1. Introduction

In his famous 1959 lecture “There’s plenty of room at the bottom”,[20] Richard Feynman introduced the idea of very small machines that can be used to move through their surroundings and potentially perform a myriad of tasks, from manufacture to microsurgery. While we are still a good deal away from this futuristic vision, the last decade or so saw the development of the first microstructures, with sizes between hundreds of nanometers and several micrometers, which can be actuated and controllably propelled through various fluids.[7,21] And even with these relatively simple systems, researchers have not been shy about foreseeing and proposing all kinds of applications, from biomedical uses like nanosurgery,[22,23] drug delivery and cargo transport,[3,22,24-26] and remote sensing and diagnostics,[22,24,27,28] to self-assembly of superstructures,[29] and environmental remediation.[3,30,31] However, none of these have at this point been implemented beyond a proof of concept demonstration.

While some of these envisioned applications might be more realistic than others, almost all of them require certain improvements and further developments in order to be at all feasible, and in order to determine how promising the intended applications actually are. Necessary advances include external hardware development, for issues like power transmission and imaging, as well as modifications to the microstructures themselves. The present work deals exclusively with the latter. The type of particle investigated here is a helical screw-shaped one, which includes a magnetic section and can be propelled by the application of an external rotating weak magnetic field, which causes the particle to rotate and consequently translate due to its inherent chirality. The advantage of this approach is the absence of fuels used by other designs, and thus the avoidance of additives which are potentially toxic or otherwise harmful to the respective surrounding, and which are furthermore generally subject to a concentration decline over time.

To bring these micropropellers a little closer to useful applications, first and foremost fabrication techniques have to be optimized for high relative and absolute yields. Just a small number of these actuated particles by themselves will only be of limited use in many applications, particularly those where more than a very limited area, say one single cell, needs to be targeted. And large amounts of debris that are not able to navigate to the targeted site will in many cases undo precisely those advantages that actively propelled particles might have over conventional approaches. Fabrication approaches that preceded the work presented here generally achieved only one of the above mentioned objectives. They produced micropropellers either in high numbers[7] or high yields with a minimum amount of debris.[32] Recently, a technique was demonstrated which could potentially achieve both by template electrosynthesis, although no values for the yield were reported.[33] In Chapter 3 an approach is presented that optimizes an already established method to produce large numbers of helical colloids with defined shape and functionality.[8] By reducing the number of fabrication steps, yields are improved significantly. This, among other potential benefits, enables them to be used as model systems to investigate various phenomena and molecular processes, in experiments that require very clean and uniform colloidal systems. This is demonstrated by visualizing on a colloidal scale the “propeller effect”, which was proposed for molecules by Baranova and Zel’dovich in 1978,[10] but has so far not been observed experimentally on a molecular scale.

Other necessary developments for many applications include strategies for actuation in biological fluids. This encompasses two objectives: The micropropellers would have to be stable in the respective medium, and be able to propel through it. The stability in several biologically relevant solutions of the magnetic section of micropropellers has been achieved by various coatings.[1,34] Concerning the propulsion capabilities however, earlier demonstrations were almost always preformed in low viscosity Newtonian fluids like water or serum.[1,2,7,35] Venugopalan *et al.* achieved both stability and propulsion of magnetic microhelices in blood, which is a non-Newtonian fluid due to a shear thinning effect caused by the suspended cells.[34] Nevertheless, blood still has a rather low viscosity, as it is specifically designed to flow through narrow channels at high velocity. Many other biological fluids and tissues in which applications of micropropellers might be attractive, however, have much more complicated rheological properties, often including highly viscoelastic behavior caused by extended three dimensional networks of various biopolymers, in addition to cells, proteins, and other components. Chapter 4 presents one viable approach for controlled actuation of particles in biologically relevant viscoelastic gels. Hyaluronan, which was used as a model biological fluid in this work, forms networks with mesh sizes on the order of several tens of nanometers. Whereas the micropropellers reported previously, with diameters of hundreds of nanometers, are not able to move through these solutions, much smaller helices with filament diameters of only 70 nm are able to do so. Whereas these nanopropellers, which are the smallest of its kind reported to date, do not effectively propel through water due to strong thermal motion, they do propel in solutions of higher viscosity, and penetrate the viscoelastic HA gels even more effectively than Newtonian fluids.

Naturally, every biological fluid is different, and most likely a different propulsion strategy would have to be devised for each targeted medium. In addition, while the results mentioned above demonstrate that the size can be crucial when it comes to delivering particles into a biological system, strategies that do not rely on an exact propeller size are generally desirable, as they allow for more flexible designs that are tailored to the respective application without being limited by a maximum diameter. In Chapter 5, an approach for the propulsion of micropropellers in solutions of gastric mucin is presented. The previously used HA is in many respects a relatively simple model of a viscoelastic biological fluid, since the polymer chains do not interact measurably with the colloidal helices. Gastric mucin on the other hand is known for its tendency to adsorb strongly to surfaces, a phenomenon termed muco-adhesion, and to reduce particle motility in the process.[36,37] In fact, with mucus being the first layer of defense on every surface of the body where substance exchange with the environment takes place, as for example in the airway system and gastro-intestinal tract, mucin is specifically designed to allow for the transport of small molecules like nutrients or oxygen, but prevent the penetration of micron-sized structures that include most pathogens.[38,39] But for this reason it is of high interest to achieve efficient propulsion in this system, particularly because mucin polymers are ubiquitous in nature, and an approach to realize efficient propulsion of micropropellers with (almost) arbitrary diameter in this medium presents an important step towards eventual applications. Since gastric mucin generally occurs at low pH values in the lining of the stomach, a passivation technique is presented that stabilizes the magnetic layer against oxidation in acidic environments. In addition, approaches to reduce muco-adhesion are explored. As a final step to realize navigation of micropropellers through mucin gels, a strategy copied from the bacterium *Helicobacter pylori* [18] is demonstrated, which employs urease to alter the local pH value and lower the gel's viscoelasticity in the process to allow for propulsion through the mucus. This approach has a certain elegance, since it changes the surrounding fluid's properties reversibly, and is therefore minimally destructive to its environment.

The results presented in this thesis have in part been published (or will be published in the near future). In particular, figures and excerpts were taken from the following sources:

Chapter 3:

Schamel, D.; Pfeifer, M.; Gibbs, J. G.; Miksch, B.; Mark, A. G.; Fischer, P.: Chiral Colloidal Molecules And Observation of The Propeller Effect. *J. Am. Chem. Soc.* **2013**, *135*, 12353-12359.

Chapter 4:

Schamel, D.; Mark, A. G.; Gibbs, J. G.; Miksch, C.; Morozov, K. I.; Leshansky, A. M.; Fischer, P.: Nanopropellers and their Actuation in Complex Viscoelastic Media. *ACS Nano*. **2014**, *8*, 8794-8801**.**

Gibbs, J. G.; Mark, A. G.; Lee, T.-C.; Eslami, S.; Schamel, D.; Fischer, P.: Nanohelices by Shadow Growth. *Nanoscale.* **2014**, *6*, 9457-9466.

Chapter 5:

Walker, D.; Käsdorf, B.; Jeong, H.-H.; Lieleg, O.; Fischer, P.: Enzymatically Active Biomimetic Micropropellers for the Penetration of Mucin Gels. *Sci. Adv.* **2015**, accepted manuscript.

In addition the following work has appeared, but is not included in this thesis:

Walker, D.; Kübler, M.; Morozov, K. I.; Fischer, P.; Leshansky, A.: Optimal Length of Low Reynolds Number Nanopropellers. *Nano Lett.* **2015**, DOI: 10.1021/acs.nanolett.5b01925.

Anderson, L. J. E.; Kirchner, S. R.; Schamel, D.; Fischer, P.; Lohmüller, T.; Feldmann, J.: Light-driven Rotation of Helical Microstructures in a Fluidic Environment. *Conference on Lasers and Electro-Optics (CLEO) - Laser Science to Photonic Applications*. San Jose, CA, USA, **2014**.

Qiu, T.; Schamel, D.; Mark, A. G.; Fischer, P.: Active Microrheology of the Vitreous of the Eye Applied to Nanorobot Propulsion. *IEEE International Conference on Robotics and Automation (ICRA)*. Hong Kong, China, **2014**.

Qiu, T.; Gibbs, J. G.; Schamel, D.; Mark, A. G.; Choudhury, U.; Fischer, P.: From Nanohelices to Magnetically Actuated Microdrills: A Universal Platform for Some of the Smallest Untethered Microrobotic Systems for Low Reynolds Number and Biological Environments. In *Small-Scale Robotics: From Nano-to-Millimeter-Sized Robotic Systems and Applications*; Paprotny, I., Bergbreiter, S., Eds.; Springer: Berlin, Germany, **2014**, 53-65.

2. Theoretical Background

The present chapter is intended to give an introduction to general concepts, as well as state-of-the-art techniques related to micro- and nanopropellers, and their applications. Chapter 2.1 covers the basics of propulsion at small length scales. It gives an overview of available actuation strategies, followed by an analysis of the propulsion mechanism of magnetic propellers in a Newtonian fluid at low Reynolds numbers. Finally the influence that Brownian motion has on helical propulsion is discussed. Since the propulsion strategy employed here requires particles with low symmetry and magnetic properties, Chapter 2.2 provides an overview over available fabrication techniques for low-symmetry micro- and nanoparticles. Glancing Angle Deposition (GLAD), the technique used in this work, is described in more detail. Finally, Chapter 2.3 introduces the additional challenges that one faces when navigating small structures in biological fluids. Model fluids used in this work are described, and the effect that their chemical, as well as their complex rheological properties have on propulsion in and penetration of biological systems, is discussed.

2.1 Controlled Motion of Microscopic Structures

One of the first questions that need to be asked when attempting to controllably navigate very small structures, is how should they move? More specifically, how can they be powered, and how can their motion be controlled? The following section is intended to give an overview about strategies that have been designed to actuate and steer micro- and nanostructures. Magnetic propulsion, which is the focus of this thesis, is analyzed in detail.

2.1.1 Actuation Strategies and “Microrobot” Designs

One of the most precise methods to control and manipulate microscopic structures involves optical tweezers. They make use of an intensity gradient in a focused laser beam to trap and