hydrophobic [adsorption](http://en.wikipedia.org/wiki/Adsorption) or encapsuation, making the nanocoral a possible multifunctional [nanosensor.](http://en.wikipedia.org/wiki/Nanosensor)

# Imaging and magnetolytic therapy [12,13]

Also in 2010, Janus nanoparticles synthesized from hydrophobic magnetic nanoparticles on one side and polystyrene-block-allyl alcohol) on the other side were used for imaging and magnetolytic therapy. The magnetic side of the Janus nanoparticles responded well to external magnetic stimuli. The nanoparticles were quickly attached to the cell surfaces using a magnetic field. Magnetolytic therapy was achieved through magnetic field-modulated cell membrane damage. First, the nanoparticles were brought close in contact with the tumor cells, and then a spinning magnetic field was applied. After 15 minutes, the majority of the tumor cells were killed. Magnetic Janus nanoparticles could serve as the basis for potential applications in medicine and electronics. Quick responses to external magnetic fields could become an effective approach for targeted imaging, therapy *[in vitro](http://en.wikipedia.org/wiki/In_vitro)* and *[in vivo](http://en.wikipedia.org/wiki/In_vivo)*, and cancer treatment. Similarly, a quick response to magnetic fields is also desirable to fabricate smart displays, opening new opportunities in electronics and [spintronics.](http://en.wikipedia.org/wiki/Spintronics) In 2011, silica-coated Janus nanoparticles, composed of [silver oxide](http://en.wikipedia.org/wiki/Silver_oxide) an[d iron oxide](http://en.wikipedia.org/wiki/Iron_oxide) ( $Fe<sub>2</sub>O<sub>3</sub>$ ), were prepared in one step with scalable flame aerosol technology. These hybrid plasmonic-magnetic nanoparticles

bear properties that are applicable in bioimaging, targeted drug delivery, *in vivo* diagnosis, and therapy. The purpose of the nanothin  $SiO<sub>2</sub>$  shell was to reduce the release of toxic  $Ag<sup>+</sup>$  $Ag<sup>+</sup>$  ions from the nanoparticles surface to live cells. As a result, these hybrid nanoparticles showed no cyctotoxicity during bioimaging and remained stable in suspension with no signs of agglomeration or settling, thus enabling these nanoparticles as biocompatible multifunctional probes for bioimaging. Next, by labeling their surfaces and selectively binding them on the membrane of live-tagged Raji and [HeLa](http://en.wikipedia.org/wiki/HeLa) cells, this demonstrated the nanoparticles as [biomarkers](http://en.wikipedia.org/wiki/Biomarker) and their detection under dark-field illumination was achieved. These new hybrid Janus nanoparticles overcame the individual limitations of  $Fe<sub>2</sub>O<sub>3</sub>$  (poor particle stability in suspension) and of [Ag](http://en.wikipedia.org/wiki/Silver) (toxicity) nanoparticles, while retaining the desired magnetic properties of  $Fe<sub>2</sub>O<sub>3</sub>$  $Fe<sub>2</sub>O<sub>3</sub>$  and the plasmonic optical properties o[f Ag.](http://en.wikipedia.org/wiki/Silver)

Catalyst in hydrogen peroxide decomposition [14] In 2010, spherical silica Janus nanoparticles with one side coated wit[h platinum](http://en.wikipedia.org/wiki/Platinum) were used for the first time to catalyze the decomposition of [hydrogen](http://en.wikipedia.org/wiki/Hydrogen_peroxide)  [peroxide](http://en.wikipedia.org/wiki/Hydrogen_peroxide)  $(H_2O_2)$ . The platinum particle catalyzes the surface chemical reaction:  $2H_2O_2 \rightarrow O_2 + H_2O$ . The decomposition of hydrogen peroxide created Janus catalytic nanometers, the motion of which was analyzed experimentally and theoretically using computer simulations. The motion of the spherical Janus nanoparticles was found to agree with the predictions of computed simulations. Ultimately, catalytic nanomotors have practical applications in delivering chemical payloads in [micro fluidic](http://en.wikipedia.org/wiki/Microfluidics) chips, eliminating pollution in aquatic media, removing toxic chemicals within biological systems, and performing medical procedures.

#### Water-repellent fibers [15]

In 2011, Janus nanoparticles were shown to be applicable in textiles. Water-repellent fibers can be prepared by coating [polyethylene terephthalate](http://en.wikipedia.org/wiki/Polyethylene_terephthalate) fabric with amphiphilic spherical Janus nanoparticles [10]. The Janus particles bind with the hydrophilic reactive side of the textile surface, while the hydrophobic side is exposed to the environment, thus providing the water-repellent behavior. Janus particle sizes of 200 nm were found to deposit on the surface of fibers and were very efficient for the design of water-repellent textiles.

# Applications in electronics [16,17]

The potential application of Janus particles was first demonstrated by Nisisako *et al.*, who made use of the electrical [anisotropy](http://en.wikipedia.org/wiki/Anisotropy) of Janus particles filled with white and black [pigments](http://en.wikipedia.org/wiki/Pigments) in both hemispheres. These particles were used to make switchable screens by placing a thin layer of these spheres between two [electrodes.](http://en.wikipedia.org/wiki/Electrodes) Upon changing the applied [electric field,](http://en.wikipedia.org/wiki/Electric_field) the particles orient their black sides to the [anode](http://en.wikipedia.org/wiki/Anode) and their white sides to the cathode. Thus the orientation and the color of the display can be changed by simply reversing the electric field. With this method, it may be possible to make very thin and environmentally friendly displays.

Janus particles handling by dielectrophoresis [17,18,19]

Janus particles Au/fluorescent polystyrene are fabricated and their flip/flop rotational effect is studied in a micro fluidic channel thanks to dielectrophoresis, providing a new type of local light switch. A method for producing large amounts more than 10<sup>6</sup> particles/ml of Janus particles is first presented. Those particles were then injected in an electromicrofluidic chip and stabilized in the fluid by a dielectrophoretic trap. The spanning frequency of this trap allowed performing a "flip-flop" effect of the Janus particles by recording their fluorescent intensities. Flip Au top side and flop PS top side frequencies are identified. Experiments were performed on the time-triggered commutations between flip and flop frequencies to define the capability of each Janus particle to sustain speed control of their flip-flop.

#### **Conclusion**

Janus particles give desirable control over not only surface chemical composition, but also the capacity to produce large quantities of monodisperse .Janus particles. Looking to the future, Fundamental research of this kind will continue to elucidate our understanding of the principles of the self-assembly process. This in turn implies that the observed structures are likely to be equilibrated. To this end, it will be necessary to find synthetic pathways in the laboratory to implement the multivalent structures that have been proposed in large quantities and in monodisperse form.

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