IRIS
Institute of Robotics and Intelligent Systems

BIO MICRO ROBOTICS: Robotics for Exploring Life

Robots are currently exploring many environments that are difficult if not impossible for humans to reach, such as the edge of the solar system, the planet Mars, volcanoes on Earth, and the undersea world. The goal of these robotic explorers is to obtain knowledge about our universe and to answer fundamental questions about life and human origins. Microrobotics has entered this field by exploring life at a much smaller scale and more fundamental level. Microrobotic systems for physically exploring the structures of biological cells are being developed, and robotic motion planning strategies are being used to investigate protein folding. Microrobotic mechanisms have been used to investigate organism behaviors, such as the flight dynamics of fruit flies as well as the neurophysiology that govern many other biologically interesting behaviors. These recent research efforts and others like them illustrate how several areas of robotics research are rapidly converging to create this new discipline I refer to as BioMicroRobotics. These new directions in robotics represent only a beginning and indicate that robotics research, and biomicrorobotics in particular, has the capability of making significant contributions in the understanding of life.

Over the past decade the science of microrobotics has emerged as a subset of the general field of robotics. Microrobotics can be divided into two main categories: the manipulation of micron sized objects with larger robots and the fabrication of small intelligent robotic systems from micron sized parts. The main research challenges in microrobotics consist of understanding the predominate physical forces that govern part interactions at these scales, and the development of appropriate sensing and actuation strategies that can effectively and robustly operate in this domain. Furthermore, microrobotics means integrating these sensing and actuation strategies with a cognitive aspect that enables intelligent, complex interactions with the microworld.

Biomicrorobotics is an emerging field in which microrobotics is defined within a purely biological domain. A number of fascinating robotics research efforts fall within the category of biomicrorobotics, which the following research projects illustrate.

Robot Motion Planning and Protein Folding

Proteins, the basic units of life, are 3D structures formed by linear amino acid sequences folding themselves into a specific shape. The structure provides valuable clues to the function of a specific protein. The attempt to understand the mechanism that drives a protein into its unique, biologically active structure, and to predict this structure and thus the protein's corresponding function from knowledge of its amino acid sequence, is called the protein folding problem. Because of the great significance of understanding the protein folding problem, such as for designing new drugs and for more fully understanding the molecular biology of many diseases, several methods have been proposed for predicting protein structures. Prof. Wuethrich of ETH is clearly at the forefront of this field with his work in molecular modeling using NMR techniques. One strategy that has been quite successful from a computational standpoint comes from the motion planning community in robotics. For more than two decades robotic researchers have worked to solve the robot motion planning problem. The problem can be stated as follows: given a starting state of a robot and a goal state of that same robot, determine a path for the robot to take that will connect the two without colliding with objects in the environment or forcing the robot into physically impossible geometric or dynamic configurations. Computationally this problem is incredibly difficult to solve. Many roboticists, however, have developed insightful approaches that have been used to guide mobile robots in cluttered environments and robot snake-like arms with many degrees of freedom. Similar techniques have been used to plan radiation therapies for treating brain cancer that maximizes the radiation dose to the tumor, while minimizing damage to healthy tissue. Roboticists such as Prof. Latombe of Stanford, Prof. Amato from Texas A&M, and Prof. Kavraki from Rice Universty, realized that the protein folding problem can be described in a similar mathematical framework and that, with appropriate modification, their tools can be used to determine protein fold pathways correctly and efficiently on PC platforms. This provides molecular biologists with quick and accurate ways of investigating protein structures and the paths these structures may take to arrive at the correct, or in the case of many diseases, incorrect folds. Figure 1 illustrates the protein folding problem from a robotics perspective and shows the similarities and differences between traditional robot motion planning and protein folding.

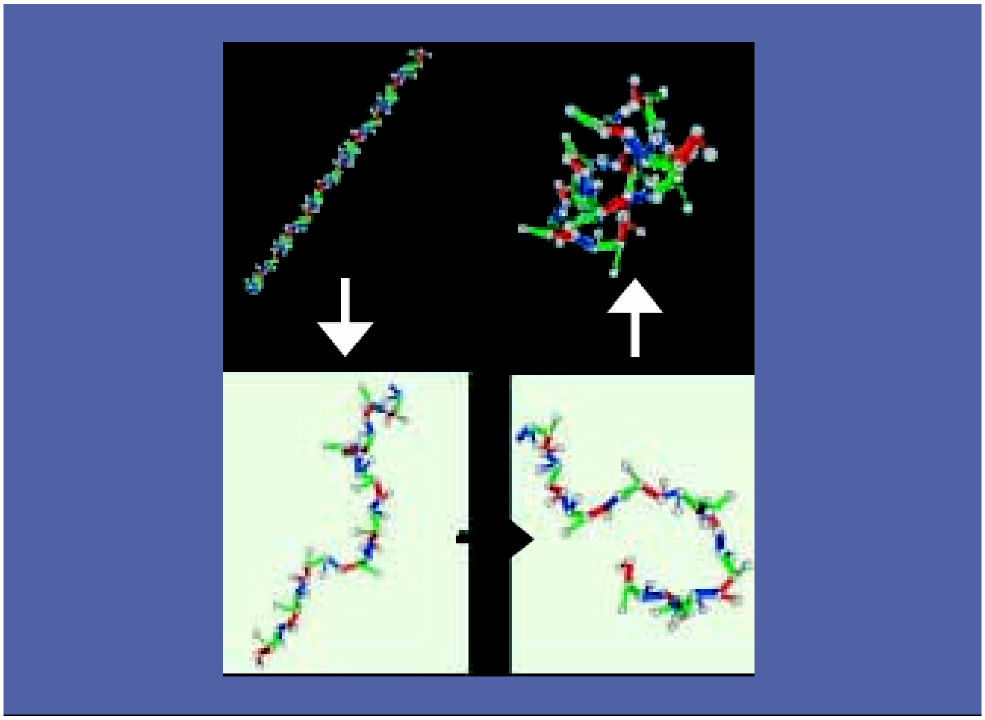

Figure 1. Robot motion planning and protein folding (the 10-ALA folding case is shown courtesy of Prof. Amato at Texas A&M

Microrobotic Cell Manipulation.

Progressing from molecules to cells, biomicrorobotics is developing intelligent robotic systems that have the potential to change the way in which biological cells are studied and manipulated by creating complex biomanipulation techniques. From a robotics standpoint, the manipulation of biological cells and materials presents several interesting research issues that extend well beyond biomanipulation. Biological structures are usually highly deformable objects, and the material properties of these objects are often not well quantified, so developing strategies for manipulating deformable objects must be addressed. Most biological cells are between 1 and 100 microns in diameter, depending on the cell type, so micromanipulation issues must be explored, including the appropriate use of high resolution, low depth-of-field vision feedback and very low magnitude force feedback. Although multi-axis force sensing capabilities would be useful for handling cells, sensors capable of multi-axis force sensing at the force scales required are currently unavailable. Robotic devices capable of complex manipulation of biological cells and materials are only beginning to emerge, and robotic systems capable of integrating a variety of novel sensory information for biomanipulation are still very much an open research topic. By pursuing robotic manipulation of small-scale biological structures, many interesting robotics research avenues such as micromanipulation, deformable object handling, multi-sensor integration, and force and vision feedback assimilation must be explored.

At the Institute of Robotics and Intelligent Systems (IRIS) we are fabricating microsensors for measuring cell forces at micro to nanoNewton levels and developing computer vision algorithms for tracking cell deformations in real-time. We have recently investigated the mechanical membrane changes that take place during “zona hardening” in which oocyte (egg cell) membranes harden after fertilization. This work has important implications for reproductive biologists working with in vitro fertilization and for biologists that develop transgenic organisms for biological research studies. The results provide additional evidence for protein cross-linking that biologists have proposed as the mechanism by which zona hardening occurs.

Figure 2 shows an overview of our efforts to intelligently manipulate biological cells using microrobotics.

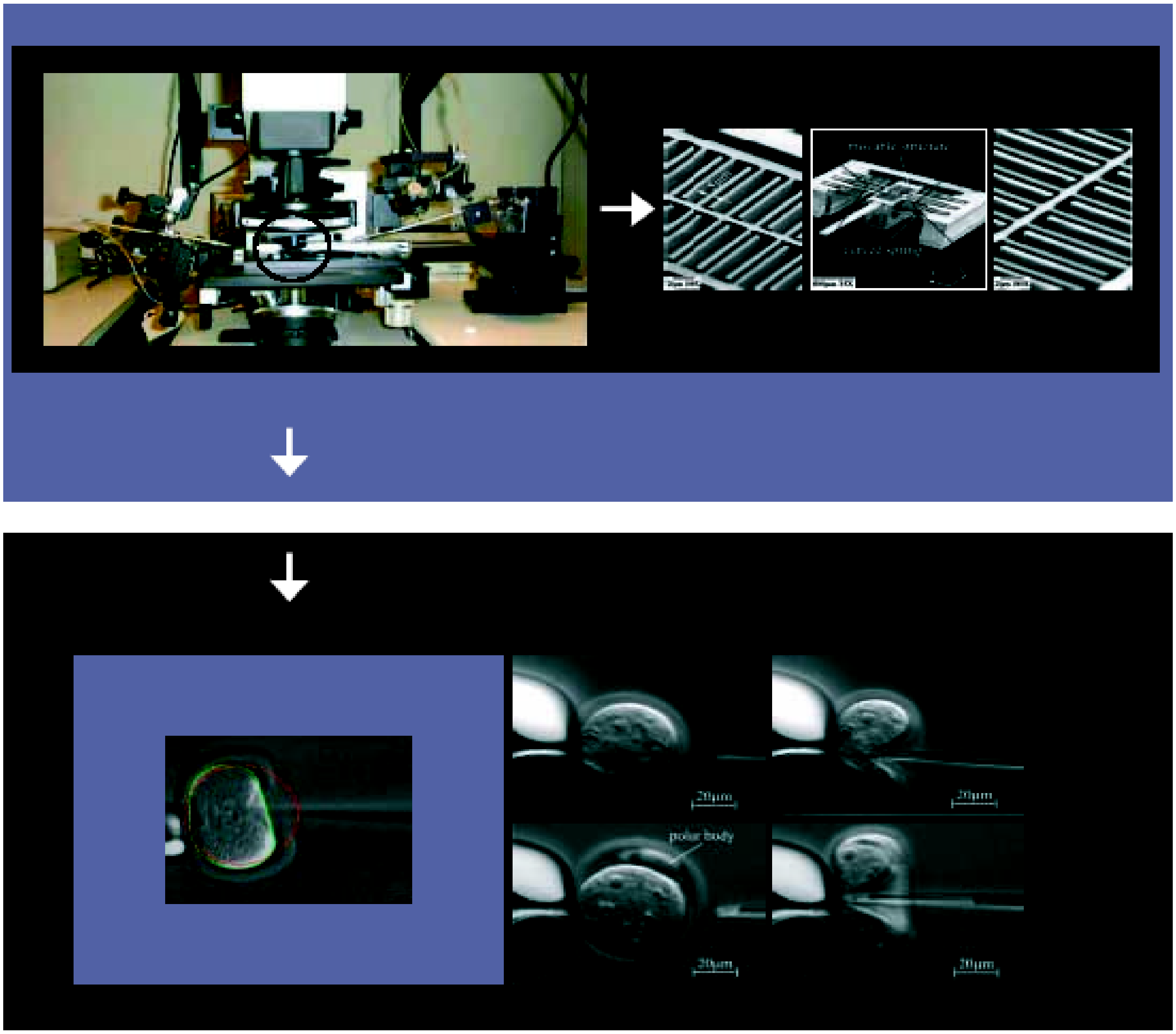

Figure 2. Microrobotic cell manipulation

Investigating Complex Organism Behavior at the Neuron Level

As scientists and engineers strive to develop more intelligent microrobotic systems, many in the field are increasingly turning towards biological organisms in order to provide design inspiration. For example, researchers have considered cockroaches, crickets, and earthworms to guide the design of small autonomous microsystems. Prof. Boehringer, a roboticist working at University of Washington, works with biologists to implant microelectrodes in sea slug brains to monitor neurological activity during locomotion. Over the past few years, the flight behavior of small insects has attracted interest for the development of flying microrobotic systems, such as the Mechanical Flying Insect (MFI) project currently being pursued in Prof. Fearing's laboratory at the University of California at Berkeley. One such insect that is particularly interesting from the standpoint of complete flight system design is drosophila, the fruit fly.

Drosophila, a model organism studied by biologists for almost a century, possess a highly developed flight control system that provides them with the capability to perform robust stable flight, as well as exceedingly rapid and precise turning maneuvers. The neurophysiology and biomechanics are inextricably linked and must be considered at the systems level. Multimodal sensory input converges on only 18 control muscles that are responsible for the fine-tuning of wing motion for maneuvering, the aerodynamic basis of which has recently been revealed. Beyond its impressive flight behavior, the fact that Drosophila is completely autonomous, extremely small, highly robust, and self replicating make this organism particularly interesting from a microrobotics standpoint. IRIS researchers have been working with Dr. Fry of the Institute of Neuroinformatics at ETH to develop microrobotic sensors that can more fully investigate the flight dynamics of drosophila. Our recent results have, for the first time, accurately measured both aerodynamic and inertial forces directly from live specimens, as shown in Figure 3, providing further data on how complex behaviors such as flight can arise from biological organisms like drosophila.

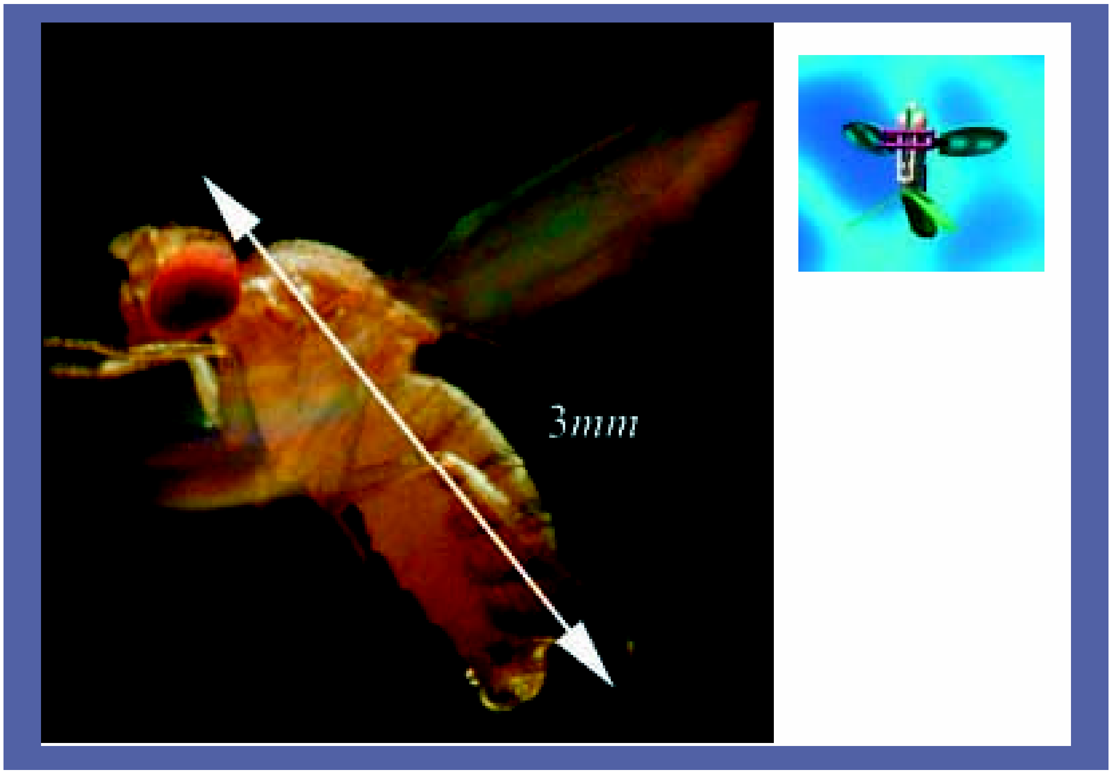

Figure 3. Fruit fly dynamics.
Exploring the dynamics of fruit flies (drosophila) using a MEMS force sensor and a conceptual drawing of the Berkeley Mechanical Flying Insect (Upper left Drosophila photo courtesy of Dr. Fry, Institute of Neuroinformatics, ETH. Upper right MFI photo courtesy of Prof. Fearing at the University of California-Berkeley).

BioMicroRobots for Exploring Organisms such as the Human Body

A new research project at IRIS is building autonomous microbotic machines that can explore the interior of organisms without being physically connected to the outside world. This effort integrates our past research in robot control using computer vision feedback, MEMS, deposition of permanent magnetic materials for the fabrication of microsystems, and the manipulation of deformable objects, into wireless magnetically guided microrobots. Figure 4 shows the system concept. Recent theoretical and experimental work has demonstrated the feasibility of this concept, and we are currently working to realize a complete working prototype. A microrobotic system like this will dramatically change our ability to explore the human body, gather information on its inner workings and, possibly, perform delicate microsurgeries and deliver drugs in difficult to reach locations, such as in the eye, the brain, or other organs.

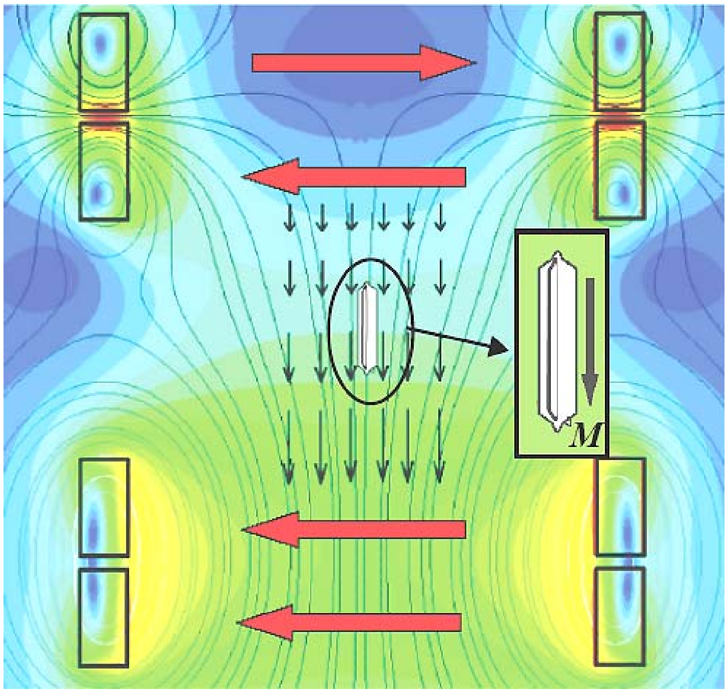

Figure 4. Conceptual drawing of a magnetic microrobot steered with external magnetic fields. The microrobot (shown enlarged in the inset) is magnetized along its major axis. Four solenoid coils are placed coaxially with the large arrows indicating the direction of current flow. The superimposed fields of the coils are shown with flux lines also drawn. The inner two coils are in a Helmholtz coil configuration creating a uniform magnetic field at the center and aligning the microrobot along the central axis. The outer two coils are in a Maxwell coil configuration, generating a uniform magnetic field gradient at the center and applying the steering force on the microrobot.

Robotics as a Key Component of Nanoscience

As Dr. Heinrich Rohrer pointed out at the 2003 St. Gallen Nanofair, the field of nanoscience represents a steady convergence over the past fifty years of three distinct areas. First, our ability to fabricate solid state electrical and mechanical components at smaller scales has vastly improved. Second, molecular biology has also made impressive strides in understanding the structure and function of biological structures at smaller scales. Finally, chemistry, which has always been involved at nanoscales, has developed a much deeper understanding of chemical and material properties at these levels. As these fields converge, nanoscience and nanotechnology have become defined. At the nanoscale level, the drive towards more intelligent behavior, towards better sensors, actuators, and the intelligent connection between sensing and actuation, is apparent. This drive suggests that techniques and strategies developed by the robotics research community over the past fifty years can play a key role. The field of BioMicroRobotics is rapidly emerging and is moving towards this exciting convergence.