Chapter - 2

Literature Review

2.1 Introduction

In the previous chapter, the existence of life at micron level and locomotion of micro-organisms is discussed in literature as presented in section 1.1. The importance of artificial nanoswimmer in biomedical applications along with different designs of flagella bearing mastigonemes is discussed briefly. For nanoswimmers, on-board volume is a precious and limited commodity, consequently there is a need of design of on-board energy transduction system using piezoelectric biocompatible material for locomotion of artificial nanoswimmer as presented in Chapter 1.

Locomotion at micro/nano domains is a challenge and has drawn attention from researchers from last few decades. Inspired from nature, researchers have proposed and mimicked the natural swimming nano-bio-organisms, which use rotating or beating flagella to locomote a nanoswimmer. The mode of propulsion, also known as flagellar propulsion has been explored extensively in literature to study propulsive characteristics of artificial nanoswimmer such as propulsive force/thrust force, rotational velocity and propulsive efficiency in various fluidic medium via different propulsion mechanism. However, chemical and magnetic methods have gained interest of researchers in past decade owing to advantages like high thrust force and wireless control. A hierarchical classification of the propulsion of an artificial swimmer is shown in Figure 2.1. The review summarizes chronologically the flagellar propulsion attempted at macron scale for planar and helical modes of propulsion. In literature it was mentioned that planar wave is more efficient (3 to 7%) than helical wave motion (0.2 to 1%) for same geometric parameters [1]. Therefore, planar wave motion is preferred more than helical motion. Different theories have been developed and published in literature which is also being validated through experimental analysis at scaled up level. The chapter is divided in two parts the artificial swimmer investigated experimentally at macro-scale as well as micron-scale. In the succeeding section locomotion at macron scale is discussed in detail to corroborate the theoretical models.

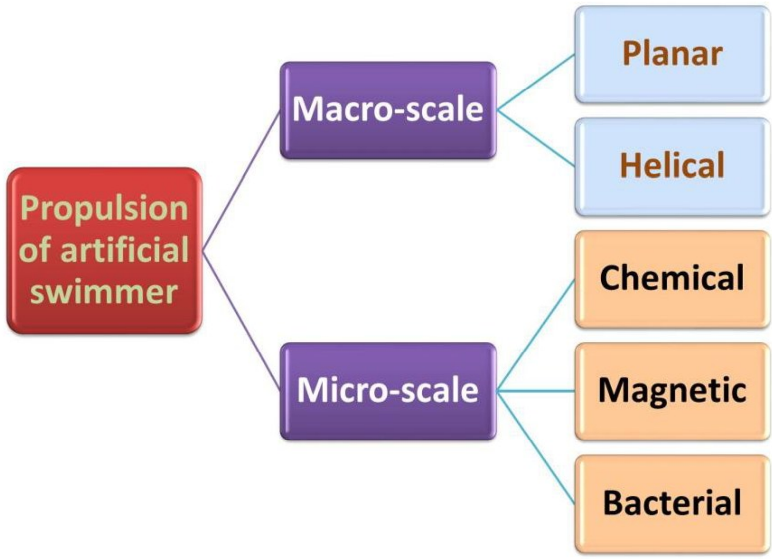


Figure 2.1: Classification of propulsion mechanism for artificial swimmer

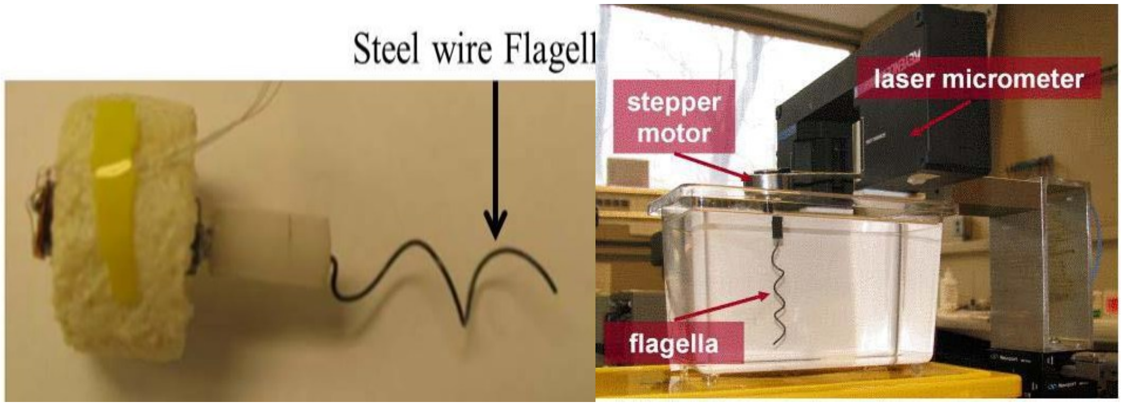
Most of the research of locomotion at micron-scale is attempted in last two decades while flagellar propulsion has been studied for over seven decades. Researchers are also interested to study the propulsive characteristics of flagellated nanoswimmer. Two major modes of propulsion displayed by microorganisms are planar propulsion and helical propulsion. Flagellar propulsion is one of the mechanical modes of propulsion which needs to be reconnoitred. Contribution of biologists, physicists, mathematicians and engineers leads to development of various theories and validation of it through experimental investigation over last seven decades. Since 1951, modelling of physics of planar and helical flagellar propulsion has been explored through resistive force theory (RFT), slender body theory (SBT), boundary element method (BEM) and bead model (BM) [1]. Few experiments have been attempted towards realization and validation of these theories. The following sections present the macro scale experimental studies attempted in the field of flagellar propulsion. To progress the design of nanoswimmer, material is also one of the major point needs to be considered and which should be biocompatible for biological applications. Further gaps in the research work are presented and problem statement is decided to be worked out.

2.2 Locomotion of Macro-Scale Biomimetic Artificial Nanoswimmer

Researchers have performed experiments to design flagellated artificial nanoswimmers, by using variety of stiff materials and have investigated their propulsive characteristics in terms of swimming speed, rotational velocity, propulsive efficiency and thrust force generated in various mediums via different actuation methods. Due to certain technological limitations, it is difficult to design, fabricate and study such a micro scale phenomenon and experimental set-up. In order to overcome this issue, researchers have designed test-rig and conducted scaled up experiments to prove the theoretical studies performed to date. The dynamic similarity in between the actual phenomena and macro-scales experiments is achieved through Reynolds number similitude. The geometrical parameters are scaled-up to a desired value using Buckingham Pi theorem and the other parameters such as fluid medium and actuation frequency is selected accordingly. It must be seen that Reynolds number for bio-microorganisms are very low. In this instance, viscous forces are more dominant for propulsion and inertia can be ignored. So, it is essential to design a propulsion system for flagellated nanoswimmer that works for low Reynolds number. So as to realize, we did literature review chronologically, on the experimental investigation attempted to locomote flagellated nanoswimmer at scaled up level through planar and helical mode of propulsion at low Reynolds number also shown in Table 2.1.

In 1996, Honda et al. [2] fabricated centimetre size robot and immersed in silicon oil having viscosity 10 St and 100 St instead of water to maintain low Reynolds regime. $SmCo_5$ magnet was attached to spiral copper wire so as to remotely control the swimmer. $SmCo_5$ magnet rotates when rotating and alternating magnetic field was applied perpendicular to the axis of spiral copper wire. The driving mechanism was propelling in direction opposite to the wave propagation and changing its speed while changing direction of rotation. Spiral wire connected to magnet was placed inside the 1.5 mm diameter of test tube. The magnetic-field was applied by peripheral magnet. The amplitude of swimming velocity was increased on increasing excitation frequency. The swimming frequency was observed 10-33 Hz and 2-5 Hz for 10 St and 100 St silicon oil. The experimental investigation has been confirmed by the results of Lighthill's theory. Swimming velocity was observed to be increasing on increasing length of wire because propulsive force increases against the drag on $SmCo_5$ magnet.

In 2005, Behkam and Sitti [3] developed a propulsive mechanism at scaled up level using Buckingham Pi theorem. Rotating flagella generated a thrust force in silicon oil medium matched well with RFT model. They also proposed that multi-flagella system may increase speed and efficiency of swimming robot as future which needs to be investigated and attempted in the research work (Figure 2.2). The advantages and disadvantages of magnetically propelled micro-swimmer were mentioned such as magnetically propelled swimmer does not require external power source while speed limitation is the main drawback. When driving frequency increases the rotational frequency of external magnetic field is not able to synchronize and hence velocity of micro-swimmer decreases. Such spiral type machines can swim in wide range of viscosity. Besides the speed constraint there are some other issues of magnetic field such as patient having metallic implant cannot acquire magnetic swimmer inside his body; patient need to stay for longer time inside the magnetic-field system as it will cause heating due to eddy current. By considering these issues, Behkam and Sitti proposed a miniaturized, safe propulsion system. A propulsion mechanism mimicking *peritrichous* flagella (*E. coli*) has been designed. Through mathematical modelling it was concluded that velocity and efficiency of biomimetic system depends on geometric parameters. An increase in diameter of flagella and diminution in size of the swimming robot leads to enhancement in efficiency and velocity of the system. A scaled up prototype is being designed by analysing the system parameter through Buckingham Pi theorem. The experiment is being carried out in silicon oil having viscosity 350 cSt rather than water to match the scaled up system with swimming micro-organisms. The flagellum made up of steel wire is connected to the prototype body consist of two-phase stepper motor which is mounted perpendicular on steel cantilever beam. A deflection data from laser micro-meter has been used to calculate thrust force. As we increased the frequency form 5 Hz to 15 Hz, thrust force also increases in accord with it. Experimental results has been conforming the theoretical results. They have mentioned the imprecision in experimental results due to uncertainty in measuring instrument, user and beam calibration process. In RFT both flagella end has been considered as free ends while performing experiments, flagellum is being attached at one end which changes the flow of surrounding fluid.



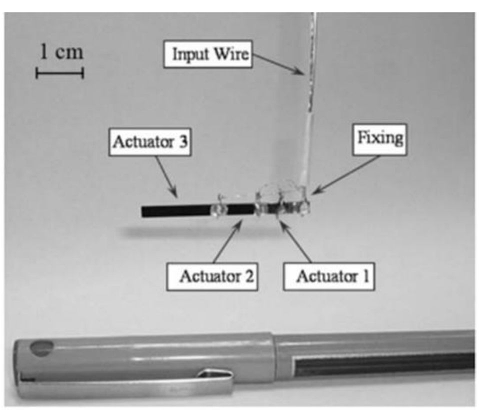
(a) **(b)**

Figure 2.2: (a) and (b) Rigid helical flagella designed to study propulsion system at scaled up level experimentally [3]

In 2006, Yu et al. [4] designed a planar propulsion system using scotch yoke lever mechanism, to oscillate flagella made up of stainless steel (Figure 2.3). A Robo-chlam body has given its name after algae *chlamydomonas* which is 8 cm in length consists of dc motor. Base angle was angularly propelled sinusoidally. Fabricated tail has been immersed in silicon oil of viscosity 3.18 Pas and to maintain low Reynolds number condition as exhibited by micro-organisms in the range of 10^{-2}-10^{-3}. The tail shape and propulsive force of beating flagella were measured and results were in comparison with the existing linear and nonlinear theories or RFT. Scotch yoke lever mechanism coupled with flagella was fastened to a cantilever beam and strain gauge has been affixed on opposite side of beam to measure deflection generated due to flagellar propulsion. As per their findings there could be sources of error in validation of theoretical results with experiments such as thermal drift and wall effects in the experimental investigation.

Figure 2.3: Designed elastic tail swimmer oscillate through DC motor [4]

In 2007, Kosa et al. [5] fabricated a tail made up of piezoelectric material and developed a planar propulsion system at macro scale. Fabricated microrobot contains payload and two piezoelectric tails made up of PZT material divided into three segments as shown in Figure 2.4. Propulsion has been achieved by applying voltage of same frequency (2800 Hz) but with different phase to different segments of tail. The propulsive force generated was coming around 4 mN which was comparable to the theoretical results. The fluidic elastic model has been analysed and verified experimentally at scale up level. 0.8 grams was the weight of fabricated PZT based actuator tail having width 0.6 mm and length 35 mm. The swimming tail has been dipped into gear oil (SAE80W90) to mimic natural swimming bio-organism in low Reynolds regime. A square wave of 60 V and 2800 Hz has been applied for piezoelectric actuation. Tail moved by 8 mm when actuator was activated. The propulsive force achieved during experiments was 0.403 μN while analytically propulsive force observed was 0.467 μN. In 2008, Kosa et al. [6], observed that the swimming tail moves backward and forward with propulsive force of 5.7 μN and 10.3 μN with frequencies from 1-150 Hz but Reynolds number was 300 which is larger to mimic micro bioorganism condition. It was observed from the experimental results that at lower frequency, propulsive forces were larger in value. They also mentioned effect of the head on the swimming of microrobot. If volume of head (925 mm^3) of swimming robot was 12 times the volume of swimming flagella (52.5 mm^3) then there was a reduction in propulsive force approximately 50%. It was observed from the data that as frequency decreases, propulsive force increases.



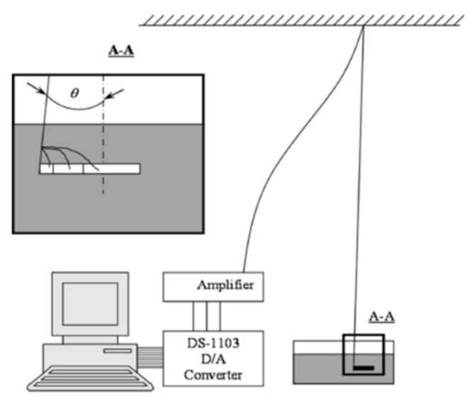


Figure 2.4: Showing the swimming tail divided into three segments and schematic of experimental system [5]

In 2009, Coq et al. [7] rotated elastic flexible filament at rotation speed varied from 0.01 to 10 RPM (Sp. Number – 10^{-1} to 10^{4}) inside a glycerine filled tank. The length of the tail was varied in the range of 10 cm to 2 cm by consecutively cutting it while it was attached to the motor. The Reynolds number was lying below 10^{-2} at available speed and viscous medium during the range of length. The experimental results have been matched with the theoretical values of thrust and torque. It was observed from the image capture that for $Sp<1$, the filament remains straight and for $Sp \approx 10$ filament bent.

In 2010, Ha and Goo [8] studied linear swimming velocity of single helical flagella attached to the ellipsoidal body using RFT. The macro-scale biomimetic helical swimmer was 6.5 mm in diameter and 55 mm in length. The wavelength, length and amplitude of aluminium wire which was used as filaments were taken as 9 mm, 27 mm and 2.5 mm. This aluminium filament was then connected to DC motor through coupler. Swimming velocity of macro-swimmer inside silicon oil medium having viscosity 350 cSt was measured on applying voltage 0.5 V to 3 V at step size of 0.5 V to DC motor. It was observed that velocity of swimmer increases on increasing voltage supplied to DC motor in the range of 0.5 V to 3 V. A finite element software ADINA was used to study the flow pattern around the helical filament with respect to Reynolds number. In simulation results flow pattern was observed same for different Reynolds number (0.01, 0.1 and 0.56).

In 2010, Fountain et al. [9] used non-uniform magnetic field to control magnetic helical microrobot leads to placement of it closer to the patient of body. It was better than uniform magnetic field system in terms of cost and size. Two techniques have been used to control microrobot; axial control and radial control. Change in direction of rotating permanent magnet (RPM) leads to change in direction of microrobot. A scaled up magnetic microrobot was fabricated from spring and cylindrical NdFeB magnet and immersed in water.

In 2011, Singleton et al. [10] investigated experimentally the multiple helical flagellum mimicking bacterial flagella attached to the single rotation axis as shown in Figure 2.5. To rotate each flagellum independently in multi-flagella arrangement was difficult and it also leads to negative thrust so as to eradicate these issue multi-flagella arrangement was attached to cylinder actuated magnetically. From the experimental results, it has been observed that flexible helices provide enhanced performance than stiff helical arrangement. Voltage applied to motor was such that frequency of motor remains in the range of 0.5 to 5 Hz. They also tested the practicality of using external magnetic field to propel the flexible helical system by submerging it inside 30000 cSt silicon oil filled in 44 mm diameter and 96.5 mm long acrylic tube, to keep Reynolds number 10^{-3}. They utilized multi-helical flagellar system to enhance the propulsive characteristics. At frequency 3.5 Hz, 15 mNm torque was generated by robot.

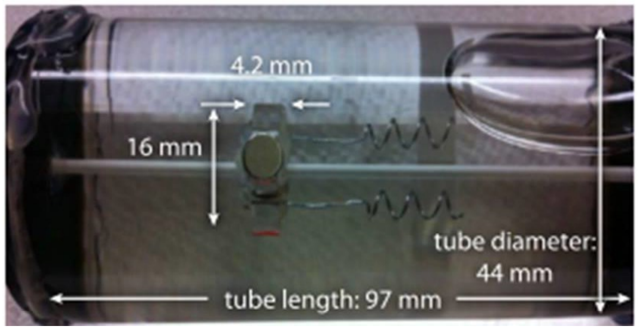


Figure 2.5: Prototype of swimming micro-robot inside a glycerol filled tube [10]

In 2011, Temel et al. [11] inspected experimentally the screw like motion of helical microrobot of 2 mm in length with radius in micrometers producing swimming speed in mms^{-1}. Head was fabricated from permanent magnet NdFeB. Four magnetic coils have been used to move designs of rigid helical microrobot having different dimensions in glycerol (10 Pas) under applied magnetic field in the range of 6.85 mT to 7.60 mT. Forward and backward motion of microrobot is achieved by rotating magnetic-field under applied rotating frequency of 5 Hz to 50 Hz. Experimental results have been validated through RFT. It was noticed that in glycerol medium the size of head and tail is important. The swimming microrobot with smaller head and larger tail with more helical turns move faster. In his succeeding work, Yesilyurt fabricated 12 different designs of helical macro-swimmer (1 mm diameter and 48 mm length) based on helical radius and pitch. Experimental investigations of these designs have been done in glass tube filled with silicon oil and linear and angular velocity was validated through RFT model. In 2012, Temel et al. group [12] conducted experiments in glycerol (1.412 Pas) filled Y and T shape channels as shown in Figure 2.6 made up of acrylic glass and under applied magnetic field (1-5 Hz) helical swimmer was moving forward and laterally. In their work copper helical tail was connected to NdFeB magnetic head for propulsion inside glycerol filled chamber. To study different swimming modes helical tail is rotated with frequency

1 and 5 Hz. On increasing the frequency of rotating helical swimmer, the position of swimmer is changed and move with faster velocity approximately 2.94 mms^{-1} while at lower frequency due to traction forces, swimmers try to roll itself.

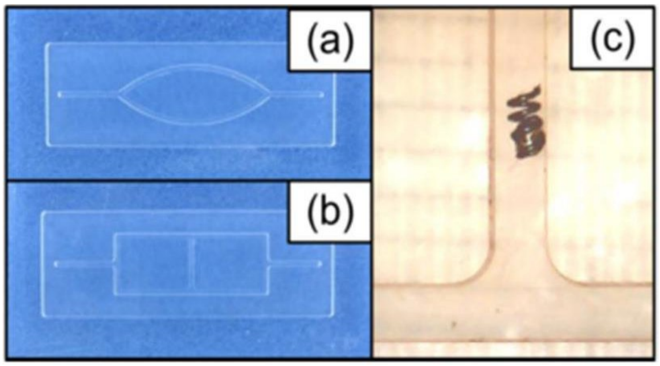


Figure 2.6: (a) Y-shape and (b) T-shape channel for millimeter size helical swimmer (c) [12]

In 2013, Rodenborn et al. [13] compared the experimental results of helical flagella (radius-6.3±0.4 mm and length-130±5 mm) immersed in silicon oil with results obtained by RFT, SBT and stokeslet method. The thrust force was measured for clockwise and anticlockwise rotation of flagella. It was shown that experimental results are in agreement with SBT and stokeslet method at low Re number. By varying the pitch of helical macroscopic flagella, the thrust force, drag and torque were observed as 80 mN, 66 mN and 6 mNm. The difference in value obtained by Gray and Hancock's and Lighthill for normal and tangential drag coefficients and forces in case of small pitch and longer flagella was mentioned. It was also stated that RFT got failed by neglecting hydrodynamic interactions created by different parts of flagella between flows.

In 2014, Xu et al. [14] observed that head did not influence the shape of propulsion characteristics but effect the cut off frequency value. The propulsive characteristic of scaled up helical nanobelts (SHN) as shown in Figure 2.7 was proposed first time. Comparison of propulsive characteristics has been made of helical swimmer with magnetic head and those with magnetic tail. To make the helical tail magnetic, they opted to cover it either by small magnets or by coating it by ferromagnetic material. The propulsive characteristics of these different types of magnetic tail have been compared. It was shown that square head produced larger drag torque than spherical and cylindrical heads and magnetic head was not mandatory to move the helical swimmer. Glycerol was used as medium to maintain low Reynolds number for scaled up helical swimmer. Reynolds number is varied for SHN in the range of 0.008 to 3. Orthogonal arrangement of electromagnet was used to propel SHN. It was shown through experimental investigation that magnetic head is not necessary to propel magnetic tail swimmer.

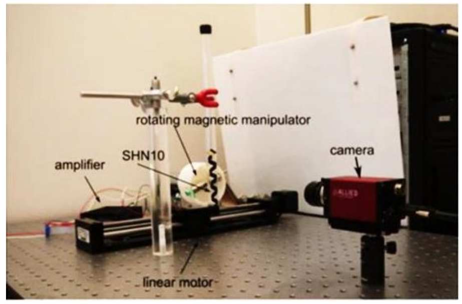


Figure 2.7: Experimental set up used to study propulsive characteristics of scaled up helical nano-belts [14]

In 2014, Ye et al. [15] introduced swimming millimetre scale flexible flagella, which showed enhancement in propulsive force and velocity on increasing number of attached flagella (Figure 2.8). Swimming microrobot has been fabricated by planar photolithography, micro-moulding and manual assembly. It was noticed that swimming speed increased on increasing number of flagella from one to four in 350 cSt silicon oil medium and decreases as number of flagella increase to 6. This may be because of decrease in flagellar spacing, results in strong hydrodynamic interaction. The experimental investigation has been performed for a range of viscosities. It was also investigated that even at 5 cSt viscous silicon oil (Re=0.5), artificial flagella generated the enough propulsive force to swim. It implies that microrobot may work potentially well in certain range of fluid. The measurements in lesser viscosity medium were not preferred such as water because swimmer get sink into medium before any significant measurement. Using multiflagella system lower frequency can provide desirable swimming speed which is suitable for future medical application. Hydrodynamic interaction of multi-flagella swimmer has no significance in the resulted experimental investigation, linearly increase in speed has been observed on increasing number of flagella. Increase in linear viscous force and propulsive force has been observed on increasing flagellar system.

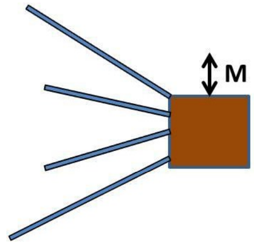
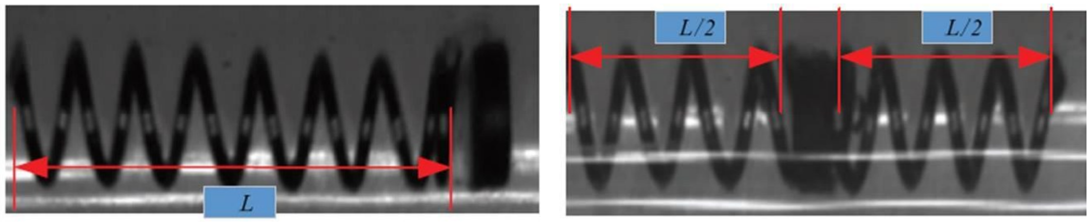


Figure 2.8: Schematic diagram of magnetic-field controlled multi-flagella design fabricated through soft lithography technique [15]

In 2015, Temel and Yesilyurt [16] studied three different swimming modes of micro-swimmer such as rotation frequency and effect of gravity, traction and fluid forces through CFD model in COMSOL simulation software at different range of frequencies. Dimensions of helical tail were length 1.1 mm and diameter 0.09 mm was placed inside a rectangular channel filled with glycerol (1.412 Pas) as shown in Figure 2.9. Actuation frequency applied to swimmer was in the range of 1 Hz to 50 Hz and observed swimming velocity 1.5 mm/s at 1 Hz. Experimental investigation has been carried out in the presence of three pairs of electromagnetic coils. Through backward and forward motion of magnetic helical swimmer effect of surface roughness and swimming direction is being studied through CFD simulation. Backward and forward speeds observed experimentally at 1 Hz are 0.05 mm/s and 0.06 mm/s.

Figure 2.14: Schematic diagram of helical swimmer inside rectangular channel filled with glycerol [17]

In 2017, Wang et al. [18] fabricated five designs of double end helical microswimmer (tungsten wire) by varying the helical pitch. A design having helical pitch 2.7 mm was optimized because of producing maximum velocity and experimental results are supporting the theoretical results. It was also observed that swimming velocity also increases on increasing helical length. Some error in the results were noted when RFT was adopted for validation because RFT was not considering the interaction of fluid between each pitch so producing error. Experimental results of single end helical swimmer have been compared with double end helical swimmer (Figure 2.10). Viscosity of medium is 1000 mPas and speed of helical rotation is 20pi rad/s. The salient work in the field of experimental investigation at scaled up level is tabulated below in Table 2.1.



(a) Single end helix **(b) Double end helix**

Figure 2.10: (a) Single end helix and (b) Double end helix design for comparison of enhanced propulsive characteristics [18]

Table 2.1: List of Macro-scaled experiments performed to study modes of propulsion of nanoswimmer

Year/Author	Mode of Propulsion	Material/Medium	Remarks
1996-Honda et al. [2]	Helical	Copper Wire/Silicon oil (10St-100St)	Experimental results are supported the Lighthill's theory.
2005-Behkam and Sitti [3]	Helical	Steel wire/Silicon Oil (350cSt)	Thrust force generated by rotating flagella was increasing linearly with frequency and theoretical results are in accordance with experimental results.
2006-Tony et al. [4]	Planar	Stainless steel/Silicon Oil (3.18Pas)	First time experimentally investigated the planar mode of propulsion at macro scale.
2007-Kosa et al. [5]	Planar	Piezoelectric unimorph Si-PZT actuator/Gear Oil (607.6cP)	First time examined the analytically coupled mechanical-electrical-fluidic model of propulsion.
2008-Kosa et	Planar	Magnetic coil tail wounded using copper	Analytically shown the impact of head on the

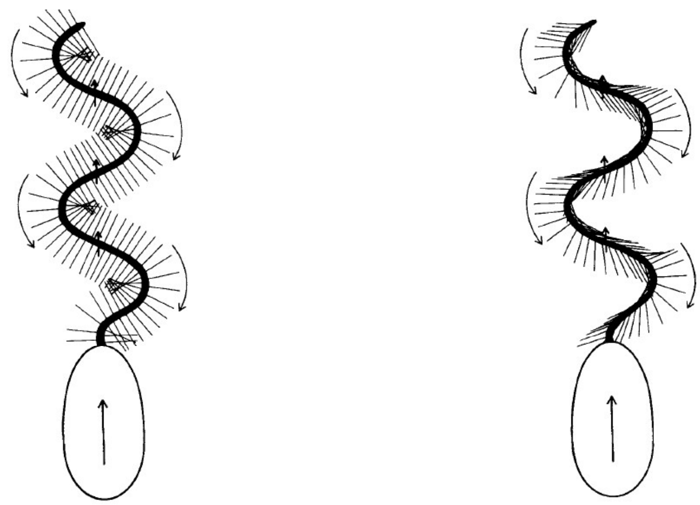
al. [6]		magnet wire/Water	swimming microrobot.
2009-Coq et al. [7]	Helical	Polyvinylsiloxane polymer + Iron carbonyl particle/Glycerine	Validated the hydrodynamics coupling and geometric nonlinearities along with discontinuity in the torque-force relation to characterize filament profiles.
2010-Ha and Goo [8]	Helical	Aluminium wire/Silicon oil (350cSt)	RFT has been applied to study the propulsive speed and efficiency of designed model.
2010-Fountiain et al. [9]	Helical	Steel Spring/Water	Proposed the rotating permanent magnet to control magnetic helical microrobot.
2011-Singleton et al. [10]	Helical	Steel Spring/Silicon Oil (30000cSt)	Five different designs of scaled up microrobot with multiple helices were investigated experimentally to study thrust force generation.
2011-Temel and Yesilyurt [11]	Helical	Non-magnetic metal wire/Glycerol (10Pas)	Observed propulsion of microrobot through external magnetic-field in water and glycerine environment.
2011-Erman and Yesilyurt [19]	Helical	Steel wire/Silicon oil (0.0056Pa.s)	Presented characterization of 12 different designs of rigid helical tail connected to head with the help of revolutary joint.
2013-Temel et al. [12]	Helical	Copper wire/Glycerol (1.42 Pas)	Forward and lateral motion of magnetic swimmer was observed under applied magnetic field.
2013-Rodenborn et al. [13]	Helical	Stainless steel/Silicon oil(100Kg/ms)	Compared the experimental results with RFT, SBT and regularized stokeslet method.
2014-Xu et al.	Helical	Titanium/NdFeB/Ni	Optimized the design of

[14]			helical swimmer.
2014-Ye et al. [15]	Helical	NdFeB-Polyurethane-PDMS (straight)/Silicon oil (5cSt and 350cSt)	Investigated the enhancement in propulsive speed by multiflagella arrangement instead of doing geometric parameter optimization.
2015- Sitti et al. [20]	Not available	Not available	Review on current progress and challenges on untethered swimming microrobot in biomedical field.
2015-Temel and Yesilyurt [16]	Helical	NdFeB- helical copper wire/Glycerol (1.412Pas)	A bioinspired millimetre size microrobot inside rectangular channel has been studied under applied magnetic field.
2017-Wang et al. [18]	Helical	NdFeB-Tungsten wire	Proposed double end helical swimmer at millimetre scale.
2017-Erin et al. [21]	Not available	NdFeB –sphere magnet inserted inside cylindrical cavity created in polylactides	Robot is a rectangular prism of 3.3 mm width and height
2019-Danis et al. [22]	Helical	Steel wire- 10 mm pitch length and 6.25 mm helix diameter, Silicon oil viscosity 350 cSt and 30000 cSt	Generated thrust force approximately 1 mN comparatively low predicted through RFT.

2.3 Mastigonemes Bearing Flagella

In the previous section, review has been done where scientist has shown great interest in mimicking planar and helical flagellar propulsion having smooth flagella at macro scale. While in nature there exist some other types flagella such as *Ochromonas* in which flagella is bearing hair like structure on it which is called as mastigonemes. Mastigonemes are present on flagella of many species of protozoa to increase the effective surface area of flagellum. Researchers have observed planar motion of *Ochromonas malhamensis, O. danica under* micro-cinematography [23]. Flagella has been classified on the basis of occurrence and arrangement of mastigonemes [24] such as

(a) flagellum without any mastigonemes; (b) pantonematic flagellum having two rows of mastigonemes; (c) stichonematic flagellum carrying single row of mastigonemes; (d) acronematic flagellum presenting a single terminal filament and ; (e) pantacronematic flagellum showing two or more rows of mastigonemes along with terminal filament. *Ochromonas malhamensis* is a pantonematic type of flagellum. Mastigonemes helps to increase the effective movement of flagella in comparison to flagella without mastigonemes. The presence of mastigonemes and its motion of *Ochromonas* are shown below in Figure 2.11



(a) **(b)**

Figure 2.11: (a) Schematically shows 90° orientation of mastigonemes for *Ochromonas* and (b) the effective swing movement of mastigonemes between 0° to 90° [23]

Pitelka and Schooley [25] and Manton [26] defined the presence of small flexible fibers at the end of mastigonemes of *Ochromonas*, which further increases the efficiency of the system. They also mentioned that mastigonemes are also held at different angles other than 90° because of flexibility which needs to be investigated. In 1964 Jahn et al. [23] described qualitatively direction of reversal of flagella due to mastigonemes presents on it.

In 1967 Holwill [27] studied the drag coefficient, average frequency of beating and swimming speed for *Ochromonas* computationally initially given by Gray and Hancock in 1955. Holwill also observed the swimming behaviour of *Ochromonas* flagella using stroboscopic which is found to be planar rather than helical in nature. Through electron micrograph it was noticed that mastigonemes are arranged in two rows at opposite sides of the flagella. In 1971 Bouck [28] described that mastigonemes of *Ochromonas* are of two types (1) Fibrous mastigonemes of diameter 50-100 A° and 1-3 μm long and; (2) Tubular mastigonemes having 200 A° in diameter and 1 μm long.

In 1975 Brennen [29] validates the theoretical hydrodynamic analysis of *Ochromonas malhamensis* through experimental analysis. He assumed mastigonemes a rigid structure presented normal (at 90° orientation) to the surface of flagellum. The observed value of propulsive velocity (55-60 μms^{-1}) is in close approximation to the predicted value (60 μms^{-1}). It was mentioned and observed that if angle of mastigonemes is changed from 90° to any other angle such as shift of 10° there is decrement in propulsive velocity. Mastigonemes should be rigid enough to produce effective propulsive velocity.

In 1996 Nakamura et al. [30] studied that monoclonal antibody of mastigonemes are react to mastigonemes which was noticed in immunofluorescence microscopy. In literature it is mentioned that the amputated flagella regenerate in 90 minutes to 120 minutes to their original length. Mastigonemes are regenerated in the new flagella at distal end embedded inside the flagellar surface. It is also mentioned that mastigonemes helps in increasing propulsive force by increasing effective surface area of flagella. In the experimental it was mentioned that tubular mastigonemes are responsible for reversal of direction and thrust of the flagellum.

In 2009 Kobayashi et al. [31] performed the computational study of micro-propulsion of mastigonemes bearing flagella modelled in water. The effect of number of mastigonemes and dimensions of mastigonemes on thrust force through computational fluid dynamics has been studied. It was stated that flagella without mastigonemes propels in the opposite direction of wave propagation due to more tangential drag coefficient than normal drag coefficient as shown in Figure 2.12.

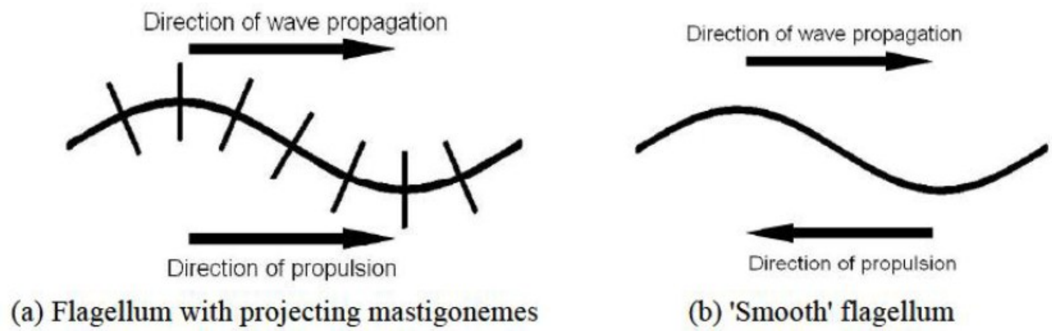


Figure 2.12: (a) and (b) showing direction of propulsion of flagellum with mastigonemes and without mastigonemes [31]

From 2011 to 2018, Onck et al. [32], [33], [34], [35], [36] performed computational study to investigate the direction of propagation of flagella bearing mastigonemes. The equation of solid mechanics and fluid dynamics were solved together to study propulsion behaviour of flagella inside fluidic medium. The hydrodynamic study has been done theoretically to investigate the effect of number of mastigonemes, height of mastigonemes, mastigonemes rigidity and flagellar wavelength and amplitude. In literature flagella is a design concept for locomotion of an artificial nanoswimmer while cilia based structure is used for fluid mixing, fluid flow and micro-object manipulation at micro and nano scale. 2D stokes flow is implemented to present the fluid environment and fluid structure interaction model is considered for micro-object manipulation inside fluid. Five important parameters of flagellum consisting mastigonemes has been considered such as (1) amplitude of the wave deformation, (2) length of base flagellum, (3) the wavelength, (4) height of mastigonemes and (5) spacing between mastigonemes. The mastigonemes are assumed rigid enough to see the effective thrust force. When number of cilia density increases fluid flow increases.

In 2013, Tottori and Nelson [37], fabricated the mastigonemes shaped magnetically actuated artificial helical swimmer using three dimensional lithography and electron beam evaporation of ferromagnetic thin films. If the length and spacing ratio of the mastigonemes changes swimming speed and direction of propulsion can be changed this has been studied experimentally and theoretically. A few experimental attempts have been made by researchers to study mastigonemes bearing flagella. So, there is a lot of scope to study further in this field. In the next section, various actuation mechanisms to propel micro-scale artificial swimmer is discussed.

2.4 Locomotion of Artificial Swimmer at Micro-scale

Nanotechnology enables us to create devices or machines of nanometer size range which can locomote themselves autonomously. Production of autonomous machines like nanorobot requires joint intellectual efforts from chemists, biologist, physicists, pharmacist and engineers. A major challenge for nanorobot design is locomotion and various nanoswimming mechanisms and energy resources have been tested. This is a review of techniques for propulsion of an artificial nanoswimmer.

In quest to mimic nature, researchers have done a lot of work to imitate propulsion of artificial nanoswimmer with flagellated bacteria [38]-[50]. The first published discussion about in vivo locomotion of a swimming nanorobot [51] addressed many issues, including movement through the blood stream, walking, traversing and swimming through various tissues and membranes, identification of defective cells, and swimming medical robots reaching a target area inside the human body. Advancements in nanotechnology have enabled us to realize machines and devices which are $1/100^{th}$ the size of human hair [52]. The nanoswimmer is one such small machine which is required to navigate along predefined path in fluids, ranging from water, blood, or urine, to more complex environments, such as cerebrospinal fluids, gastrointestinal tract, or brain matter [53] and for environment monitoring [54]. Nanoswimmer have potential in various biomedical applications, e.g. brain tumor [55], Alzheimer's disease [56], plaque [57], coronary artery disease [58], angioplasty surgery [59], heart transplantation [60], gout and kidney stone [61], nano-dentistry to ensure oral health by regulation over the oral anesthesia, tooth repair and repositioning [62], and targeted drug delivery, using pharmacytes of 1-2 μm size to carry a payload to the specific location inside the human body to treat cancerous cells [63]-[65].

Propulsion techniques [66] such as chemical, magnetic and thrust force generated by the movement of natural bacteria [67] have been used for locomotion of artificial nanoswimmers [1]. Different fuel system can be used to generate power to propel artificial nanoswimmers, e.g. hydrolysis of adenosine triphosphate (ATP), a concentration gradient of different ionic species and an interfacial gradient due to asymmetrical catalytic reaction [68]. The reported literature presents the current medical nanorobots [51], [69], design issues [70], challenges and solution [71],[68],[72] related to propulsion, powering, control and transport of payload to the specific target. Figure

2.13 is showing the amount of work done to date to locomote artificial nanoswimmer through different techniques at micron-scale in the form of Pi chart.

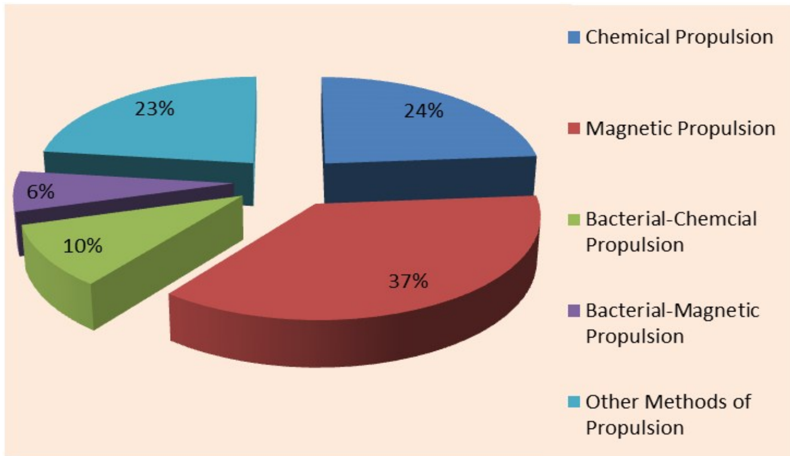


Figure 2.13: Pi Chart in terms of percentage of papers published at micro-scale nanoswimmer using various propulsion techniques

2.4.1 Chemical propulsion of nanoswimmer

Chemical propulsion has been studied extensively in the last decade due to its advantages including higher thrust force and ease of operation. Chemical propulsion is based on the thrust generated when two chemical species react. There are three types of chemical species which are used as propellant namely solid, liquid and gas. Of the three, liquid propellant has been used most widely as a mean of propulsion for artificial nanoswimmers as it lasts for a longer time than the other chemical propellants.

The presence of foreign bodies like bacteria triggers the immune system to produce hydrogen peroxide by some cells of the body [73]. Thus, hydrogen peroxide solution has been used as fuel for propulsion of nanoswimmers. Some of the innovative work was based on bubble propulsion mechanism, using platinum (Pt) as a catalyst has been reported[74]-[88]. Nanoswimmer propulsion has also been observed in water [89], bromine solution [90], diluted human serum, H_2SO_4 and HCl under applied electric field [91]. Nanoswimmer have mostly been fabricated from gold (Au) [75],[76],[77],[92],[80],[84],[81],[93] because it is biocompatible and can be functionalized easily by using biological material.

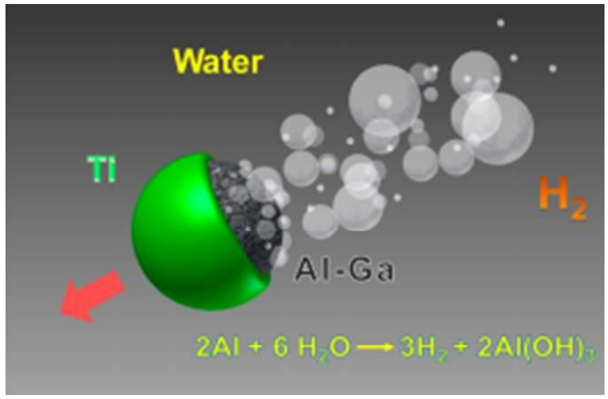


Figure 2.14: Bubble propulsion mechanism in water as medium in the presence of Ti as catalyst [89]

In Figure 2.14, Titanium (Ti) act as catalyst and in the presence of Ti, water molecule breakdown and lead to bubble generation for propulsion of microsphere. The objective of fabricating artificial nanoswimmer using biocompatible material and it's propulsion inside the body fluid seems to be full filled by catalyzing fuel like water (Figure 2.14), hydrogen peroxide alone or in combination with surfactant and other fluid or by reinforcing CNT, which intensify its motion. Researchers have proposed chemical propulsion method using hydrogen peroxide and water. There is still scope of exploring propulsion of nanoswimmer using other medium as well, at same physiological condition because same medium is not present everywhere in the body. According to medical management guidelines [94], an excess amount of H_2O_2 leads to side effects. The permissible concentration of peroxides does not generate the necessary thrust force to propel a nanoswimmer. Experiment conducted at low concentrations of hydrogen peroxide solution (up-to 0.2% [85]) leads to decrease in speed of nanoswimmers. It was attempted to increase the efficiency or speed by adding surfactant [87] to the solution or by incorporating Carbon Nanotubes (CNT) [76]. Though synthetic propulsion of chemical based nanoswimmers have been fabricated from noble metals and synthetic polymers that possess biocompatibility and biodegradability issues [95]. Thus advancement of such biocompatible and biodegradable synthetic artificial nanoswimmer capable to transport and release drug at particular location is still a challenging task to date. Various designs of micro/nano motors show certain advantages and disadvantages. Some of the chemical based nanoswimmer used high concentration of ionic media and produce low power. To overcome this issue tubular micromotors and janus particles have been designed and utilized for enhanced bubbled propulsion of nanoswimmer. In literature, Hydrogen peroxide and hydrazine is utilized most widely for most of the bubble propulsion mechanism of nanoswimmer, due to its biocompatibility issue, it is being restricted to use in biomedical applications. Hence, enzyme based micro/nanoswimmers have been designed and experimentally investigated which seems promising towards biological applications [96]. Enzymes are present naturally and act as 'engines' convert chemical energy into mechanical motion in biological systems. Challenges faced by enzyme based micro/nanoswimmer includes high viscosity, strong flow, complexity of biological fluids, stability and sensitivity towards pH, temperature and poisonous chemicals are some of the disadvantages [97].

2.4.2 Magnetic propulsion of nanoswimmer

Magnetic propulsion is another potential means of nanoswimmer locomotion, and the most successful to date because it is non-invasive method and offers easy control and navigation of the targeted nanoswimmer. In expedition to realize magnetic propulsion, researchers have fabricated a nanoswimmer made up of ferromagnetic material and maneuver it using magnetic fields [98],[99]. Magnetic propulsion has been attempted for both micro and macro size objects under a clinical MRI (Medical Resonance Imaging) system [2],[100],[101]. Both Helmholtz coil [102]-[105] and electromagnetic coil [106]-[108],[12] have been used to generate magnetic fields for propulsion of ferromagnetic particle. Magnetic nanoparticle for tracking and wireless controlled transport of micro-objects have been demonstrated extensively in viscous environment like silicon oil [2],[100],[109],[107],[110], water [2],[9],[111],[107], paraffin oil [102], at different concentration of methyl cellulose in water [53], [104], [105], organic media (N,N-dimethylformamide, DMF), and glycerol [12], [108] to mimic human body environment. In 2007, Chanu and Martel [112] fabricated magneto-elastic Fe-Ni based biosensor for monitoring pH inside the human body, whose motion was guided by MRI system. The pH was detected by measuring the change in resonant frequency of polymer coated poly(acrylic acid-coisoocylacrylate) magneto-elastic core. The change in polymer mass or size has been observed due to swelling of polymer as a result of change in pH which leads to change in resonant frequency, detected by MRI RF coil. In 2008, Guo et al. [113] fabricated the structure of microrobot body, made up of styrol and flexible fins (polyimide film) attached to the permanent magnet, which helped in propulsion of microrobot in pipe to mimic blood vessel. Biocompatible thermo-responsive [114], [115] and pH responsive [112] polymer/ hydro-gel have been used to make nanoswimmer, carrying a payload to release a drug at specific site. For studying the nanoswimmer propulsion, MRI has proven to be better than other imaging modalities like X-ray, ultrasound, infrared imaging (IR) and radioactive dye because it can provide information of various internal organs such as head, chest, blood vessels, abdomen, bones, spine and structure of heart and does not contain any ionizing radiation. The biocompatibility of *in-vivo* and *in-vitro* of magnetic nano-propellers need to be investigated. The challenge of using magnetic microrobot is how to eliminate it after completing their mission. Either we can guide them and remove them using minimal invasive surgery or we can fabricate magnetic nanoswimmer using bio-degradable polymer [116]. Challenges associated with magnetically controlled artificial nanoswimmers are; patient with metal implants may feel difficulty because it may experience magnetic force, cutting and compression of tissues. Patients are also need to stay for longer duration for locomotion of low speed magnetic-nanoswimmer, the gradient of magnetic fields generate eddy current which leads to heating inside human body [3].

2.4.3 Bacterial based propulsion of nanoswimmer

Besides the attempts to fabricate artificial nanoswimmer, researchers have also worked upon manipulation, pickup and transport of micro-object by utilizing thrust force of living prokaryotic and eukaryotic cells such as sperm cell as shown schematically in Figure 2.15. Bacterial motion depends on concentration gradients of light, magnetic fields, chemical concentrations, and temperature. The response of bacteria towards external stimuli has encouraged many researchers to investigate their motion under various conditions. *V. (Vibrio) alginolyticus* mutant strain VIO_5 [117], *Escherichia coli* cell strain (YS34/pYS11/pYS13) [118], *S. (Serratia) marcescens* [119]-[121], *S. (Salmonella) typhimurium* strain [122] have been used for transporting micro-object to a target location.

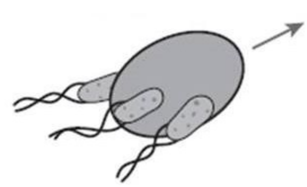


Figure 2.15: Motion of polystyrene beads by utilizing thrust force of living attached bacteria

The presence of amino acids inside the human body makes the VIO_5 strain driven micro-object, a potential means of propulsion of nanoswimmer because bacterial strain moves towards the attractant (amino acid) and away from the repellent (amino acid) and may also control the direction and speed of flagella according to the presence of environmental stimuli such as chemical gradient [117]. In 2008, Behkam and Sitti [121] explored the speed of patterned microbeads and obtained speed value of approximately 28.2 μms^{-1}. The propulsive force of bacteria has great potential for transporting drug loaded micro-objects for targeted drug delivery inside the human body. However, there are some drawbacks to bacterial driven nanorobot. First, the propulsive force produced by bacteria has not been utilized fully because bacterial flagella attached to the Polydimethylsiloxane (PDMS) substrate and polystyrene (PS) beads are not able to swim freely. Second, the motion and orientation of these bacteria are not controllable. Third, as the size of the micro-objects increases, bacteria are not be able to propel efficiently [123].

In addition to chemo-taxis, magneto-taxis manipulation of micro-objects has been observed by utilizing the motion of different types of magneto-tactic bacteria (MTB) under medical MRI. Martel and his group in the series of work [99], [124]-[127], proposed the steering of ferromagnetic particle rather than propulsion because it was bit difficult to propel nanoswimmer in some part of the body such as in highly vascular network of tumor cell or inside the capillary of very small diameter, which require more magnetic gradient amplitude to propel ferromagnetic particle. The living MTB driven micro-object under applied magnetic field has been proposed first time. Three bacteria [125] have been considered for propulsion and manipulation under applied magnetic fields: MV-4, the smallest MTB, *magnetococcus* sp. (MC-1), the fastest MTB, and *magnetospirillum gryphiswaldense*. The latter has bundle of flagella on both ends while MV-4 and MC-1 MTB have bundle of flagella on one end. The best results were reported with a longer chain of *magnetospirillum gryphiswaldense*. Martel and his co-workers described the purpose of using MC-1 MTB due to its high average and peak speed (200 $\mu ms^{-1}$and 300 μms^{-1} in water and blood) than artificial flagella synthesized by many researchers and also able to move in lesser diameter capillary inside human body. They also brought into light the incapability of MC-1 MTB to survive in the high blood flow rate in larger blood vessel. No imaging modalities are capable of imaging smaller diameter capillary and vessel, where ferromagnetic nanoswimmer (25 μm in size) proves to be better at same physiological condition. In 2011, Felfoul et al. [128] stated that bacteria are responsive to external stimuli like chemicals, light, temperature and amount of oxygen and these properties of bacteria are difficult to control and manipulate inside the human body. So, they simulated and experimented *in vitro* with MTB (MC-1 cell) to reach deep inside the tumor, using magnetic guidance; however swimming bacteria near the boundaries did not follow the direction of the magnetic field. Martel [127] stated that use of chemical and phototaxis may not be better for blood vessels and going deep inside the human body. The effect of chemicals and oxygen level on the movement of MTB has been decreased by applying magnetic fields slightly higher than the earth's magnetic field, i.e. around 0.5 gauss resulting in more controllable movement of the MTBs. Ferromagnetic nanoparticles [129] attached to bacteria for transportation of micro-objects have been used because they glow with a different color, when illuminated with UV light, which helps to track the path of nanoswimmers when traveling inside the body. Pickup and transportation of micro-objects *in-vivo* and *in-vitro* by MTB have been observed.

2.4.4 Other methods of propulsion of nanoswimmer

Other actuation methods have been tested include myosin-actin, kinesin-tubular protein molecular-motors[130],self-acoustophoresis[131]-[139] self-diffusiophoresis, thermo-phoresis [140], electro-osmotic propulsion [141],[142], surface tension [143] and laser light [144]. Drug release, incorporated inside thermo-responsive hydrogel and transport of micro-object by *S. marcescens* bacteria and *Chlamydomonas reinhardtii* (CR) [131], have been demonstrated when exposed to UV light. An ultrasonic wave produces a radiation force which helps in propulsion of micro-objects. Researchers have utilized the property of piezoelectric materials, e.g. lead magnesium niobate- lead titanate (PMN-PT) [5],[145],[146] have been used to generate power for propulsion of nanoswimmers. In 2012, Kagan et al. [138] obtained an average speed of microbullets approximately 6ms-1. Different models [147]-[155] have been proposed to generate power for propulsion of nanoswimmers in human body. Optical tweezers [156] and atomic force microscopes [157] have been used as micro-robots for manipulation. Some drawbacks [158] are associated with *in-vivo* ultrasonic propulsion, e.g. the heating effect, mechanical effect, shrinking and expanding of micro-bubbles present in the lungs and genetic defects after prolonged exposure. A low frequency (20-100 KHz) [159], [160] ultrasonic wave has been used in various biomedical applications including eye surgery, dentistry, breaking kidney stone, to image internal organs. The propulsion of silica colloidal particles coated with magnetic Pt(2 nm)/Py(100 nm)/Pt(2 nm) [160] stack has been observed due to a temperature gradient generated by applying an AC magnetic field around the magnetic cap in water. Electro wetting on dielectric (EWOD) technology [161] has been used to propel the smallest MEMS (Micro-electromechanical systems) base device with no moving parts in water with a speed of 8 mm s^{-1}. The back and forth motion of the device has been observed due to movement of trapped bubbles on the surface of the silicon swimming robot when voltage was applied to the electrode. A piezoelectric resonant motor coupled with axial and torsional displacement has been designed by Watson et al. [162] with a helically cut stator 70% smaller in diameter (250 μm) than previous stators. They observed an angular velocity of approximately of 135 rad s^{-1} by flagellar propulsion. This group also modeled and designed a piezoelectric ultrasonic motor with a stator of diameter 241 μm which helps to drive an *in vivo* microrobot for biomedical applications [163]. Light driven (UV and NIR) micro/nanoswimmer produce harmful effects on human body and may generate unnecessary thermal effects [164]. So, control manipulation of micro-swimmer is still a challenge. In table 2.2, the locomotion of swimmer at nano/micro scale through external stimuli is presented.

Table 2.2: Achievements in the field of artificial nanoswimmer

Year/ Author	**Mode of Actuation**	**Material used to make**	**Remarks**
2016-Ma et al. [165]	Chemical	Silica nanojets (220 nm)	-Nanojet was powered by urea act as substrate. In the absence of urea nanojets showed Brownian motion.
2016-Solano et al. [166]	Chemical	Spherical silica particle half coated with carbon caps.	-First time demonstrated the enhanced motion of spherical janus nano particle in non-Newtonian fluid.
2016-Li et al. [167]	Magnetic	Nanofish- head made up of Au, 2 Ni segments as body and 1 Au segment as fin (diameter- 200 nm and Length- 4.8 μm).	-Oscillating magnetic field propel the Ni body. -Speed-30 μm/s.
2016-Stanton	Bacterial	E.coli coated on PS janus	-Observed attachment of

et al. [168]		particle capped with Pt. Ti, Fe and Au.	*E.Coli* better with Pt. Bacteria carried 2 μm and 600 nm payload to the target. -Average velocity- 0.4 μm/s/.
2017-Ochoa et al. [169]	Chemical	Commercial cellulose adhesive tape coated with MnO_2 catalyst is folded in tapered cylinder of millimeter size	-Ferro-fluid on other end of swimmer is also used for controlled motion of mm size swimmer -Speed- 7.2mm/s at 20% H_2O_2 solution.
2017-Ali et al. [170]	Magnetic	Silica+Ni	-Generated rigid hollow helical nanoswimmer using *Salmonella typhimurium* as biotemplates. -Speed-22 μm/s at 112.5 Hz rotation rate of flagellar motor. -Swimmer move in and out due to significant Brownian motion.
2017-Li et al. [171]	Magnetic	Ni-Ag-Au-Ag-Ni-nanoswimmer -Ni and Au are rigid rods and Ag act as elastic joints between them	-Free style swimming using oscillating planar magnetic field is more efficient than propulsion of helical nanoswimmer using rotating magnetic field. -Observed speed 38.7 μm/s at 17 Hz.
2017-Wang et al. [172]	Light driven	Silicon Nanowire	-Reported visible and near IR light driven nanomotor in hydroquinone and H_2O_2 solution.
2018-Louf et al. [173]			-Reported as fastest nanoswimmer reported to date. -Speed is 0.05 to 350 mm/s by applying acoustic waves (250-450 KHz).
2018-Chen et al. [164]			-Reviewed nano/micro motors powered by light.
2018-Zhang et al.	Magnetic	PDMS+Carbonyl iron powder	-Synthesized artificial cilia to generate circulatory fluid flow speed upto 250 μm/s.
2018-Wang et al. [174]	Magnetic	Fe_3O_4 nanoparticale based Gelatin-	3D soft helical microswimmers are

		methacrylol	fabricated
2019-Woodward and Sitti [175]	Magnetic	Magnetic Spring-152 μm in diameter	Generate pull force of 3.12 N.
2019-Erkoc et al. [176]	Not available	Not available	Presented therapeutic effects of drugs, cells and genetic material through microrobotic system is reported.

In the previous section, the several issues and research advancement in realization of nanoswimmer was reviewed. The various types of actuation mechanisms of locomotion at micro-scale for discussion have been considered. Each and every actuation mechanisms have some pros and cons, so we need to address some alternative such as piezoelectric material based energy harvester to locomote artificial nanoswimmer. In the following section, we are reviewing the piezoelectric based actuation mechanism in aiming to design on-board actuation scheme of an artificial nanoswimmer after finding suitable design of flagellated swimmer.

2.5 Piezoelectric Based Actuation of Artificial Nanoswimmer

Various types of actuation mechanisms have been explored till now such as chemical actuation [91], bacterial actuation [177], magnetic actuation [178] and thermal actuation mechanism [144] for artificial nanoswimmer and it possesses some limitations [179]. To overcome those limitations of different actuation mechanism, piezoelectric based on-board energy harnessing scheme is an alternative for artificial nanoswimmer.

Energy transduction mechanism implies conversion of mechanical or vibrational energy from surrounding environment into electrical form by electrostatic [180], electromagnetic [181] and piezoelectric approach [182]. Piezoelectric conversion technique is most suitable for energy harnessing purpose at micron scale because it does not require any external means in comparison with electrostatic and electromagnetic mechanism. Selection of material becomes essential parameter for fabricating and navigating artificial nanoswimmer inside human body environment. Piezoelectric material such as lead-zirconate-titanate (PZT), lead-titanate (PbTiO2), lead-zirconate (PbZrO3), and barium-titanate (BaTiO3) are being employed in energy harnessing process in last few decades. Due to some constraints of piezo-ceramics [183], piezoelectric polymers Polyvinylidenefluoride (PVDF) has been synthesized and can be used for energy harvesting application [184]. PVDF seems most appropriate piezoelectric material because of flexibility, biocompatible, light weight and inexpensive [185] to design on-board powering scheme for artificial nanoswimmer.

To harvest energy for an artificial nanoswimmer, a well-designed on board energy transduction system is required, which must overcome various challenges and issues significant in nano-domains. Scientists and engineers have shown a great interest to conceptualize model, analyse and realize various actuation scheme for artificial nanoswimmer in last two decades by fabricating it, using polymers, nanoparticles, biocompatible materials such as gold, piezoelectric materials, shape memory alloy and so on. Piezoelectric materials prove to be a more feasible material in the field of realization of energy transduction mechanism of a nanoswimmer due to low cost, biocompatibility [10], flexibility, and light weight, generation of electricity on stretching and vice a versa. So, it is desirable to have artificial nanoswimmer which may actuate by utilizing piezoelectric properties.

The potential to design on-board energy transduction system for nanoswimmer is the topic of discussion from past decade. In pursuit to harness energy from piezoelectric material, scientists are endeavouring to make a cantilever beam, when vibrate may induce stress which leads to electric potential or power [186], [187], [188]. A piezoelectric coefficient of cantilever beam has been measured by loading it manually. According to the piezoelectric effect, voltage response is proportional to the stress, what is described by piezoelectric coefficients [189]. A cantilever beam based piezoelectric energy harvesting device has been proposed by researchers to delve substantial energy from ambient vibration. The effect of geometric parameter such as beam length, width and thickness on the voltage generation and power has been studied by doing mathematical modelling [190]. The model is developed using piezoelectric application mode for the simulation of the mechanical and the electrical behaviour of the converter when a voltage is applied using electrostatic application mode [191]. As per the reported literature, a cantilever based piezoelectric energy harvesting system has been employed to convert mechanical energy provided by vibrating element into electrical energy. A few attempts of energy harvesting in fluid flow condition have been done [192]. A simulation approach is used to prove the concept of voltage generation on piezoelectric device inside flowing fluid channel. A modelling of cantilever based energy harvesting under base excitation has been studied by many researchers as presented below in Table 2.3.

Table 2.3: Exploration of cantilever based energy harvester in literature

Author/year	Material	Dimensions	Achievements
2004, Minteo et al. [190]	PZT-PIC 255	Dimensions are in meter.	At 13.4 Hz, Power-2.6 mW.
2007, Zurkinden et al. [186]	PVDF	Cantilever beam 30mm long, placed in a 0.6 m deep wave flume; a flexible foam core 3.75 mm thick is sandwiched by two 1.25 mm thick and 30mm long piezoelectric polymer layers.	At Frequency 0.89 Hz, 3.28 V is achieved.
2008, Zhu et al. [193]	PSI-5H4E with brass.	Dimensions are in mm.	ANSYS simulation shows power-372 μW, and V-16.1 V. Experimentally 370 μW and 15.5 V was achieved.
2009, Penic et al. [189]	PZT	10 cm long and 18 mm wide stainless steel strips (cantilever) of thickness 0.5 mm were cut by milling and then pressed between two rigid stainless steel plates acting as a fixed support.	Frequencies ranging from 20 Hz to 10 kHz, at excitation voltage of 10 mV, find out d_{31}. Piezoelectric constant through ANSYS simulation.
2009, Berdy et al. [188]	PZT	Cantilever dimensions in mm.	Power output of 7.2 μW at 0.2 g acceleration and 49 Hz has been experimentally achieved through ANSYS simulation.
2011, Prakash et al. [191]	ZnO	Cantilever is made up of copper with dimensions 500 μm×100 μm×2 μm.	Resonates at a frequency of 110 KHz output and voltage obtained is 0.0956 V using COMSOL.

2012, Park et al. [194]	PVDF	Dimensions are in mm with different shapes of cantilever beam.	Carried out finite element model by ANSYS at 10-80 Hz.
2012, Manoharan and Nedumaran [195]	PZT		Voltage is 1-5 V and results are validate through COMSOL and experimental at pressure in the range of 100-500 KPa .
2012, Tiwari et al. [196]	PVDF	Width-1-5 mm, length-above 5 µm	A maximum tip deflection is observed for thickness of 5 µm at 100 V using COMSOL software.
2013, Bangi [192]	PZT	Larger dimension in micrometer. D shape bluff body and cantilever beam.	At Velocity-1 to 5 m/s, stress-3088 Pa and voltage-2.9 mV at 5 m/s is observed. Obtained larger potential from vortex shedding in fluid flow condition.
2015, Graak et al. [197]	PZT	The length of the cantilevers is fixed as 60 µm and the width is fixed at 10 µm. Taken a Si layer of thickness 1.5 µm and an upper layer of thickness 0.5 µm.	A constant force of 0.5 µN is applied on all the cantilevers. Piezoelectric voltage of 0.0386 V and power is 29.2 µW is achieved.
2015, Fengchi et al. [198]	PVDF	L-100 mm, b-10 mm, h-0.05mm.	The flag is immersed in the air whose velocity varies from 1 m/s to 10 m/s. When the velocity attains 4 m/s the circuit voltage is tending towards stability while the maximum output power increases continuously.
2016, Saker et	PZT	L-0.01 m, b-0.003 m, t-	Generated 0.4 V for given geometric

al. [199]		0.0001 m.	dimensions.
2017, Usharani et al. [200]	PZT	L-76.5 mm, b-25 mm, t-05 mm.	Generated voltage in the range of 3.99 V to 57.25 V.
2018, Lee et al. [201]	ZnO	L-15 µm, b-3 µm, t-50 nm.	Observed voltage as 0.04 V.
2018, Nain et al.	PZT, PVDF, AIN	L-50 µm, b-2.5 µm, t-2.5 µm.	Observed maximum electric potential 188 nV for PVDF based cantilever beam
2019, Xiong et al. [202]	PZT	L-40 mm, b-20 mm, h-0.2 mm.	Observed output power approximately 10.7 mW.

2.6 Gaps in Existing Research and Investigations

- Through literature review it is evident that very less research has been endeavored on planar propulsion which is more efficient mode of propulsion than helical propulsion. Shape of flagella has been considered most widely to study locomotion of nanoswimmer while mastigonemes bearing flagellar propulsion is still need to study for propulsive characteristic of nanoswimmer. Hence, main purpose of the current study is to develop conceptual design of swimmer that is innocuous, biocompatible and simple.
- It is clear from the above literature review that very less attempt has been made to actuate nanoswimmer using biocompatible material. Among efficient actuation schemes in miniaturized domains, piezo-actuation finds a prominent place. Though extensive research has been carried out on chemical and magnetic mode of propulsion, investigation on piezo-actuation for nanoswimmer is very little and need to be investigated.
- Despite many attempts, no feasible design with on-board powering of a nanoswimmer has been proposed. Though researchers have proposed and investigated several techniques to locomote and control nanoswimmer but on-board actuation scheme of nanoswimmer have yet to be conducted to confirm their credibility.

- Miniaturization of devices has many advantages like resource conservation, low cost, low power consumption, less space requirement and easy disposability. So, there is a need to design a miniaturized actuation system, which may consume on-board less power and less space. This study will try to overcome the existing gaps in the research and will investigate various designs of biocompatible artificial swimmer.

Based on the literature review attempted in the present chapter, objectives are defined as:

1. To develop and design the test rig for propulsion of macro scaled flagellated artificial nanoswimmer.
2. Investigation of various designs of branched flagellated swimmer through design of experiments (DOE) at scaled up domain.
3. Comparative analysis of various designs of artificial nanoswimmer through COMSOL multiphysics FEM simulation for on-board powering concern.

Organization of the thesis

Neither standard design of artificial branched flagellated swimmer is available nor is the set-up available off the shelf therefore a customized design of experimental set up consisting of cantilever beam as displacement transducer; scotch yoke mechanism to develop a planar oscillating mode of actuation to flagella; controllable DC power supply, DC motor and silicon oil medium have been fabricated and purchased towards working on further investigations. Planar propulsion is embraced over helical propulsion because of high efficiency generation. The design of test rig for planar propulsion of branched flagella is presented in Chapter 3.

Different designs of flagella reported in literature for propulsive force investigation at macro-scale is reviewed in Chapter 4. In nature *Ochromonas malhamensis* exist in nature in which small hair like structure (mastigonemes) called as branches in our work is embedded on the surface of flagella and is not studied much in literature. The present approach endeavours a biomimetic branched flagellated swimmer to study planar mode of propulsion in Chapter 4. How does number of branches, orientation of branches and gap between the branches affect the propulsive force of branched flagella? The effects of above mentioned parameters of branched flagella in terms of propulsive force along with environmental parameters such as speed of DC motor and viscosity of silicon oil need to be examined for contribution of each factor through statistical methodology Taguchi analysis.

After investigating various designs of branched flagellated swimmer at scaled up level, we are endeavoring to realize artificial branched flagellated nanoswimmer on-board energy harnessing for locomotion in complex surrounding media. PVDF (Polyvinylidene Fluoride) stands out as a suitable piezoelectric material for *in-vivo* applications as an energy transducer in nanoswimmers. No attempts have been made to date using biocompatible PVDF-based branched flagellated artificial nanoswimmer. The focus of Chapter 5 is to simulate an actuation scheme for an artificial nanoswimmer using PVDF piezoelectric material which is able to generate electric potential when get deformed or stretched due to fluidic pressure, in COMSOL multiphysics FEM software to prove the design concept of branched flagellated nanoswimmer for on-board powering.

2.7 Summary

1. We have presented literature review available for propulsion of an artificial nanoswimmer and we observed there is a need to design flagella by varying geometric parameters for propulsive force enhancement. The literature review is divided into macro-scale and micro-scale propulsion of artificial swimmer and introduces in Section 2.1.
2. Section 2.2, entails the scaled up experiments performed to study the planar and helical mode of propulsion of flagellated swimmer.
3. In section 2.3, mastigonemes bearing flagella design is discussed for its further investigation experimentally at scaled up level to investigate propulsive force enhancement.
4. In section 2.4.1, chemical propulsion mechanisms based on catalytic decomposition of fuel are reported. In section 2.4.2, propulsion of nanoswimmer for *in-vivo* and *in-vitro* applications under applied magnetic field is presented. In section 2.4.3, manipulation of a payload, exploiting chemo-taxis and magneto-taxis bacterial flagella is presented. Propulsion schemes based on external stimuli, electro kinetics, ultrasonic and thermal methods are discussed in section 2.4.4.
5. In section 2.5, on-board actuation mechanism concept for artificial nanoswimmer using piezoelectric material is introduced for energy transduction mechanism. The gaps in the existing research and objective of the current

proposed work has been described briefly in section 2.6, which will be investigated in Chapter 3, Chapter 4 and Chapter 5.

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