

WTEC ROBOTICS WORKSHOP

RESEARCH AREA SUMMARY

Medical Robotics; Biological and Pharmaceutical Applications; Assistive/Rehabilitative Applications

by

Yuan F. Zheng
The Ohio State University

In the U.S., research in the areas of medical, bio/pharmaceutical, and assistive/rehabilitative applications is very active. Although technologies in the other countries are yet to be assessed, it is safe to state that the U.S. is leading the world in these three related areas.

1. Medical Robotics

1.1 The Advantages of the Medical Robots

Medical robots have a number of advantages including: a. expanding the capabilities of the doctors in performing surgery, b. improving consistency and quality of surgical treatment to produce better outcomes, and c. enabling non-invasive surgeries to reduce the pain and recovering period during and after the surgery. The technologies have been developed for about 15 years in this country. Primary focus is on the computer-integrated robotic surgery. Today, some of the robotic technologies have become mature and led to the development of commercial products while others are still extensively studied in the laboratories.

1.2 Research Issues

According to Russell Taylor of the Johns Hopkins University computer-integrated robotic surgery includes the following three activities: pre-operation, intra-operation, and post-operation. Computer information processing is involved in all the three operations. In the pre-operation process, the data from the patient and atlas is processed which develops the patient model and “designs” the plan of the surgery. During the operation, the patient model and the surgery plan are updated based on the information provided by the sensors such as computer vision, and the medical robot executes the operation. The post-operation assesses the result of the surgery under the assistance of the computer again.

The three operations processes involve the integration of many research issues in robotics. In terms of the hardware, a computer-integrated system needs a precise mechanical manipulator, an imaging device, and a high-speed computer connected to the network. On the software side, the medical robot needs mechanisms of advanced image and sensor data processing, computer-aided planning and control, human-machine interface, anatomic atlas and surgical task modeling, efficient data retrieval, and system

integration. Although technologies exist in these areas, **invention, improvement, and integration** of new and effective components are the major research issues of this particular field. The goal is to have a grand unified system to perform “plug and play”, “information-intensive” surgery and “one-stop shopping therapy” with a robot and computer-assisted surgical team.

1.3 Major Laboratories and Investigators

In the United States, there are a great number of research laboratories and investigators performing research on medical robots. **Russell Taylor** at the Johns Hopkins University has an NSF funded Engineering Research Center (ERC) for Computer-Integrated Surgical Systems and Technology which cooperates with **MIT, CMU, Morgan State, Georgetown, Harvard, and Penn.** Activities of the ERC represent the most advanced development of the field in the United States.

1.4 Major Accomplishments

A large number of robotic surgery topics have been studied in this country. In terms of technologies, researchers have investigated the **modeling and analysis** technologies for patient-specific modeling and analysis, **interface** technologies to extend the sensory, motor, and human-adaptation abilities of computer-based systems in an unusually demanding and constrained environment, and **System Science** technologies for developing architectures, building blocks, and analysis techniques that facilitate rapid development and validation of versatile computer-integrated systems and processes with predictable performance. The progress of those three areas will determine the progress of the medical robot applications.

In terms of practical applications, experiments have been performed on a number of surgeries and therapies including:

- steady-hand sinus surgery with virtual fixture derived from CT models
- high precision ultrasound guided needle placement, bio-manipulation with a steady hand robot
- telesurgical robot for throat surgery
- robotic joint replacement surgery
- steady hand guiding for microsurgery
- telerobotic surgery augmentation
- 3D ultrasound guided and robot aided prostate brachytherapy and TRUS-guided prostate therapy
- robotically assisted lung biopsy
- intra-cavity robot in closed MRI
- robotically assisted spinal pain blocks

In summary, research on medical robots has made great progress in this country. Research laboratories continue to study the technologies related to the three fundamental issues, i.e., modeling and analysis, interface technology, and systems science. It is predicted that the impact of computer-integrated medical robots on medical care in the next 20 years will be as great as that of computer-integrated manufacturing on the manufacturing industries over the past 20 years.

2. Biological and Pharmaceutical Applications

2.1 The Need of Robotics in the Area

In this particular area, robotics are applied to the automated handling of biological samples, including cells and body fluids, drug delivery, and dispensing of various biomaterials some of which are highly viscous. This area is growing strongly in recent years because biological research has become a priority in both universities and pharmaceutical industry. The goal is to study the biologic structure at the protein level such that effective drug can be developed, or various compositions of drugs can be screened automatically and efficiently. Another goal is to operate on tiny biological objects such as cells or bio-chemical samples directly to cure disease or to perform genetic operations. Researchers in the U.S. are studying robotic technologies for the following applications:

- Cell manipulations – for genetic research such as automated cell injection for pronuclei DNA injection
- Drug discovery – for high through-put handling of chemical samples
- Drug delivery – for targeted delivery of drug in human body
- Protein folding – for study the principle of protein folding such that effective drug can be discovered.
- High throughput applications such as biomaterials dispensing – for drug screening, and protein crystallization studies, etc.
- DNA and protein sequence analysis
- High-throughput molecular screening and drug discovery systems
- Bio-sample preparation (blood, sputum, gynecological, colorectal, fine needle aspirates)
- Production and analysis of DNA and protein microarrays
- Lab-on-a-chip chemistry analysis systems
- Functional analysis of living cells
- Combinatorial chemistry
- Protein crystallography
- Exploring molecular and cell biology

2.2 The Robotics Research Issues

There are a number of research issues involved in this new area of applications. These issues need a new consideration of robotics technology which represents a departure from conventional ways:

- A. **Fabrication of robotic components** – There is a need to fabricate micro-grippers, micro-actuators, and micro-sensors which can handle, operate, and sense at micro or even nano level. Non-traditional approaches such as solid-state fabrication and various MEMS approaches must be used.

- B. **Sensing** – Tiny and sensitive sensors have to be developed such as force sensors to sense the force of a micro-needle when it penetrates a cell. Other sensors include optical microscopes, AFM, SEM, TEM, etc., for seeing the bio-structure at micro- and nano-resolutions. Using capacitive and optical measurements is also an issue of study in sensing.
- C. **Actuation** – Actuation at the micro-level is extremely important for biological applications. Current technologies being studied include *piezoelectric, electrostatic, electromagnetic, ultrasonic, and molecular*.
- D. **Physical modeling** – At the molecular level, one needs to consider what the best approach is for describing the dynamics of the molecules using Maxwell or Newtonian mechanics. One also needs to develop new molecular modeling approach to understand bio-structure such as protein folding.
- E. **System integration** – For high through-put handling of biomaterials, one needs to integrate various robotic components, including robotic arms, robotic vision, micro-actuators, and robotic sensors to build an effective system, and to plan the coordination of various components. In this area, we see a number of ad hoc approaches, but not systematic developments.

2.3 Major Laboratories and Investigators

Since the area is relatively new, there are only a few laboratories and investigators in the U.S. involved in this area. Our current knowledge produces the following list:

- A. **Peter Allen** at Columbia University studies automatic harvesting of protein crystals using robot vision and micro-gripper.
- B. **Karl Bohringer** at the University of Washington studies Neuronal cell probes, cell/droplet handling which needs similar tools as Brad Nelson (see below).
- C. **Ronald W. Davis** at the Stanford University Genome Technology Research Center studies Custom instrumentation and novel technology to increase the throughput and decrease the cost of DNA sequencing and genomic analyses.
- D. **Harold (Skip) Garner** at the University of Texas Southwestern Medical Center studies applied computational biology, advanced instrumentation development, genetics, genomics and proteomics that capitalizes on bioinformatics/computational biology findings and instrumentation capabilities.
- E. **Ian Hunter** at MIT and **Sylvain Martel** at the University of Montreal Ecole Polytechnic has developed the Nanowalker, a mobile microrobot with a suite of scientific instruments for investigating large numbers of bio-materials with potential for high throughput assays.
- F. **Eric Lander** at the Broad Institute (MIT, Harvard, Whitehead Institute) studies high-throughput robotic systems for large-scale DNA sequencing, SNP analysis, and haplotype mapping, and tools for genomic medicine.
- G. **Deirdre Meldrum** at the University of Washington studies two major topics. One is the high-throughput robotics and automation systems to prepare samples (DNA, protein crystallography, etc.) and the other is to develop integrated

modular microsystems to measure multiple parameters in living cells in real-time for molecular and cellular biology.

- H. Brad Nelson** at the University of Minnesota studies the automated intracytoplasmic cell injection (ICSI), DNA pronuclei injection, zebrafish embryo injection, drosophila characterization, highly targeted drug delivery. These application areas need fabrication of micro-end-effectors and sensors. Brad Nelson is currently with the ETH-Zürich in Switzerland, on leave from the University of Minnesota.
- I. Yuan F. Zheng** at The Ohio State University studies the mechanisms for automating the protein crystallization process, and for automatic harvesting of protein crystals. Major research issues are technologies for high-throughput dispensing of bio-materials, especially materials with viscosity, and of various combination of chemical samples for screening conditions of protein crystallization as well as vision and micro-gripper coordination for effective harvesting of protein crystals.
- J. Novartis Research Foundation's Genomics Institute** studies high-throughput screening robot to test 1 million compounds a day (Kalypsys, Inc.) with on-line storage capacity of 2.2 million compounds.

In addition to the above, quite a few researchers study **structural computational biology** through computation and theoretical tool, including **Herbert Edelsbrunner** and **Pankaj Agarwal** at Duke, **Jack Snoeyink** at UNC, **Jean-Claude Latombe** and **Leo Guibas** at Stanford, **Lydia Kavradi** at Rice, **Nancy Amato** at Texas A&M, **Greg Chirikjian** at Johns Hopkins, and **Bruce Donald** at Dartmouth.

2.4 Major Accomplishments in the U.S.

Researchers have collectively made many contributions in the field, which include the following aspects. First, a number of robotic systems for bio-materials and liquid handling have been developed for high-throughput screening. Automated manipulation including sample dispensing, storage and retrieval. This development perhaps represents the most notable accomplishments which are useful not only to research laboratories but also to the pharmaceutical industry. Another important development in high-throughput system is the automated DNA sequencer and large-scale DNA processing pipeline which have enabled sequencing of the human genome and other organisms.

Micro robotic technologies have enabled the automated handling and operating of tiny biological objects such as automated cell injection for pronuclei DNA injection using visual servoing, while microarray technologies for DNA and proteins have enabled whole genome studies of gene expression, protein expression. In addition, lab-on-a-chip and similar miniaturized technologies have enabled integration of process steps in analyzing DNA, cells, etc. for fundamental understanding, therapy, and eventually prevention of disease.

Theoretically, biomechanics membrane modeling for force/vision feedback fusion "Zona hardening" quantified mechanically was done for the first time by Nelson and students. Robotic modeling of the process of protein crystallization processing was studied by Zheng and his student. In structural computational biology, researchers have

studied many topics including accurate computations for shape and volume, kinematics and conformational analysis of large molecules, search methods for notoriously difficult problems such as protein folding, and methods for computer-assisted drug design that take into account molecular flexibility, better analysis of experimental results from X-ray and NMR, and better understanding of the computational complexity of several computational biology problems.

In summary, robotics research and activities on bio-applications in the U.S. are relatively young for less than five years. Within such a short period of time, researchers in the U.S. have accomplished a great deal. From the information available at this point of time, we believe that the U.S. should lead the world in the bio-applications of the robotic technologies.

3. Assistive/Rehabilitative Applications

3.1 The Needs of Robotics in the Area

Assistive/rehabilitative robots have been studied for a long time. The goal of the development is to assist people with physical disabilities. For assisting mobility, early efforts were made by European scientists in the 1960s which aimed to develop exoskeletons to be worn by disable people. The efforts were not that practically successful but led to the development of legged walking robots and chairs in recent years. For manipulation, prosthetic arms and feeders for assisting the patients who have lost arms or hands are available commercially in a simple way.

In the U.S., there are 5 million wheelchair users. The cost for assisted living on the other hand is rising and so is the cost for rehabilitation. Consequently, assistive/rehabilitative applications represent one of the most important areas of robotics research. In the United States, there are quite a few institutions involved in the field, and some high-end products with advanced technologies are already commercially available.

3.2 Research Issues

There are two sets of research issues for mobility and manipulation, respectively, each of which is listed below.

A. Mobility

Mobility is to assist the elder and handicapped people in both locomotion and navigation, and is the most essential function that the assistive/rehabilitative robots have to perform. Although there are many robotic wheelchairs available, most of them are still limited to be a mechanical device, not able to assist in an intelligent way. Most challenging issues of research are: a. **understanding human intention and adapting to it**, and b. **developing mechanism of control for human-in-the-loop navigation**. Most important issues of technology are: a. **flexible input devices**, and b. **low-cost robotic wheelchairs**. The former is to make the robotic device more flexible in adapting to the needs of the people, and the latter is for improving the affordability of the device such that many people can use it.

B. Manipulation

The issues of research for manipulations are: a. **identifying movement training algorithms that maximize motor learning and neural recovery, by combining robotics, brain imaging, and neurocomputational modeling**, b. **designing automated tools to aid the diagnosis and assessment process** (parametric to enable customization), and c. **developing safe and effective human-robot interaction for hands-off assistive robotics**.

The issues of technology which have to be addressed by the industry include: a. develop **combined therapeutic/assistive rehabilitation robotic systems** that are lightweight enough to be worn while performing activities of daily living, and b. develop **inexpensive, safe, and back-drivable robots**.

3.3 Major Laboratories and Investigators

There are quite a few laboratories led by active investigators in the U.S. to study the assistive/rehabilitative robots. This list includes:

- **David Reinkensmeyer** at University of California at Irvine (UCI) studies the Robotic training algorithms which can speed-up learning of a motor skill in healthy subjects.
- **David Reinkensmeyer** at UCI and **Venkat Krovi** at State University of New York at Buffalo demonstrated the feasibility of web-based, robotic, tele-movement training.
- **Neville Hogan** at MIT develops various robotic assistive technologies
- **Maja Mataric** at University of Southern California develops robots interacting with stroke patients.
- **Krovi, Vijay Kumar at the University of Pennsylvania**, and **Wellman** develop wheeled/legged wheelchairs for mobility.
- **Johnson and Johnson** has developed an iBot wheelchair which is a very advanced system by industry.

3.4 Major Accomplishments in the U.S.

For mobility, a number of advanced technologies have been developed by universities including: automated navigation of wheelchairs, input modalities to mobile systems providing access to users who may lack fine motor control which include mechanisms of gesture recognition, voice command, and vision-based interaction plus devices of sip and puff, and ability to drive on all terrains (stairs/curbs).

A number of intelligent chairs have been developed by the universities or companies including TinMan II developed by Miller and Slack which performs tasks such as turning and moving forward and contains an obstacle avoidance mode that overrides the user's commands, a device called Wheelesley by Yanco, et.al. which is able to follow a path while avoiding obstacles, and NavChair by Simpson, Levine, and et.al. which has the wall following modes. Finally, the Penn SmartChair by the Patel, et.al. combines deliberative and reactive behaviors.

For manipulations and rehabilitative training, even more accomplishments have been

achieved by the U.S. researchers. One of them is the development of robot which interacts with stroke patients to encourage them to exercise the affected limb(s). For stroke patients, assistive technologies including robots, graphics, and video games for stroke rehabilitation as well as mechanisms for neuro-rehabilitation and assessment/evaluation have been developed. Technologies for mass commercialization of assistive devices are also available. The U.S. researchers have developed robotic training algorithms that can speed-up learning of a motor skill in healthy subjects, for which the feasibility of web-based, robotic, tele-movement training has also been demonstrated.