This document contains the draft version of the following paper:


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I. INTRODUCTION

MICRO MANIPULATION refers to robotic manipulation, involving any combination of push, pull, orientation, deformation, and even sometimes dissection and fusion, of microscopic objects such as colloidal particles, cells, biomolecules, and biomimetic viruses. Just like in macro domain robotics, micro manipulation systems consist of actuator, sensor, controller, and actual manipulator hardware, along with software for sensor data processing, and manipulator planning and control. However, some of these system components are often quite different from their macro domain counterparts owing to the unique challenges posed by operations at the small length scale. For example, while most large robot arms are actuated by pneumatic, hydraulic, or electrical technologies, a majority of micro manipulation systems employ piezoelectric, magnetic, chemical, optical, or hybrid, like optoelectronic or optofluidic, forms of actuation. Similarly, while large robots sense using vision, laser scanning, inertial measurement, or a combination of multiple of these, micro robots primarily rely on imaging using either optical and electron microscopy and sometimes force sensing. As the microscopy techniques only provide images of the cross-sectional planes, sensing the full 3D workspace is quite challenging for micro robots. While multiple sensors or vertical translation of the sensors offer feasible solutions, real-time 3D state estimation is still impeded by hardware limitations and computational complexity.

The manipulators themselves are often quite different at the micro scale as compared to the macro domain. They are either physical structures attached to the rest of the system, such as micro grippers, micro pipettes, and nano probes, or specially designed micro objects like magnetotactic bacteria, or external sources like electric currents, fluid flows, lasers, or electromagnets. The physical structures exert contact forces on the manipulated objects, while the other two types belong to the class of non-contact micro manipulation. We refer the interested readers to [1] for a survey on the challenges of handling micro parts using grippers, [2] for a discussion on the similarities and differences between micro and macro manipulation force models, [3] and [4] for reviews on micro gripper technologies, [5] for a detailed survey on contact micro manipulation strategies, and [6] for an overview and classification of nano manipulation systems that is almost directly applicable to micro manipulation systems.

Micro manipulation is increasingly playing a vital role in realizing the potential of micro systems technology in almost all the current thrust areas including communication, energy, and human health care [7], [8]. It is being used to assemble micro-scale parts of varying shapes and types, and for directed repair and fabrication of specific parts in larger structures, to yield products such as switches or energy-storing devices with much improved material properties as compared to their conventional counterparts made out of macro-scale parts. It
is also ushering a revolution in biology and medicine by providing new modes of precise drug delivery (see [9] for a relevant discussion), drug discovery, cell sorting for genetic screening and analysis, cancer studies via regulated intercellular signaling and mechanotransduction, and development of a fundamental understanding of physiological processes like DNA transcription and folding.

However, in addition to design and actuation issues, manual or teleoperated control, which provides limited reliability, repeatability, and efficiency, poses one of the main challenges for widespread adoption of micro manipulation in both industries and clinical laboratories. That is why, there has been a lot of interest in bringing about automation to micro manipulation over the past decade or so using a variety of planning and control methods. An early review of the issues pertaining to feedback control and task planning in micro manipulation is found in [10], a more recent survey of specifically force sensing and control methods is available in [11], and a review of the challenges in controlling magnetic micro robots is given in [12].

In this paper, we survey all the planning and control methods that required some software module and did not result in automation only by virtue of controlling the tunable parameters in the hardware. We provide a high-level method taxonomy based on the underlying models and algorithms, and discuss each method in either Section IV or V, both of which are organized into sub-sections based on the presented taxonomy. We emphasize the salient aspects of the methods that enabled them to be successful in the micro domain, where the physics is significantly different from the macro domain due to one or more of the following reasons: (a) the scaling effect due to the dominance of surface forces such as adhesion and drag over body forces like gravity, (b) random Brownian motion of objects in fluid media resulting in constantly changing workspace conditions, (c) application of external force fields leading to coupled physics problems, (d) uncertainty in action execution, (e) sensing uncertainty, and (f) the need for computing actions within a few milliseconds. We also highlight the major experimental results reported in the papers and point out some of the main limitations. We then identify the common trends across all the methods, analyze the relative utilities of the methods under varying operating conditions, and discuss promising research directions.

II. DIFFERENT MICRO MANIPULATION SETUPS

We first provide an overview of the various micro manipulation setups that utilize fundamentally different forms of manipulators with own set of advantages and limitations to facilitate a better understanding of the automated planning and control methods. For each setup type, we discuss some of the earliest works along with notable advances in instrumentation, and point the readers to review articles for more details. Note that we only cover those setups for which a large number of automated planning or control methods have been developed and validated. There are other forms of micro manipulation using chemotaxis, dielectrophoresis, acoustics, ultrasonic levitation, fluid flow, or hybrid techniques that are not discussed here.

A. Magnetic micro robots

One of the popular ways of manipulating micro objects is by using external electromagnetic coils. An early example of such a system was presented in [13], where the authors developed untethered nickel micro robots that could be guided inside the human body to perform a variety of diagnostic and surgical operations. They achieved good control over the position and orientation of the robots by creating uniform magnetic fields through a combination of co-axial Maxwell and Helmholtz coils as is usually done in magnetic resonance imaging (MRI) systems. Pawashe et al. [14] then designed another micro robot composed of neodymium-iron-boron, which performed stick-slip motion due to periodically varying magnetic fields generated by a system of four electromagnets, two of which were arranged horizontally and the other two vertically. Frutiger et al. [15] later developed a new type of magnetic micro robot, called the artificial bacterial flagella (ABF), that has now become very popular. The ABF had comparable shape and size as the natural bacterial flagella, consisted of a helical tail and a thin-soft magnetic head, and could be controlled precisely by three rotating orthogonal electromagnetic coils. A different form of magnetic micro robot design was presented in [16]. Instead of external magnetic fields, this system comprised of magnetotactic bacteria as manipulators, each of which had two flagellar bundles for propulsion and a chain of magnetosomes for directional control, and could be used to push non-magnetic objects.

B. Mechanical micromanipulators

Mechanical micromanipulators are direct analogues of large-scale robot arms that can grip or hold, move, rotate, and release or inject micro objects. The two common types of micro manipulators are microgrippers and micropipettes. One of the earliest designs of microgrippers was provided in [17], where a pneumatically-driven microcage was used to manipulate biological objects in fluid media. The manipulator consisted of multiple chromium/aluminium cantilevers that were arranged in an asterisk pattern by residual stress slip motion due to periodically varying magnetic fields generated by a system of four electromagnets, two of which were arranged horizontally and the other two vertically. Frutiger et al. [15] later developed a new type of magnetic micro robot, called the artificial bacterial flagella (ABF), that has now become very popular. The ABF had comparable shape and size as the natural bacterial flagella, consisted of a helical tail and a thin-soft magnetic head, and could be controlled precisely by three rotating orthogonal electromagnetic coils. A different form of magnetic micro robot design was presented in [16]. Instead of external magnetic fields, this system comprised of magnetotactic bacteria as manipulators, each of which had two flagellar bundles for propulsion and a chain of magnetosomes for directional control, and could be used to push non-magnetic objects.

C. Optical tweezers

Optical tweezers (OT) consist of tightly focused laser beams that can tweeze or trap micro objects in fluid media and hold them in stable configurations near the beam foci. They are particularly suitable for manipulating biological objects using
infra red wavelength lasers. The first successful demonstration of an OT system was provided in the seminal work of Ashkin et al. [21]. Ashkin later explained how optical trapping works for dielectric particles with diameters greater than the laser wavelength through counteracting optical gradient and scattering forces in [22]. A detailed survey of the role of OT in manipulating objects of varying material properties and shapes leading to fundamental advances in atomic, molecular, and biophysics can be found in [23]. For a long time, these systems mostly comprised of single or dual laser beams, which restricted the number of objects that could be manipulated at a time. Curtis et al. [24] developed holographic OT that could manipulate several (up to hundred) objects simultaneously with complete individual control over each of the trapped objects in 3D. This multiplexing capability has contributed largely to the growth in popularity of optical tweezing.

D. Scanning probe microscopy

Microscopy techniques typically use nanoprobes consisting of cantilever beams that are made of platinum, iridium, silicon nitride or gold, and have thicknesses of the order of a few nanometers. The beams contain pointed tips at the free end to probe, i.e. push, place, or orient, micro-scale objects. Unlike the mechanical micro manipulators, they are capable of simultaneously imaging the probed surfaces by scanning the probes in rasterized manners and recording the interactions as functions of the probe positions. The two most common types of nanoprobes are atomic force microscopes (AFMs) and scanning tunneling microscopes (STMs). One of the earliest works on using AFM for micro manipulation was presented in [25]. Both AFMs and STMs have been extensively used for biomanipulation, and hence we refer the interested readers to [26], [27], and [28] for detailed surveys on the different techniques and experimental successes.

III. PLANNING AND CONTROL TERMINOLOGY

We now formalize our terminology of planning and control and make an important distinction between the traditional and new architecture before discussing the specific methods in the following sections. Based on the terminology proposed in [29] and [30], the literature is categorized into planning and control based on the spatial and temporal granularity of the proposed method. A work is classified as planning if the method is designed to generate global paths or grasps or task sequences for one or more objects across relatively long time horizons (several seconds or more) and lengths (several microns). On the other hand, control methods are meant to output local translations or grasp motions or individual tasks (collectively called actions) for the objects over relatively short time spans and distances.

Thus, while planning focuses on optimizing operation goals such as avoiding collisions and/or minimizing completion time, control is required to ensure that the desired actions can be executed stably while often optimizing over system-level entities such as effort or deviations from reference states. Hence, a planner may generate action sequences where the individual actions are not controllable, whereas a controller may yield actions that may not best satisfy the operation requirements when performed in a sequence. That is why, recent research has closely linked the two fields. Planners use high-fidelity system dynamics models, continuous or finely-discretized state, action, and time representations, rapid local adjustments to global plans, or feedback control stability during plan computation to guarantee controllable action generation. Similarly, controllers incorporate operation-level requirements within the process models and cost functions to better meet the overall goals. Hence, even though every method is listed in either the planning or control section depending on the presentation emphasis of the corresponding article, we make an effort to specifically mention how many methods address the above-mentioned issues of stand-alone planners and controllers.

IV. PLANNING METHODS

Feddema et al. [31] showed the utility of motion planning in picking up, holding, and releasing micro spheres with rectangular tools. The authors concluded that while the principles of free configuration space and geometric assembly constraints are directly applicable from macro domain planning, precise motion planning needs to account for surface forces such as van der Waals and electrostatic. Thus, they laid the foundation for the development of sophisticated methods that are based on well-known macro scale planning algorithms but are tailored specifically for micro scale physics. We classify the methods into three types based on the models and algorithms, and discuss them one by one.

A. Graph search

Graph search methods have proved to be extremely efficient for robot path planning in the macro domain. One of the earliest applications of graph search for micro manipulation in the form of orienting micro parts without sensing can be found in [32]. The authors proposed a pair of manipulation primitives, namely squeeze and roll, and developed a complete algorithm that could find the shortest paths from the graph node representing all the manipulator states (pairs of edges and jaws) to the nodes containing a minimal number of states. Much more recently, Mitra et al. [33] developed graph search algorithms for path planning in complete or selective washing of droplets in both array-based and irregular geometry biochips. They modeled the problem of reducing the path length and washing time with or without capacity constraints of the droplets as variants of the well-known NP-Hard Chinese Postman or Traveling Salesman problems. While both of these works provide valuable theoretical contributions, it would be useful to investigate their performances in physical experiments.

A* and D* (and its variants, namely Focused D* and D* Lite) are two popular classes of heuristic graph search
algorithms that provide complete and optimal paths between the nodes which represent origin or start and destination or goal configurations in the discretized workspace with fast computation times. Encouraged by the success of these algorithms and the pioneering work by Makaliwe and Requicha [34] in formulating the planning problem for automating nanoparticle assembly tasks, Malima and Sabanovic [35] developed a proof-of-concept system that used A* to push particles around static obstacles toward destination points in a virtual micro-assembly workstation. Das and Popa [36] proposed a precision-based path planning algorithm, where the path precision was used as the cost metric instead of the path distance to achieve high yield micro assembly conditions. Cappelleri et al. [37] later used A* to determine the optimal assembly sequences and initial part locations in the workspace for planar micro assembly task planning, and achieved full control over the part states by applying rotation, one-sided pushing translation, and caging transport motion primitives.

Wu et al. [38] developed an A* algorithm to automatically transport living cells using optical tweezers. The authors modified the standard A* heuristic function that consists of the sum of the path-cost function and an admissible heuristic estimate (lower bound) of the cost to reach the goal from the current location. Experiments with yeast cells at 10 mW laser power in aqueous medium showed the usefulness of the approach in moving a cell around other cells with acceptable deviation in cell position from the trap center using moderate penalization values; however, the actual transport times were not reported. Wu et al. [39] incorporated a proportional integral (PI) control scheme within the above approach to further reduce the possibility of the cell escaping from the optical trap and enhance transport efficiency. Experiments demonstrated collision-free path generation for transporting cells in moderately crowded workspaces. Further work would be needed to extend the method for real-time transport of multiple cells in 3D.

Chowdhury et al. [40] used an A* algorithm in conjunction with inverse kinematics-based feedback control of object positions to automatically manipulate cells that are vulnerable to photo damage indirectly using optically-trapped dielectric micro particles (beads) as grippers. Indirect manipulation is commonly used to investigate the biomechanical properties of nucleic acids and motor proteins, and we refer the interested reader to [41] for a detailed survey of various experimental set-ups. However, this is an area of ongoing research for cells, and recent works (see [42] and [43]) highlight the benefit of providing enhanced cell viability as compared to direct laser exposure. Experiments showed effective gripper formation control during transport, and provided comparisons of maximum transport speed and minimum laser power requirement for different formation types. However, the experiments used 5 \( \mu m \) silica beads as substitutes for cells which calls for further investigation.

Chowdhury et al. [44] recently developed a D* Lite algorithm to automatically create a uniform distribution of yeast cells in an optical tweezers-assisted microfluidic chamber. The chamber contained a large number of microNets that were designed to capture cells in a regular and precise arrangement for inter-cellular signaling studies. Optical tweezers were used for cleaning the microNets that had surplus number of cells and transporting the surplus cells to nearby microNets that had deficiencies. The major contributions of this work were in robust selection of destination microNets by accurately simulating cell motion using a combination of computational and analytical tools, and leveraging the fluid flow during cell transport to minimize laser power and operation time by using a modified cost function. Further work is needed to integrate indirect manipulation for photo-sensitive cells and synchronize the microscope stage motion with cell transport.

B. Decision-theoretic

Decision-theoretic methods are popularly used where the effects of executing actions to cause robot state transitions are often stochastic, and the states themselves may not be known exactly and are estimated (measured) probabilistically. The planning problems are most commonly modeled as directly or partially observable (PO) Markov decision processes (MDPs), where the future and past states are assumed to be independent provided the current states are estimated. Any MDP or POMDP algorithm outputs a policy that maps states to actions and optimizes the expected, discounted long-term reward (value) for a known or learned reward function which provides the immediate cost/benefit of executing an action, and state transition and measurement probability distributions. Thus, one-time policy computation provides a viable alternative to constant re-planning for highly stochastic systems with fast and/or partially unmodeled dynamics and large state estimation errors.

Banerjee et al. [45] and [46] explicitly accounted for the motion and sensing uncertainties arising in optical tweezers-based object transport operations due to the constant Brownian motion of the micro spheres and image processing noise, and modeled the path planning problem as a POMDP. Simplified trapping probability models, developed in [47] to encode the probability of trapping an object as a function of the relative displacement of the object from the trap focus, trap speed, trap power and object size, were used to compute the effective collision zones around other freely diffusing objects (obstacles). A modified value iteration form of an approximate POMDP algorithm, known as the QMDP algorithm, was developed to provide real-time performance. Both simulation and physical experiments with 2\( \mu m \) silica beads demonstrated effective collision avoidance via a combination of circumvention and additional obstacle trapping in workspaces containing fifteen to twenty obstacles. However, just like any other POMDP algorithm, scalability with increasing state dimensionality would be a major issue.

Banerjee et al. [48] and [49] incorporated the previous POMDP algorithm within a decoupled path planning framework to transport multiple objects simultaneously. A maximum bipartite graph matching algorithm was first used to assign goal locations to target objects. The modified QMDP algorithm was then applied on every target object to yield paths that would avoid collisions with the obstacles but might result in collisions among each other. Branch and bound optimization
was later performed to assign priorities to all the target objects so that the highest priority object would follow the optimum path, and all the others would follow the most optimal paths that did not cause collisions with any other higher priority object. Experiments demonstrated successful coordinated transport of two and three 2 µm silica beads across distances of 30 µm in moderately to densely crowded workspaces. As in their previous work, the main limitation is the lack of scalability of the algorithm with increasing state space dimensionality involving more target objects and obstacles, smaller object size, and 3D motion.

C. Others

Pawashe and Sitti [50] used the wavefront expansion algorithm to arrange up to five 4.5 µm polystyrene and 5 µm silica micro spheres using an atomic force microscope (AFM) nanoprobe into user-defined patterns while avoiding collisions with workspace obstacles. Lynch et al. [51] used a combination of cell decomposition and wavefront expansion algorithms to trace navigable paths for controlled pushing of up to twelve 4.5 µm polystyrene particles on a glass substrate using an AFM probe tip. Improved particle release strategies would however be required to achieve greater precision in both the works.

Xie and Régnier [52] combined grasp and trajectory planning of twenty 3-4 µm nylon microspheres into 3D micropatterns using a gripper comprising of two individually actuated AFM cantilevers, each of which was equipped with an optical sensing system consisting of a laser and a photodiode. Amplitude feedback from the dithering cantilever operating at its natural resonance frequency was first used to search for suitable grasping points by laterally scanning the microspheres. Shortest path method was then applied in conjunction with real-time force sensing to compute linear trajectories during pick-and-place operations. The same techniques were used in [53] to construct 3D microstructures in ambient conditions. While these simple techniques provide real-time performance, they would not work successfully if collision avoidance is required with other workspace objects.

Chapin et al. [54] applied a simple set of local traffic rules to plan collision-free 2D paths for micro spheres using sculpted wavefronts of holographic optical tweezers (HOT). Path planning was then used along with real-time particle detection and trapping to create regular grid-pattern assemblies of twenty five 1.0 µm silica particles or separate a mixture of 1.0 µm and 1.9 µm silica particles. Tanaka et al. [55] later extended these rules and combined them with group theory principles and a destination assignment algorithm to simultaneously transport, sort, and arrange groups of up to thirty six optically-trapped silica beads with diameters varying between 1-3 µm into rectangular arrays. While these simple local rules are very effective for manipulations across short distances, global approaches are required for long distance-range manipulation as evident from the more recent literature on HOT-based particle transport.

Among other relevant works, Malima and Sabanovic [35] investigated the performance of Euclidean shortest distance, artificial potential fields, and A* algorithms in transporting micro particles in a virtual workspace. Cappelleri et al. [56] used a rapidly-exploring random tree (RRT) algorithm, a popular sampling-based motion planning method, in conjunction with quasi-static models for manipulation of planar parts with surface friction, to compute open-loop plans for peg-in-the-hole micro assembly tasks. Ju et al. [57] utilized an RRT algorithm to transport individual yeast cells while avoiding collisions with other cells in the workspace using HOT. Most recently, Thakur et al. [58] developed a framework that combined system identification, Kalman filter-based state estimation, local feedback planning, and genetic algorithm-based parameter optimization to indirectly push cells using an optically-trapped silica bead as the end effector and another intermediate untrapped silica bead to further reduce the photo damage to sensitive cells. Belharet et al. [59] adapted the anisotropic fast marching method to demonstrate minimum feasible energy path planning in simulation for arterial navigation of magnetically actuated neodymium micro robots.

V. CONTROL METHODS

Fearing [60] laid the foundation for controlling micro robots by highlighting the examples found in Nature. More specifically, he considered the simple unicellular Paramecium protozoa as a model organism that can regulate its trajectory based on external control signals. He then applied electric potential and visual sensing to enable the micro devices to perform primitive closed-loop trajectory following in the plane. Later on, Zesch and Fearing [61] considered the problem of aligning parts using force controlled pushing by an AFM probe that was equipped with a piezoresistive sensor. By using a set of simple macro or primitive actions, the proposed local controller could successfully align millimeter-scale cuboidal Si blocks on the horizontal plane with micron level accuracy and without causing collisions or loss in contact conditions. These two early works demonstrated the feasibility of controlling small objects and led to the development of a whole host of methods over the past decade that are discussed next.

A. Visual servoing

Kasaya et al. [62] provided one of the first examples of successful applications of visual servoing, when they applied it to control 30 µm solder spheres under scanning electron microscopes. While the positioning error and the time taken to create an arrangement of three spheres were rather large, this work laid the foundation for extensive research on visual servoing over the past decade. Sun and Nelson [63] played a pioneering role by using it for automated embryo pronuclei DNA injection. The visual servoing control error was defined with respect to the image feature parameters that changed as a result of the manipulator motion. The control scheme switched to precision position control once the servoing controller was able to position the pipette within the detected embryo nucleus region. Experiments on five viable mouse embryos showed 100% success rate. This was, indeed, a very promising result that opened up several research possibilities.

Wang et al. [64] then used visual servoing in conjunction with proportional integral derivative (PID) control of the
injection micro pipette motion for automated injection of foreign material, namely fluorescent dye and a fluorescein-tagged morpholinos that targets the gene no tail called ntl-MO, in 600 µm zebrafish embryos. They achieved an injection rate of 15 embryos per minute with a very high survival rate of 98% and success rate of 99% for the fluorescent dye injection, and a phenotypic rate of 98% for the ntl-MO injection. While the success and survival rates are nearly perfect, there is a scope for further improvement in injection rate as compared to manual injection of 10-20 embryos per minute by operating more than two manipulators in parallel. Further experiments are also required to investigate the usefulness of the approach for smaller-sized embryos that exhibit greater diffusion. Wang et al. [65] later used visual servoing on a micro positioning system to automatically track the locomotion of Caenorhabditis elegans worm online at a rate of 30 Hz. 128 worms of four different strains were continuously tracked for 3 minutes per sample.

Among other visual servoing-based mechanical manipulation works, Anis et al. [66] applied it for automated selection and transfer of individual living cells suspended in liquid growth media to microwell arrays etched on a silica substrate that was fixed to the bottom of a Petri dish. Experiments with three human cell lines demonstrated 93% success rates of transferring single cells in a well and 100% cell viability rate after transfer. However, as in other previous works, the cell transfer speed was not that high, and could be improved by operating the motorized stages at maximum speeds and including a picoliter fluid manipulator capable of aspirating multiple cells in the micro pipette. Zhang et al. [67] used visual servoing to achieve fast and accurate release of micro objects from a novel MEMS micro gripper consisting of three electrostatic actuators to drive two regular gripper arms and a plunger for active release. Experiments on 7.5-10.9 µm borosilicate glass spheres in ambient environment showed a 100% release success rate with an accuracy of 0.45 ± 0.24 µm. 3D patterns were also formed at a rate of 6 s per sphere, which was an order of magnitude better than the previous state-of-the-art. The system, however, could not be used to release irregularly-shaped micro objects.

Liu et al. [68] applied visual servoing for orienting the polar bodies of mouse embryos away from the site of micropipette injection to prevent damage. Experiments showed an initial calibration of the first embryo in a batch) orientation speed of 15°/s, and a subsequent orientation speed of the remaining embryos at 720°/s with a translation accuracy of 1.3 µm and rotational accuracy of 0.24° of the position controller. However, the image tracking algorithm had an accuracy of 70%, which made user clicking of polar body on the control interface essential to the overall success of the method. In other related works, Lu et al. [69] used visual servoing to control multiple micro positioning devices for aspirating single cells with an operation time of 30 s per cell and a success rate of 80%, and Liu et al. [70] used it to deliver recombinant BCL-XL protein into early-stage mouse zygotes with a high degree of success to enhance pre-implantation embryo development.

Tamadazte et al. [71] combined computer aided design (CAD) model-based 3D tracking of MEMS structures with a visual servoing control law for sequential micro assembly operations. Experiments with assemblies of two or more 400 µm × 400 µm × 100 µm Si objects with clearances of (1 - 5) µm resulted in a mean position error of 0.3 µm and an orientation error of 0.35 × 10^-2 rad. Later, Tamadazte et al. [72] used mono-view and multi-scale visual servoing in 2D to sequentially construct 3D micro structures using a piezoelectrically-actuated two-finger gripper system. Micro assembly tasks involving two and five micro parts yielded positioning and orientation errors of 1.4 µm and 0.5° respectively, and a cycle time of 40.8 s for the two part assembly. As in their previous work, the results were encouraging and it would be very useful to extend the method for smaller sized parts with more complex geometries.

Other works in this field include that by Ouyang et al. [73], who developed an automated biomanipulation system comprising of a dual-hand compliant, piezo-actuated mechanism that was controlled in 2D using a proportional derivative (PD) controller. While a representative transgenic operation involving injection of gene solution into a male pronucleus was successful, further experiments need to be conducted to ascertain the reliability and repeatability of the system. Xu et al. [74] used visual servoing to control a compliant, piezo-actuated, parallel micro manipulator by employing a PD plus two integrator control strategy. Experiments showed a manipulator workspace size of 260 µm × 260 µm in 2D with positioning accuracy and repeatability of 0.73 µm and 1.02 µm respectively. The precision can be further improved by increasing the natural frequency of the manipulator and enhancing the resolution of the vision system. Wason et al. [75] developed a multiprobe system to assemble 3D micro structures from 2D planar microfabricated parts by combining pre-planned manipulation sequences with vision-based motion and grasp force control using two cameras. Experiments with parts as small as 100 µm × µm demonstrated stable planar manipulation and limited success in 3D assembly operations due to the difficulty in orienting the part using the proposed camera configuration. Hence, future work would involve adding cameras and developing flexible algorithms capable of adapting to varying part geometries to construct more complex spatial mechanisms.

Application of visual servoing for non-mechanical micro manipulation includes the work by Onal and Sitti [76], where they used it for 2D pattern formation of micro particles under an optical microscope using a sharp nano probe. Experiments on six 4.5 µm polystyrene particles resulted in less than 0.64 µm average positioning errors. Further work would be required to extend the method to non-spherical objects, perform manipulation in 3D, and integrate force sensing for ever better accuracy. Katochivil et al. [77] used a combination of visual tracking and PID control for resonant magnetic actuators to realize decoupled motion of multiple untethered micro robots. A high-level A* planner was developed for waypoint selection and obstacle avoidance of the micro robots. Experiments showed that the frequency selectivity of the actuators could be used to enable independent operation of the robots on the same substrate in response to a common control signal. However, experiments were not performed to show robot motion on a
variety of substrates and in fluid media. These limitations were overcome in a subsequent work by Frutiger et al. [78]. The robots could also be used to push a variety of micro objects such as 150 µm × 20 µm gold disk on a SiO$_2$ surface and 50 µm glass beads underwater on a polished silicon surface. Future work would involve investigating the applicability of the proposed system for biomanipulation tasks.

Fukui et al. [79] developed a visual feedback-based PID controller for regulating the voltage of a piezoelectric actuator attached to a microchannel for fatigue testing of red blood cells (RBCs). Experiments conducted after 1 hour and 5 days of removing an RBC from a human subject showed that while the cell could withstand 95 cycles before undergoing plastic deformation in the first case, it immediately deformed after just 1 cycle in the second case. In future, it would be useful to place the designed system in a larger platform to perform several fatigue tests in parallel. Diederichs [80] developed a field programmable gate array (FPGA)-based camera system capable of tracking multiple micro robots with an error of less than 2 µm for visual servoing applications, which was later shown to have smaller latency and jitter as compared to state-of-the-art software methods in [81]. Zhang et al. [82] recently demonstrated 3D visual servo control of magnetically actuated micro beads by combining a proportional controller for stabilization and actuator force calibration with a non-linear model-based controller to minimize the variance of the bead’s Brownian motion. While experiments on following a rasterized scan pattern, stepping along a path at 100 nm intervals, and traversing the boundary of a 10 µm cube by a 2.8 µm bead were all successful, further work is needed to reduce the position fluctuation due to Brownian motion and realize the full force generation capacity of the actuator.

**B. Force control**

Unlike all the previous methods that used image-based visual servoing for X-Y motion, i.e. position and/or velocity, control of micro manipulators, Bilen and Unel [83] developed an integrated vision and force control scheme to place micro spheres within pre-defined configurations by adding rotational control to the positioning stage of the manipulators. Earlier, Carrozza et al. [84] used a PI controller for force control of a micro gripper using strain-gauge sensors, Gorman and Dagalgakis [85] developed a robust non-linear force controller for the linear motor stages that could be used in robots performing micro assembly tasks, and Shen et al. [86] attached a polyvinylidene fluoride (PVDF) sensor at the end of a composite cantilever beam manipulator to perform hybrid position and force control for batch assembly of micro devices.

Huang et al. [87] combined position control in the horizontal plane with Z-axis impedance force control of the injection micro pipette for batch biomanipulation tasks. Addition of force control enabled manipulation in a large area that was not restricted to the field of view of an optical microscope. Experiments with zebrafish embryos resulted in a maximum horizontal position tracking error of 1.5 µm, a force error of 60 µN, and a vertical positioning error of 6 µm. The operation speed was about 10 embryos per minute with a success rate of approximately 98%. Thus, the success rate was very high just like in the case of the visual servoing-based methods, while operation speed could be further improved. System modifications would also be required to perform injection in smaller mammalian cells.

Xie et al. [88] later extended the force control method for micro injection on fish embryos. They included two control loops for force control — the inner loop consisted of the impedance controller proposed in [87] and the outer loop comprised of a force tracking non-linear controller based on a feedback linearization approach. The proposed force controller was successful in directly regulating the penetration force to follow the desired force trajectory during the injection process in ten madaka fish embryos with a relative RMS error of less than 4.5%. More recently, Xie et al. [89] developed a new force-sensing scheme for injection on zebrafish embryos by combining the PVDF sensor with mechatronical electrical transduction of a simply supported beam structure. Experiments showed 100% injection success rate, survival rates between 73.9% - 92.3% 24 hours after fertilization, and survival rates between 73.9% - 90.3% 55 hrs after fertilization. No data was, however, reported for the injection speed; it would also be interesting to examine the viability of the approach for smaller embryos.

Among non-biomanipulation applications, Rabenorosoa et al. [91] implemented an incremental static controller and combined it with a direct-drive controller for hybrid force/position control of a micro gripper comprising of two piezo-actuated fingers. While the control scheme could achieve stable grasping of a 1500 µm × 1000 µm × 100 µm part when the substrate was perturbed, further evaluation is required for more complex guidance tasks of smaller-sized parts.

**C. Potential function**

Inspired by the flocking behaviors of natural organisms like birds, fish, and bacteria, where they act in a coordinated manner by following some simple objectives, flocking has become a popular tool for controlling large robot teams. Chen et al. [93] developed a region-based flocking control algorithm, comprising of two objectives, to move micro particles to predefined rectangular goal regions using optical tweezers. Each particle was assigned a specific goal within the rectangular region (global objective) and needed to maintain a certain minimum separation from every other particle (local objective). Experiments with nine 2 µm silica particles showed that they reached a stable flocking configuration after 34 s. A detailed convergence proof of the designed controller along with an allocation algorithm for assigning goal locations to individual particles was later provided in [94]. Experiments with twenty 3 µm silica particles showed faster configuration formation than in [93].

A modification of the previous work using only the local potential function to pair particles from two different groups and move the paired particles to a rectangular array configuration was presented in [95]. Detailed theoretical proofs of convergence to a stable array configuration with a controllable distance between the paired particles were reported in [96].
Experiments demonstrated that the method was able to create arrays by pairing two groups of ten 2 \( \mu m \) silica beads and 5 \( \mu m \) yeast cells with better positioning accuracy than the approach presented in [54] and without resulting in any collisions. An extension of this method to limit the maximum particle velocity was made in [97]. While all of these potential function-based controllers are very promising for computing collision-free trajectories of micro particles to form regular arrangements, questions remain about the applicability of the method for smaller and faster moving objects in 3D, and for long range transport operations.

D. Synchronization control

A closed loop synchronization control scheme was developed by Hu and Sun in [98] to transport multiple cells while maintaining a fixed pattern using optical tweezers. Utilizing a first-order dynamics model for cell behavior in an optical trap [99], the authors formulated the synchronization control problem as that of guiding and positioning multiple cells around the boundary of a 2D compact set that was parameterized by a planar curve. Experiments with yeast and Jurkat T Cells showed smaller errors in satisfying the synchronization constraint using the proposed controller instead of a non-synchronous controller with a maximum error value of less than 0.2 \( \mu m \). Further work would be required to apply this method for transporting cells in 3D and by avoiding collisions with other obstacles.

E. Others

A variety of other control strategies have been used to automate different micro manipulation operations. One of the earliest works was by Varholomeos et al. [100], who developed a multi-level controller where navigation functions were used for online multi-robot navigation, blended polynomial laws were used for trajectory control of the robot effectors, and genetic programming was applied to learn the parameters of the open loop model that mapped velocity to effectors, and genetic programming was applied to learn the parameters of the open loop model that mapped velocity to feedforward controllers for piezo-actuated \( H_\infty \) controller with a maximum error value of less than 0.2 \( \mu m \). Further work would be required to apply this method for transporting cells in 3D and by avoiding collisions with other obstacles.

In connection to micro assembly operations, a linear quadratic regulator was designed for optimal control of PVDF micro force sensors in [101], a linear robust \( H_\infty \) controller for piezoelectric cantilevers was developed in [102], a PI controller for a 2 degree of freedom (DOF) stick-slip positioning device was implemented in [103], feedforward controllers were designed for oscillating piezoelectric cantilevers in [104], and an \( H_\infty \) controller was synthesized for piezo-actuated cantilevers in [105]. Cappelleri and Fu [106] developed a coordinated control method to automate 3D manipulation and assembly tasks using multiple micro manipulators consisting of single point probes. Das et al. [107] designed a hybrid controller that switched between open loop and closed loop control for micro assembly of compliant MEMS structures, Xiao et al. [108] used a model reference adaptive PID controller for an electromagnetically actuated XY micro positioning stage, Xu and Li [109] combined output integral sliding mode control with model predictive control for a micro/nano positioning piezostage, and Xu [110] developed a discrete-time sliding mode generalized impedance controller with adaptive switching gain for both position and contact force control of a piezoelectric micro gripper.

In the domain of biomedical applications, Hagiwara et al. [111] presented a feedback controller comprising of PI control and a disturbance-based observer for precisely positioning a magnetically driven micro tool for enucleation of oocytes in a microfluidic chip, Li and Cheah [112] developed a feedback controller for cell manipulation using holographic optical tweezers, and Pawashe et al. [113] designed model-based, iterative learning controllers for automating pushing of micro objects using a permanent magnet actuated by oscillating external magnetic fields. Zhang et al. [114] developed a closed loop robust controller for automated aspiration and positioning of cells inside a micro pipette. Ou et al. [115] developed a model predictive control approach for the motion control of magnetotactic Tetrahymena pyriformis cells, and Shen et al. [116] used a PID controller for the X, Y, and Z degrees of freedom of a nanorobotic manipulator for cutting single cells.

Other recent works on miscellaneous applications include the development of robust adaptive motion tracking control of flexure-based, four bar micro/nano positioning mechanisms by Liaw and Shirinzadeh [117], and an open loop and a predictive model-based 2D trajectory control of a micro bead in a dielectrophoretic device by Kharboutly et al. in [118] and [119] respectively, and robust \( H_\infty \) control for electromagnetic steering of cylindrical NdFeB micro robots in low viscosity fluids by Marino et al. [120].

VI. DISCUSSION AND FUTURE WORK

We now summarize the common trends among all the planning and control methods below.

- **Modeling of micro system dynamics:** It is borne out from the discussions of the planning and control methods that modeling the physics at the micro scale plays an important role in their successes. Developing and experimentally validating high-fidelity models of the dynamics of the manipulated objects in the presence of dominant surface forces and often under the influence of external force fields are essential pre-requisites for devising a suitable planner or controller.

- **Adaptation of macro domain methods:** All the planning and control methods are modifications of well-established approaches in macro scale robotics deployed in industrial, military, medical, and space applications. The defining characteristic of the methods at the micro scale is incorporating the micro object dynamics models within the optimization framework before using the standard form or some slight variant of a popular planning algorithm or control law to achieve manipulation success.

- **Coupling between planning and control:** Planning and control methods are increasingly being coupled together to achieve the dual benefits of optimizing operation-level requirements while ensuring controllability and stability.
of the executed actions. This coupling is particularly important for micro manipulation due to the fast response times needed for constantly changing object locations, orientations, and appearance or disappearance of objects in the workspace.

- **Enhanced effect of uncertainties:** Both sensing and action execution uncertainties play a significant role in the planning and control methods. While such uncertainties are often present in the macro domain, both spatial and temporal extents of the uncertainties are enhanced at the micro scale due to a combination of diffusion, presence of translucent and inhomogeneous objects, inherent limitations of the sensing hardware (resolutions of optical and electron microscopes), difficulty of 3D state estimation, and the settling effect of gravity. Hence, both the forms of uncertainties are either modeled explicitly by the methods to compute robust policies or control laws, or are accounted for using feedback error compensation or fast re-planning.

- **2D manipulation of a few objects:** All the methods are experimentally shown to achieve reasonable or sometimes nearly perfect precision, accuracy, and reliability in manipulating many types of microscopic objects, both biological and artificial, using different manipulation techniques. However, most of the experiments report 2D manipulation of a few (up to twenty) objects in relatively small workspaces over short time durations of the order of a few seconds.

In order to assess the relative usefulness of the planning and control methods under different operating conditions, we use four parameters, namely manipulation environment or type, manipulated object size, number of manipulated objects, and workspace occupancy. Table I shows that graph search and other non decision-theoretic methods are suitable for manipulation in both liquid media and ambient conditions, and scale polynomially with the number of manipulated objects. While graph search works best for large-sized objects (characteristic dimension \( \geq 5 \mu m \)), other methods are applicable for both small and large-sized objects. However, unlike many other non decision-theoretic methods, graph search is useful for computing collision-free trajectories in crowded workspaces. Decision-theoretic methods are most useful for manipulating a few small-sized objects in liquid media in crowded workspaces.

Table II shows that only force control is applicable for 3D manipulation if it is of contact-type; all the other control methods are restricted so far to 2D manipulation largely due to the limitation in sensing the 3D workspace as discussed in Section I. Visual servoing, potential function, and synchronization control are all suitable for every object size, whereas force control is mostly useful for not very large objects, and the other methods are primarily used for large objects. Force control is used for manipulating one object at a time, whereas visual servoing is applicable for manipulating any number of objects, and potential function and synchronization control are designed to manipulate several objects in parallel. And lastly, visual servoing works well in crowded workspaces if coupled with a planner, potential functions perform satisfactorily for local manipulation operations in crowded workspaces, and synchronization control is useful when non-manipulated objects (obstacles) are not present.

Promising future research directions where automated planning and control might play a significant role are listed below.

- **3D manipulation:** Manipulating objects in 3D is necessary to assemble functional devices with non-planar micro parts or automate critical operations in biology and medicine such as cell sorting, drug delivery, and drug screening. Some of the challenges are real-time reconstruction of the 3D workspace, computing global plans and feedback control gains on-the-fly for high-dimensional problems, and the need for incorporating multiple sensing and control modalities. Machine learning might be useful in alleviating some of the challenges by learning complex manipulation behaviors from primitive actions online, or by approximating object configurations, optimal plans, and control gains in real-time based on the models that are generated offline for similar workspace conditions.

- **Manipulating a large number of objects:** As in the previous case, most practically important applications require manipulating not just a few objects at a time, but several of them (up to hundred) simultaneously. Increase in problem dimensionality, however, renders many of the current planning and control methods ineffective. Machine learning and sparse distributed memory-based reasoning might help us in addressing this challenge. Parallel computing and GPU-based computing would also be useful in accelerating high-fidelity simulation of manipulation operations to facilitate the development and validation of such planning and control methods.

- **Manipulation in hybrid set-ups:** It would be useful to leverage the capabilities of hybrid micro manipulation set-ups, such as optofluidic or optoelectronic, to develop systems that provide both high throughput and precision. Automated planning and control is challenging in such systems due to the coupled nature of the dynamics equations. Model simplification and reduction might facilitate the process by enabling the use of computationally efficient models in real-time planning and control with bounded and tunable loss in the solution quality.

- **Automating complete operations:** The existing planning and control methods have focused on automating the individual steps, such as transport, pick-and-place, and alignment, of the biomanipulation or micro assembly operations. We now need to extend the methods to address the problem at the complete operation level. Developing an integrated system consisting of separate planning and control methods for the different operation steps, and adapting some of the latest advances in macro scale robotics such as LQR trees, RRT*, and chance-constrained optimal control, to be able to model a wide variety of problems might be useful in this regard.
Table I

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Manipulation environment</th>
<th>Manipulated object size</th>
<th>Number of manipulated objects</th>
<th>Workspace occupancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td>Graph search</td>
<td>Decision-theoretic</td>
<td>Synchronization control</td>
<td>Others</td>
</tr>
<tr>
<td></td>
<td>Useful for operations in both liquid media and ambient conditions</td>
<td>Most useful for operations in liquid media</td>
<td>Use for operations in both liquid media</td>
<td>Use for operations in both liquid media and ambient conditions</td>
</tr>
<tr>
<td></td>
<td>Useful for larger objects ($&gt; 5 \mu m$) with smaller diffusivities and imaging errors</td>
<td>Useful for smaller objects ($&lt; 5 \mu m$) with larger diffusivities and imaging errors</td>
<td>Scales exponentially necessitating approximate solutions</td>
<td>Usually scales polynomially</td>
</tr>
<tr>
<td></td>
<td>Scales polynomially with proper choice of heuristic function</td>
<td>Works well in crowded workspace</td>
<td>Works well in crowded workspace</td>
<td>May not work well in crowded workspace</td>
</tr>
</tbody>
</table>

Table II

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Manipulation type</th>
<th>Manipulated object size</th>
<th>Number of manipulated objects</th>
<th>Workspace occupancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td>Visual servoing</td>
<td>Force control</td>
<td>Method</td>
<td>Synchronization control</td>
</tr>
<tr>
<td></td>
<td>Mainly useful for all 2D manipulation</td>
<td>Applicable for 3D contact-based manipulation</td>
<td>Has been applied to 2D optical tweezing</td>
<td>Has been applied to 2D optical tweezing</td>
</tr>
<tr>
<td></td>
<td>Useful for all object sizes</td>
<td>Useful for not very large objects</td>
<td>Useful for manipulating several objects together</td>
<td>Useful for manipulating several objects together</td>
</tr>
<tr>
<td></td>
<td>Works well any # of objects</td>
<td>Useful for manipulating one object at a time</td>
<td>Varies depending on the specific method</td>
<td>Works locally in crowded workspace</td>
</tr>
<tr>
<td></td>
<td>Works well if coupled with planner</td>
<td>Meant for isolated manipulation</td>
<td></td>
<td>Works well in crowded workspaces</td>
</tr>
</tbody>
</table>

VII. Conclusions

To the best of our knowledge, this paper provides the first comprehensive survey of the state-of-the-art in automated planning and control research as applied to manipulation of micro scale objects. We first discuss the distinction between isolated and coupled planning and control architectures to emphasize the need of the latter for micro manipulation that poses some unique challenges not present in the macro domain. We then present a high-level taxonomy of the methods in the literature, and discuss their key aspects, resulting advances in experimental studies, and major shortcomings. After identifying certain common trends among all the methods, four parameters are introduced to characterize the various types of manipulation operations. Our conclusion is that while no single class of planning or control methods is useful under all operating conditions, at least one class of methods always works well in simultaneously manipulating a not very large number of micro objects in 2D using either contact or non-contact manipulation type in liquid or ambient conditions, by avoiding collisions with obstacles in crowded workspaces or by maintaining a high degree of accuracy and reliability in isolated manipulation operations. Lastly, we present future research directions in developing planning and control methods for automating complete biological and micro assembly operations involving manipulation of a large number of objects in three dimensions.

Acknowledgements

We would like to gratefully acknowledge the help of S. Chowdhry and P. Svec in preparing the manuscript.

References


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