Active colloids: Progress and challenges towards realising autonomous applications

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Article Info

Article history:
Received 31 July 2015
Received in revised form 29 September 2015
Accepted 8 October 2015
Available online xxxx

Keyword:
Active colloids

Abstract

Active colloids are small scale materials capable of producing enhanced motion within fluid environments. The field of active colloids has grown rapidly over the last ten years and is approaching maturity where viable applications are within reach. In this review, recent advances are surveyed with a strong emphasis on developments that can enable autonomous applications, where colloids execute useful tasks without external interventions. These applications are likely to prove transformative as the resulting technologies will be significantly less complex than current methods. A survey of the requirements to achieve autonomous applications is provided, considering guidance, solution compatibilities, manufacture and function; with reference to recent developments in these capacities. Following on from this, progress towards applications in environmental remediation, lab-on-a-chip microfluidics and in vivo drug delivery is highlighted.

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1. Introduction

1.1. Background

Generating and controlling autonomous motion within a fluid environment is an essential component for many proposed nanometre and micron-scale technologies. While some ability to transport materials within a fluid environment is provided by Brownian diffusion and osmotic effects, in many cases these phenomena do not display the required speed or directionality. Fluidic transport problems are also faced in nature, as evidenced by the complex structures that have evolved to augment passive diffusion. For example, protein motors are used to transport attached cargo along microtubule tracks within cells [1], achieving directed motion at scales where trajectories are otherwise rapidly randomised by Brownian effects. In addition there are many examples of larger, micron sized cells, such as spermatozoa, Escherichia coli and algae, that can produce enhanced motion by “swimming” within fluids. These cells can also navigate based on well documented sensing mechanisms such as chemotaxis [2] and gravitaxis [3]. Partially inspired by these natural examples, and motivated by the burgeoning need to transport and organise material at small scales in order to realise new applications, attention has increasingly focused on producing synthetic devices capable of similar autonomous motion behaviour.

Two strands in the development of autonomously moving synthetic devices can be followed. At first it seemed that mimicking the deformation based swimming of the motile cells mentioned above is a promising strategy. This motivated the development of colloidal assemblies that could be manipulated to produce motion, that can be traced from a famous early example where a chain of magnetic beads executed swimming to enable applications are hard to isolate. In this context, a second approach, which is less obviously, if at all, utilised in nature; applying external field gradients to individual magnetic colloids also allows them to be efficiently transported, rotated, and manipulated [7], and so the unique benefits for using more complex deformation swimming to enable applications are hard to isolate. In this context, a second approach, which is less obviously, if at all, utilised in nature; based on the ability of chemically active colloids to modify their local environment, has proven to meet the requirement of autonomy. An early example for this concept, to produce motion by chemical activity, was reported by Whitesides, where asymmetrically distributed platinum catalyst allowed a centimetre scale device to autonomously move along a meniscus by generating a surface tension gradient while decomposing hydrogen peroxide fuel [8]. The general concept of an asymmetrically distributed reaction generating motion has subsequently been elaborated upon and miniaturised to lead to the development of the
The range of materials termed active colloids which are discussed here. Active colloids are so named to distinguish them from conventional passive colloids which exhibit purely Brownian transport behaviour.

1.2. Autonomous active colloids

The range of strategies by which surface reactions can produce motion has been the subject of several comprehensive reviews which the reader is directed towards, for example those by Kapral [9] and Sen [10]. As a broad classification, active colloids can be grouped according to geometry, and propulsion mechanism, however it is worth bearing in mind that for some examples the mechanism has been the subject of debate, and it is also possible that multiple mechanisms contribute to the observed motion. The earliest examples of small scale chemically active colloids were bi-metallic nanorods, Fig. 1a [11]. These rods produce enhanced motion by catalytically decomposing hydrogen peroxide fuel via an electrophoretic mechanism [12]. Many studies have reported a range of phenomena for these devices, including correlations between rod composition and motion velocity [13], the effect of solution properties on speed, and collective behaviour [14]. A further much studied category of active colloids, first postulated theoretically [15], are spherical Janus swimmers, Fig. 1b [16]. A common example of these devices is made by coating one hemisphere of a conventional colloid with a catalytic material, for example a platinum hemisphere decomposing dissolved hydrogen peroxide fuel. Janus colloids were initially thought to produce motion by pure self-diffusiophoresis, however recently experiments have suggested that an electrokinetic mechanism [17], related to that proposed for nanorods, may dominate. Again, extensive experiments have reported motion production across a range of colloidal sizes [18, 19], for different materials [20], and investigated phenomena such as self-assembly [21]. For all reported bimetallic nanorod experiments, and the smaller sized examples for active Janus colloids, motion is produced without detectable bubble nucleation and release occurring at the colloid surface, despite the chemical reactions often producing a gaseous product. However, as devices get larger and less curved, the energetic penalty associated with bubble nucleation reduces [22], and examples of bubble propulsion, where motion clearly results from momentum transfer due to bubbles growing and detaching from the active surface are seen. Some examples of bubble swimmers include larger, more reactive spherical Janus colloids, Fig. 1c, made for example by partially masking an inner chemically active colloid with an inert overlayer [23]. In contrast to the smaller non-bubbling spherical colloids it has also been found that asymmetrical chemical activity is not a requirement to produce motion: uniformly chemically active colloids can also produce bubble propulsion [24,23]. The final much studied active colloid examples are rolled-up nanotubes [25], also termed nano-rockets, Fig. 1d. This swimmer type contains chemically active material localised inside a tubular structure, which generates bubbles that are expelled from one of the two open ends of the tube, resulting in rapid motion.

Despite this apparent diversity, all these active colloids possess the salient feature of producing motion powered solely by dissolved fuel and so offer the potential to be exploited for autonomous small scale transport applications.

1.3. Scope of review: emphasis on autonomy

This review focuses on advances made in the last three years that have the potential to contribute to the development of autonomous applications for active colloids. The remit of this review is consequently focused on active colloids that are not reliant on the application of external directing fields in order to perform a given task. This focus reflects the authors’ viewpoint that any application that requires significant external control does not fully exploit the autonomous, unactuated motion capability that motivates interest in active colloids [28]. Due to this, the emerging class of active colloids that have a propulsion mechanism requiring external actuation are not discussed. These include examples such as thermophoretic devices [29] which are locally heated with a laser beam, and other examples based on de-mixing [30], electro-phoresis [31], and ultrasonic agitation [32]. In addition, the review will endeavour to clearly indicate when tasks have to date only be achieved, by a “hybrid” approach: where an intrinsically autonomous motion producing device is steered or otherwise actuated by an external field [33]. While externally driven and controlled active colloids can enable applications, these are likely to be via relatively complex technologies requiring significant additional control and monitoring infrastructure. In contrast, by perusing the goal to retain autonomy in active colloid developments, simpler applications may be realised, and this is the strong focus of this perspective.

In this context, initially a “wish-list” for the functionality that will be required to produce fully autonomous applications is outlined. These features are compared with the currently reported behaviour for existing devices. Particular emphasis is placed on recognising that at present, as outlined above, there are a range of demonstrated active colloid propulsion mechanisms, each having relative advantages and disadvantages. Reviewing the state of the field without recognising this diversity has the danger of understating the challenges that must be met in order to implement a viable new technology based on active...
colloids. Having assessed the general prognosis for applications, recent demonstrations for active colloid utility in three application areas: environmental remediation, lab-on-a-chip transport, and in vivo drug delivery and repair are discussed and the remaining challenges to develop these concepts into working technologies are highlighted.

2. Functional requirements for autonomous active colloid applications

This section describes the toolkit of features that will be required to realise autonomous applications for active colloids. The salient features of direction control, solution compatibility, ease of manufacture and ability to perform useful functions are all discussed in turn with reference to recent developments.

2.1. Direction control

For most autonomous active colloids, Brownian randomisation of position and orientation results in trajectories that become randomised over relatively short time periods. Considering the examples introduced above in turn: non-bubbling spherical Janus swimmers trajectories have been reported to become diffusive due to Brownian rotations over a time period of 10 s of seconds [16]. Nanorods and nanotubes show greater persistence of motion, due to asymmetric drag forces, but are eventually randomised, and for spherical bubble swimmers the chaotic nature of the bubble release process also leads to highly randomised trajectories [24]. While this random enhanced motion can be exploited for some applications; for example speeding up capture or neutralisation of an evenly distributed cargo/contaminant, it is likely that many useful applications will require the direction of motion to be further controlled.

For example, having gathered a cargo, this may need to be transported towards a specific location. The importance of imparting directionality is further evident when considering lab-on-a-chip systems where pumps and valves, or other actuated fluid manipulation methods, are currently required to enable sequential operations. In order for active colloids to provide a viable flow free alternative, the ability to control transit though a device will be required. Developing methods to induce this directionality to the motion of active colloids has consequently been the focus of recent experimental attention.

An obvious way to impart directionality to asymmetric active colloids with a well-defined link between their orientation and propulsion direction, is to generate a constraining torque with sufficient energy to prevent Brownian rotation. This can be achieved relatively trivially by incorporating a magnetic component into the device, and then externally applying a sufficiently strong magnetic field [34,35]. However this is clearly not an autonomous approach. Alternatively, two recent studies have shown that a constraining torque can also be generated by the interaction of active colloids with the Earth’s gravitational field. The first study considered catalytic spherical Janus swimmers. As these active colloids are made by coating one side of a colloid with a dense metal (Platinum), they possess considerable mass asymmetry. Depending on the size of the colloid and the thickness of the deposited metal, this mass asymmetry results in a propensity for the heavy catalytically active hemisphere to point downwards. Because the propulsion vector for these swimmers is orientated away from the platinum cap (Fig. 1b), this results in autonomous upwards motion: termed positive gravitaxis, Fig. 2a [36]. A similar mechanism is also used by bottom heavy algae to navigate aquatic environments. In a second study, shape-anisotropy was found to also result in autonomous gravitaxis, Fig. 2b + c. In this latter example the propulsion mechanism relied on laser illumination, but extending this finding to chemically powered devices should be straightforward. [37]

The utility of gravitaxis is clear, as it provides a mechanism to break the otherwise isotropic motion for active colloids and impart a well-defined and controllable propulsion direction without the need to apply controlling fields. These findings could be exploited to rapidly concentrate colloids from a 3D volume to a 2D interface, and also open the potential to execute serial processes by designing suitable vertically arranged chambers, or inclined surfaces. Furthermore, the degree of gravitaxis can be potentially be altered by cargo attachment, fuel concentration and other solution properties allowing dynamic responses in the navigation behaviour and enabling sensing capabilities.

An alternative emerging route to overcome the randomisation of active colloid trajectories is to exploit interactions with physical structures. Self-motile cells have been observed to display a range of interactions with surfaces, resulting in them accumulating at planar interfaces [38], and when exposed to more sophisticated patterning, rectification and sorting according to motion characteristics has been reported [39]. In a similar fashion, the interactions between active colloids and patterned surfaces have recently been considered. In two independent studies, bimetallic nanorods [40] and Janus spheres [41] have displayed circling behaviour around the base of the colloidal obstacles, Fig. 3a. These trajectory modifications were explained by steric and hydrodynamic interactions. Heart shaped structures have also been demonstrated to autonomously localise nanotube swimmers at sharp cusps due to steric effects, Fig. 3b [42]. Taken together, these developments suggest the potential to develop a new type of small scale fluid transport where active colloids are autonomously guided allowing the development of new applications that require predictable transit of material through a fluidic environment without the need for flows or other external control.

An additional strategy for achieving autonomous directional control for active colloids is inspired by the ability of self-motile organisms such as E. coli to display chemotaxis i.e. navigate in response to solution composition gradients [2]. To achieve this function, E. coli rely on temporally sensing local levels of the target chemical and then adjusting their flagella to execute running and tumbling trajectories. While such complex sensing and response is not possible for current active colloids, there are several examples of active colloids accumulating in response to a gradient in the fuel molecules that drive their motion. The first
example of chemotaxis for active colloids was reported for bimetallic nanorods by the Sen group in 2007 [14]. However, more recently chemotaxis was investigated in more detail by establishing well defined fuel gradients using a microfluidic channel. In this study it was found that both Janus active colloids and tubular bubble swimmers showed a tendency to move towards higher fuel concentration regions [43]. Similar to the original nanorod report, so called “match-stick” shaped swimmers were also observed to move towards higher fuel regions [44]. Interestingly, these experiments are in disagreement with predictions for the direction of chemotaxis made by simulations [45], and the exact mechanism for these phenomena is unclear (readers are directed towards the review by Golestanian [46] for a description of possible scenarios). The benefit to applications for this approach is the potential for active colloids to autonomously follow signals, to allow delivery of cargo in a particular region or accumulate to perform a specific task. To achieve this it is desirable to expand the range of chemotaxis inducing signals. Solution properties including conductivity [47] and certain small molecules [48] are known to modulate propulsion velocity, and so should also allow a chemotaxis response. Indeed, one very recent report has demonstrated that metal organic framework swimmers powered by peptide assembly can be autonomously directed towards a target based on the interaction of the propulsion mechanisms with local pH gradients [49]. In addition, size changes in a responsive material incorporated within the active colloid have also been proposed to allow chemotaxis within a uniform fuel concentration solution [45].

2.2. Solution compatibilities

Another key requirement for using active colloids to enable future applications is that they can produce autonomous motion within a wide range of solution compositions. However, a restriction for many current active colloids is the requirement for a dissolved fuel source. The most common fuel for active colloids is hydrogen peroxide, often catalytically decomposed by platinum. While this combination provides an experimentally convenient room temperature catalytic reaction, the applicability for real world applications is limited due to the potential for the highly chemically active fuel molecules to be incompatible with other material contained within the solution in which active colloids are to be deployed. An example is human blood; which contains catalase, the biological enzymatic equivalent of platinum, which would also compete to decompose hydrogen peroxide fuel. In addition, the evolution of oxygen gas, a by-product of the hydrogen peroxide decomposition, is undesirable, as at high active colloid volume fractions convection inducing gas bubbles are inevitably produced which would hamper the directional control approaches described above. Fuel depletion also limits the duration of active colloid propulsion in high active colloid densities.

One approach to overcome these problems is to use different catalyst and fuel combinations. For example, a significant improvement in efficiency, which potentially ameliorates fuel depletion and bubble formation issues was recently demonstrated for active silica Janus colloids using an iridium catalyst to decompose hydrazine [50]. Rather than the 1–10% fuel contents required for the Pt–H₂O₂ system, enhanced motion was observed for N₂H₄ at 0.0000001% fuel. However, it is more desirable to remove the need to add fuel, and instead produce motion driven by the solution in which the active colloids are to be deployed. Examples of this type of active colloid are starting to appear, for example a manganese based Janus swimmer will produce enhanced hydrogen bubble propelled-motion within sea water, due to the transition metals’ corrosion properties in the presence of high chloride ion concentrations [51]. However, in common with many bubble propulsion examples, this demonstration still required the addition of a surfactant to the swimming solution, and in contrast to the Pt and Ir examples the driving reaction is no longer catalytic, so the reacting part of the colloid is consumed, limiting the motion producing period to just over a minute.

Another solution compatibility issue faced by some active colloidial systems is that the propulsion mechanism is quenched by the addition of small levels of dissolved salt. A reduction in propulsion velocity with solution ionic strength was reported at the early stage of development for bimetallic nano-rod swimmers, and a similar limitation has recently been found for single metal Janus active colloids [47,17]. This reduction in propulsion velocity does not correspond solely to a reduction in the motion producing reaction rate, but instead reflects a reliance of the propulsion mechanisms on self-generated ionic flows. In the context of current understanding of propulsion mechanisms for single metal Janus colloids this observation has led to the conclusion that a major component of propulsion velocity is generated by an electrokinetic mechanism [17], as opposed to the originally suggested self-diffusiophoresis [52]. Bubble propulsive swimmers do not suffer from the same general limitation, as bubble release is not strongly hindered by increased ionic strength, although this device type are still subject to a variety of other solution compatibility issues [53].

It is clear that despite a variety of approaches to improving the solution compatibility for active colloids, at present a number of obstacles to a widely deployable active coloidal system still exist: electrokinetic
swimmers require low salt concentrations, bubble propulsion often requires surfactants and recent fuel-free alternatives require materials to be consumed in order to generate motion.

2.3. Manufacture

While research into active colloids is currently at the lab-scale, to realise applications it is important that some attention is devoted to the cost and scalability of production. Few of the common lab based methods to produce the active colloids used in research programmes are currently either financially viable or scalable, as they often require both access to expensive instrumentation and expensive metal catalysts and result in very small batches of colloids. Much of the cost associated with manufacturing active colloids is the effort required to generate the asymmetry needed to produce propulsion. For example, bimetalllic nano-rod manufacture requires an expensive porous template, and a multistage electrochemical process, while producing Janus structures most often exploits the directionality of thermal metal evaporation, performed using expensive high vacuum apparatus. While nanotube bubble swimmers do not require a Janus structure, localising catalyst within the interior of a nanotubular structure remains challenging to scale up. However, bubble propulsion can also result from symmetrical activity at the outer surface of colloidal bodies. One recent example used this to manufacture a bubble swimmer using a solution based process where the platinum catalyst self-assembled onto a polymer lamella body [54]. Despite being easier to make, the drawback with these symmetrical bubbling devices is that their trajectories are chaotic, and they exhibit short persistence lengths, making them hard to harness for autonomous directed transport. [24] An extension then, is to develop solution based methods to not only produce chemical activity, but also to impart the asymmetry which leads to directional motion. One approach to achieve this is to exploit Pickering emulsions, where a wax like material is mixed with colloids, resulting in a suspension of larger wax particles into which the smaller colloids are partially embedded. This allows solution chemistry to be carried out selectively on the exposed surface of the colloids, providing a simple and scalable route to asymetrically chemically active structures. Despite the potential for this method, it has to date only been used in one prominent example, where selective amination of one side of the active colloid enabled decoration with the enzyme catalase, resulting in bubble propulsion via decomposition of hydrogen peroxide [55]. Considering material costs, recognition of the potential to source readily available enzymes to power active colloid motion was highlighted in a study that demonstrated that sufficient catalase was contained in various unprocessed plant materials to produce bubble propulsion, which could be further directionally controlled by applying an impermeable mask to one side [56].

2.4. Function

The final key requirement for active colloids is that in addition to being able to autonomously produce motion and be appropriately directed, they must possess the capacity to perform a useful function. Most visions for the future applications for active colloids have focused on transport, and so the ability to attach cargo, ranging from small molecules to micron sized components, at the surface of active colloids has achieved considerable attention. The promising aspects of these reports is the demonstration that active colloids of all major types (rods, tubes and Janus spheres) are compatible with additional chemical functionalization stages required to attach cargo. A particularly important older autonomous example is the demonstration of dynamic selective protein loading onto a bubble propulsive nanotube [57]. However, frequently these transport demonstrations have been at the expense of autonomy, with cargo release requiring external actuation [58], and cargo loading being performed as a separate stage before directed transport commenced. Illustratively, a recent example for cargo transport function from the Sanchez group, shows the potential to exploit the porosity of silica Janus colloids. In separate stages, this work showed small molecules could be diffusively loaded into exposed pores, that active colloid transport could be used in conjunction with physical guidance to concentrate the colloids at an enhanced rate in a well-defined location, and that sustained release from the pores was also possible [18]. While clearly showing future potential, accomplishing the loading and release phases autonomously in synergy with active transport was not possible. Incorporating responsive materials to gate release behaviour from the pore was consequently suggested as a future extension to address this issue. In addition to transport, some researchers have demonstrated more easily obtainable functions that rely simply on existing features of active colloids, for example being the demonstration that bubble propulsive nanotubes enhance mixing rates considerably due to a combination of bubble generation and enhanced motion [59]. Other autonomous functions include the very recent development of catalyst powered spiral shaped devices that can potentially drill into soft materials [60].

3. Current application areas

The remainder of the review further illustrates the extent to which the existing active colloids meet the challenge of demonstrating autonomous applications in three different areas, each requiring a different combination of the attributes discussed above.

3.1. Environmental applications

Each application area for active colloids will require differing features from the existing toolkit of demonstrated capabilities to be used in order to realise a new autonomous technology. One area that has been attracting recent attention is environmental remediation. The concept is that active colloids can perform a function such as neutralisation of a harmful agent, taking advantage of enhanced motion to result in more frequent contact with the contaminants. For this application, less demand is placed on the ability to direct active colloids towards a target, as it is viable to deploy them specifically at the site of contamination, which will often be locally homogeneously dispersed. However, the ability to produce fuel free motion is likely to be key, as the idea of releasing an additional chemical fuel into a contaminated environment is unlikely to be palatable. Two examples from the Wang group have used fuel-free bubble propulsive motors to demonstrate remediation functionality. One example combines the ability of manganese colloids to produce motion in seawater discussed above, with a functional photocatalytic layer of titanium dioxide capable of decomposing an anthrax mimic contaminant along with other chemical warfare agents. This study illustrated that the enhanced motion improved solution mixing as well as self-cleaning the functional surface, allowing a much increased rate of decontamination, Fig. 4i [61]. A second example using a similar motor particle showed that adding a hydrophobic coating enabled the function of oil droplet collection, Fig. 4ii [51]. This study used magnetic steering, however this does not appear to be crucial in order to perform the oil collection function. In both cases, while the active colloid motion was fuel free within chlorine rich aquatic solutions, a surfactant additive was required to instigate motion. This limitation does not however appear to be universal for all bubble propulsion, for example platinum based bubble swimmers decomposing hydrogen peroxide can produce motion without any additives [23]. Potentially engineering the surface roughness in these systems to increase the local gas evolution rate can overcome the need to add surfactant and realise truly autonomous demonstration of an environmental clean-up task. Environmentally relevant functions have also been demonstrated for nanotube active colloids, for example using Fenton oxidation to degrade organic contaminants, however these colloids did require added fuel to function [62].
potential solution incompatibilities are also present for lab-on-a-chip applications, where samples for analysis include biofluids, and potentially high salt content environmental samples. In an ideal implementation active colloids will be compatible with an un-adulterated sample. However, it may also be practical to implement initial sample processing stages such as the separation of components of a biological fluid, and addition of fuel as part of a lab-on-a-chip technology, thereby lessening these restrictions. Furthermore, for other important application areas such as water testing, solution compatibility challenges are in any case considerably reduced.

Against this background, two separate recent studies illustrate the potential for deploying active colloids as lab-on-a-chip transporters. The first demonstrates that multi-stage highly specific immunoassays can be conducted using nanotube swimmers [63]. A key feature of this study is that the active colloids were transferred between different connected chambers, enabling a sequential series of chemical processes to be executed to collect and label a specific protein. Active colloidal swimmers pre-functionalised with an antibody for a specific protein analyte are loaded into a chamber, then navigated to a second chamber filled with a mixture of target protein, and other adventitious proteins where binding occurs. Finally the motors are driven to a third compartment where a second "sandwich" binding colloid functionalised with a second complementary antibody can label any bound analyte, Fig. 5. The study convincingly shows that antibody functionalization of an active colloid can enable selective attachment and transport of a specific protein. This method was also extended to collect a bacterial cell with a specific protein in its cell wall. To support active colloid motion in this system, the entire network of microfluidic chambers was flooded with a solution containing surfactant and peroxide fuel, and the biological binding tolerated these conditions. In addition, the enhanced motion of the motor was found to speed up the protein binding events. Another feature of this work is a consideration of the route to manufacture was made, which has led to the use of a polymeric material as the substrate for attaching the bio-recognition molecules, in contrast to other studies that require gold substrates. However, the significant missing ingredient from this example is an autonomous guidance function, instead the motors are steered using an external magnetic field, which must be re-orientated at the correct moment to produce the desired active colloid path and residence times throughout the device. In this context, a second recent study also concerning nanotube swimmers displays both the ability for selective binding (in this case streptavidin used to attach biotinylated components), Fig. 5, and also uses heart shaped fluidic cells to autonomously concentrate the colloids within a spatially well-defined region of the cell (see Fig. 3d) [64]. Unfortunately the two operations of binding and autonomous concentration by physical structures involved manual transfer of the colloids between different solutions. However, taken together with the previous example, it is clear that the potential to implement a useful lab-on-a-chip assay autonomously using active colloids is moving closer.

3.3. In vivo applications

One of the original motivations for the active colloid field was based on futuristic visions of miniature devices moving with the body to effect repairs or deliver drugs. To this end, recently, reports of active colloids being deployed within living animals have been published, indicating the first steps towards this challenging goal are being made. In the first example of in vivo animal model testing for active colloids, bubble propulsive tube swimmers made from zinc and a polymeric matrix were administered orally to mice [65]. Within the acidic environment of the mouse stomach, the zinc reacts to produce hydrogen bubbles, producing propulsion without the requirement for external fuel or other additives. The effect of this active motion was to drive the tube swimmers into the stomach lining, thereby enhancing their residence time beyond that for inactive controls. The study also demonstrated that mixing gold nanoparticles within the matrix of the device allowed these to be released in the stomach lining as the zinc was degraded.
again showing increasing retention compared to conventional administration, Fig. 6. Assessments of toxicity were also made, with no concerns being noted. This suggests a novel route for drug delivery that can lead to a viable application. Additional separate investigations for potential in vivo toxicity have also been made for gold-platinum nanojet swimmers and these encouragingly confirmed that the viability of a cell line was not affected by incubation with the active colloids [66].

Other potential future envisaged in vivo applications for active colloids could involve them moving within the bloodstream, for example to repair arteries. For this reason, and also to move closer to the ability to implement lab-on-a-chip analysis of blood samples with minimal sample preparation, active colloid motion within fluids containing components of blood have been performed. In one report it was found that blood proteins considerably reduced the mobility for Cu/Pt microtubular motors, an observation qualitatively assigned to fouling of the catalytic surface and solution viscosity [67]. However, more promisingly, Fe/Pt microtubular motors were found to produce motion at physiological temperatures in diluted serum and red-blood cell containing solutions. Raising the temperature of the fluid above ambient served both to increase catalytic activity and reduce solution viscosity, enhancing the observed bubble release rate and the resulting propulsion speeds [68].

While it is clear that there are in vivo applications such as drug delivery to the stomach described above that do not require a navigation function, it is also apparent that more sophisticated drug delivery and repair tasks will require active colloids to have the ability to navigate and respond to their surroundings. Autonomous navigation for any motor type for an in vivo application has yet to be demonstrated. There is however potential for phenomena such as chemotaxis to be used to enable accumulation of devices in response to the many solution gradients found within the body, while another interesting possibility is to exploit the flows present in the body to align active devices [25,69].
testing [52]. In this context it appears that developing the active colloid field beyond the current state of the art will be most efficiently accomplished by fully utilising theory and models to overcome existing barriers. As highlighted above, two of the most significant attributes for a useful autonomous active colloid system are to be widely deployable in a range of solutions, and to possess a robust autonomous guidance strategy. Theory and models provide valuable insight to help address both of these aims. For example, much theoretical effort has been devoted to understanding the numerous physical and chemical properties that determine the propulsion velocity for a given device [70], and making use of this information can consequently ensure that future devices are designed to generate maximum performance from a given driving mechanism subject to specific solution constraints. In addition, due to the ability for theory and modelling to access scenarios that are currently hard to realise experimentally, studies using this approach can lead the way for new approaches to guiding active colloids. Of particular interest is the ability for models and theory to predict collective behaviours that may emerge for large numbers of active colloids beyond those that can be currently observed due to experimental restrictions such as gas evolution or fuel depletion [71]. For example, one recent study shows the general requirements for a catalyst patterned colloid to be aligned and directed by a chemical gradient, which provides a promising route towards autonomous direction as described above [46]. In addition, the lack of physical constraints then allowed a phase diagram to be generated, predicting a rich variety of multi-body interactions under differing fuel concentration and product/reactant diffusion rates that lead to collective motion phenomena. It is these and other theoretical insights that will inspire experimentalists to perform new experiments that will further expand the range of guidance methods currently available for active colloids, and ensure the continued development of the field towards future applications.

5. Conclusions

This article has presented a summary of recent advances towards autonomous applications for active colloids. Both fundamental studies reporting specific behaviours such as autonomous navigation capacity, and reports that have been presented as steps towards end applications have been considered. Table 1 presents an overview of the features and functions displayed for the major active colloid types. From this survey it is apparent that the active colloid field is approaching a maturity where viable applications are within grasp. A chief indicator for this is

Table 1
Summary of existing features for the current major types of active colloid.

<table>
<thead>
<tr>
<th>Geometry</th>
<th>Chemistry</th>
<th>Bubbles?</th>
<th>Navigation capacity</th>
<th>Demonstrated solution compatibilities</th>
<th>Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rod</td>
<td>Catalytic</td>
<td>No</td>
<td>External field [72]</td>
<td>Low salt solutions with added peroxide fuel</td>
<td>Cargo transport [73]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physical guidance [40]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spherical Janus</td>
<td>Catalytic</td>
<td>No</td>
<td>External field [35]</td>
<td>Low salt solutions with added peroxide fuel</td>
<td>Cargo transport [35]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physical guidance [41]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spherical Janus/ Symmetrical Activity</td>
<td>Catalytic</td>
<td>Yes</td>
<td>None demonstrated</td>
<td>Aqueous solutions with added peroxide fuel</td>
<td>Cargo transport [55]</td>
</tr>
<tr>
<td>Spherical Janus</td>
<td>Reactive</td>
<td>Yes</td>
<td>External field [51]</td>
<td>Acidic/basic solutions + often requires surfactants</td>
<td>Oil clean-up [51]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physical guidance [42]</td>
<td></td>
<td>Chemical remediation [62]</td>
</tr>
<tr>
<td>Tubular</td>
<td>Catalytic</td>
<td>Yes</td>
<td>External field [74]</td>
<td>Peroxide fuel + often requires surfactants</td>
<td>Selective “fly by” capture of proteins + cells [67]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physical guidance [43]</td>
<td></td>
<td>Enhanced mixing [59]</td>
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<tr>
<td>Tubular</td>
<td>Reactive</td>
<td>Yes</td>
<td>External field [27]</td>
<td>Acidic solutions</td>
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</tr>
</tbody>
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The image contains a figure labeled Fig. 6, which is not described in the text.
the very recent report where active colloids were found to have the potential to deliver drugs within a live animal model [65**]. In addition, the state of art concept demonstration for environmental remediation is only limited by the requirement for added surfactant, which does not appear to be a fundamental obstacle, based on reports for similar motors moving without this additive. Both these demonstrations are intrinsically autonomous: functions can be executed without the application of external fields or external monitoring. For lab-on-a-chip applications, such as executing multistage analyte recognition and labelling processes, both the essentials of autonomous guidance and the required selective cargo attachment chemistry have been separately demonstrated. Equally promising is the emergence of additional new fundamental autonomous guidance strategies based on gravitational fields, physical structures and chemical signals. It is appears that combining these new approaches to navigation with the existing ability to collect and transport biological materials may enable new static microfluidics systems to be realised. It is also apparent that solution compatibilities remain a key barrier to widely deploy active colloids. In this context it appears that fundamental studies to elucidate the absolute theoretical barriers to propulsion mechanisms, together with continued efforts to utilise biological and synthetic chemical reactions within these constraints has the potential to produce further gains. Finally, while the engineering considerations for active colloids such as material costs and scalability have received less attention, strategies for producing motors without adding fuel are highly desirable. This report describes a tubular active colloid meeting this requirement.


Ability to demonstrate physical guidance for Nano tubular active colloid device.


First example of a chemotaxis phenomena for active colloids that does depend on a fuel gradient.


[64] Restrepo-Pérez L, Soler L, Martínez-Cisneros C, Sánchez S, Schmidt OG. Biofunctionalized self-propelled micromotors as an alternative on-chip concentrating system. Lab Chip 2014;14(16):2914–7. This study shows that micro motors functionalised with biological material can be autonomously concentrated within a microfluidic device.


