

ROBOTICS, MOTOR LEARNING, AND NEUROLOGIC RECOVERY

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■ **Abstract** Robotic devices are helping shed light on human motor control in health and injury. By using robots to apply novel force fields to the arm, investigators are gaining insight into how the nervous system models its external dynamic environment. The nervous system builds internal models gradually by experience and uses them in combination with impedance and feedback control strategies. Internal models are robust to environmental and neural noise, generalized across space, implemented in multiple brain regions, and developed in childhood. Robots are also being used to assist in repetitive movement practice following neurologic injury, providing insight into movement recovery. Robots can haptically assess sensorimotor performance, administer training, quantify amount of training, and improve motor recovery. In addition to providing insight into motor control, robotic paradigms may eventually enhance motor learning and rehabilitation beyond the levels possible with conventional training techniques.

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INTRODUCTION

In the past decade, investigators increasingly have used robotic devices to manipulate and measure human movement, providing insight into how the nervous system learns to control movement. Here, we review knowledge generated by two new robotic paradigms: adaptation to robot-applied force fields and robot-assisted motor rehabilitation. We also provide examples of ways that robotic devices may ultimately enhance motor learning and recovery using these paradigms. Summaries of recent nonrobotic studies in motor learning (1–4) and motor rehabilitation (5–8) can be found elsewhere.

MOTOR ADAPTATION TO ROBOT-APPLIED FORCE FIELDS

Moving requires interacting with dynamic environments. Gravity, water, the ground, clothes, tools, doors, bicycles, dance partners, and our limbs themselves have dynamics describable with nonlinear differential equations that dictate, along with muscle force, the trajectory of our limbs. Recently, investigators have used robots to create novel dynamic environments and investigate the human ability to adapt them.

The typical study design follows the one used by Shadmehr & Mussa-Ivaldi (9) (Figure 1). A two degrees-of-freedom (DOF) robotic device applied perturbing forces to the hands of unimpaired subjects who reached in a horizontal plane. The robot applied a force field for which force depended on hand velocity but pointed to it obliquely. The field initially curved the reaching path of the hand. With practice, however, the subjects adapted to the forces, straightening their hand

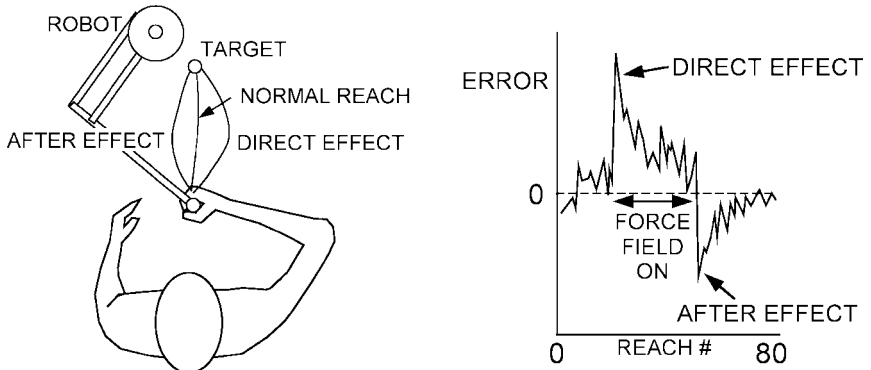


Figure 1 Robotic force-field paradigm. A robot applies a force field to the subject's hand during reaching. The reach path is curved at first but straightens with time. When the force field is unexpectedly turned off, the subject exhibits an aftereffect that persists for tens of movements, which suggests that the nervous system formed an internal model of the force field. The graph (*right*) shows the reaching error (typically quantified as the maximum perpendicular distance or area between each reach and a normative reach) as the force field is applied then removed.

paths. When the forces were unexpectedly removed, the hand path was displaced in the direction opposite the force, along a roughly mirror-symmetric path to the one observed during initial exposure to the perturbation. The presence of this aftereffect proved that the nervous system generated a prediction of the expected perturbing forces using an internal model of the environment. Feedback or impedance control strategies would not generate aftereffects, provided the desired reach path remained constant throughout the experiment; they would cause the hand to move even straighter along the desired trajectory when the external, perturbing force field was removed.

The basic observation of aftereffects, and the inference of an internal model, is perhaps not surprising. If a person picks up a suitcase expecting that it is full when it is really empty, then he moves too fast and overshoots his intended endpoint. In other words, he exhibits an aftereffect because the internal model of the suitcase was incorrect. However, what the robotic force-field paradigm provides is the ability to create a wide range of force fields, to unexpectedly alter or revert them, and to precisely measure the forces and movements associated with them. In addition, the paradigm induces adaptation in a relatively short timescale—on the order of tens of movements, which makes it possible to perform motor-learning experiments quickly. As we review below, investigators have used these features in dozens of subsequent studies to elucidate the structure of neural control.

Subjects who participate in a force-field experiment often have several interesting impressions. First is the persistence of aftereffects following unexpected cessation of the applied field. The subject thinks an external force is still being

applied for tens of movements, even though no force is being applied. Typically, the subject also decreasingly perceives the perturbation during adaptation, such that he is minimally aware that the force field is still on. Thus, conscious sense of effort appears to be heightened during periods of increased error rather than increased external force. That adaptation happens automatically, or subconsciously, for almost all subjects is also striking. Subjects who experience the force field even dozens of times still adapt to it. Put together, these observations suggest that a rather automatic or implicit process, linked to but separate from conscious control, guides internal model formation.

Technical Requirements

The robotic force-field paradigm typically uses backdriveable robots, where “backdriveability” refers to low, intrinsic, endpoint impedance (10) or simply that the passive robot linkage moves easily when pushed. Backdriveable robots allow after-effects to be measured and, more generally, a wide range of dynamic environments to be created. Most industrial robots are not backdriveable because they rely on highly geared motors to produce large forces. Backdriveability can be achieved easily for planar movement by mechanically grounding large motors that drive five bar linkages, a design often used in the robotic force-field paradigm (9, 11). Achieving high force with good backdriveability in three or more dimensions is more difficult. One commercial, haptic robot (PHANTOM, Sensable Technologies, Inc.) used in force-field experiments (e.g., 12) uses cable and capstan transmission but generates only modest forces. Nonbackdriveable robots with high-bandwidth force control are another possibility for creating dynamic environments, but typically they are not as responsive as backdriveable robots and have not been widely used to study motor adaptation. Combining force control with a springy actuator provides good active backdriveability (13).

The robotic force-field paradigm also requires selecting an appropriate force field. Most experiments have used planar, velocity-dependent, or viscous force fields as the perturbing field. Typically the 2 by 2 damping gain matrix is chosen so that the force points obliquely, often perpendicularly, to the hand velocity (a viscous curl or conservative field). Investigators use a velocity-dependent field because it does not apply force when the subject is not moving, and thus it can be turned on or off unexpectedly between movements, allowing a kinematic glimpse of the consequences of the next feedforward command (i.e., the aftereffect). Inertial force fields could also be switched on unexpectedly, but acceleration signals are often more difficult to obtain or noisier than velocity signals. Inertial force fields have been created by adding weights to outriggers on a splint attached to the arm (14). Velocity-dependent force fields with a curl component are interesting because few external environments generate them, and thus they are ostensibly novel to most subjects. Velocity-dependent force fields have also been created with revolving rooms (15). Studies have begun to investigate force fields that represent nonrigid

objects, such as a simulated mass and spring (16) or inverted pendulum (17), and suggest that internal model-based control is also used for such objects.

State Dependence Versus Rote Memorization

Feedforward control could be achieved by simply memorizing and then replaying the time sequence of muscle forces required to cancel the novel dynamic environment or by forming a mapping (an internal model) between limb state and muscle forces. If learning were rote, then performance improvements would not generalize to a movement trajectory requiring a different time sequence of commands. However, the internal model formed during straight-line reaching movements generalized well to circular drawing movements (11). Subjects also adapted to a time-varying pattern of perturbing force by producing compensating forces that depended on the position and velocity of the arm and not on time (18). Subjects adapted to a force field that varied with movement sequence only if the sequence could be approximated with a state-dependent model (19). These observations suggest that the internal model computes muscle activations from limb states, rather than from memorized time sequences.

Generalization

A motor control strategy is said to generalize or transfer if it can be used effectively in a situation different from the one in which it was learned. For example, the above experiments indicate that the internal model generalizes between different tasks (reaching and drawing circles) that share the same workspace, presumably because the model relies on a state-space representation of the field. Generalization of internal models across space, arms, directions, and speeds has also been observed.

Internal models generalize spatially, allowing subjects to compensate for a field in a region of the workspace different from the one in which they learned it. For example, subjects adapted to the field in a workspace on the right side of their bodies and then performed reaching movements in a workspace on the left side of their bodies (9). When the field was translated to the left workspace, subjects initially could not move straight. When the field orientation was rotated about the shoulder into the left workspace, however, subjects moved straight on their first reaches. Thus, the internal model learned in one part of the workspace transferred or generalized to another part of the workspace in a shoulder-centered coordinate frame. Other experiments have supported the concept that the internal model utilizes an intrinsic rather than extrinsic coordinate frame when generalizing to other regions of the workspace during same-limb reaching (20–22) or in a pole-balancing task in which the hand remained isometric (17). In contrast, learned dynamics appear to generalize from the dominant to the nondominant arm in extrinsic coordinates (23).

Instead of training in multiple directions in one workspace and then testing in other workspaces, investigators have also trained subjects in a single direction

in one workspace and then tested generalization to other movement directions within the same workspace. In this situation, aftereffect magnitude decreased with increasing angle from the learned direction, which suggests that internal models are locally represented with respect to direction (20, 24). Predictive grasping forces used during bimanual manipulation also are learned locally with respect to direction (25).

Learning of a velocity-dependent force field for a reaching movement generalized to movements of the same orientation with increased velocity or amplitude (26). This generalization was best captured by a linear extrapolation of the force field represented in state space and may help people scale learned movements in time and space.

Noise, Instability, and Impedance Control

In most force-field experiments, the force-field parameters (i.e., the gain matrix of the viscous field) were held constant throughout adaptation. In the real world, people often move in noisy dynamic environments. For example, a postal worker sorting boxes will experience a range of weights for a given size box. Trial-to-trial variability also arises from neural sources (27, 28) and is larger during childhood (29) or following an injury such as a stroke (30). When the gain of a viscous curl field was varied from reach to reach according to a normal distribution, the nervous system formed an internal model that estimated the mean gain of the field, although the estimate was low in some cases (12, 31). Children as young as age five can adapt to force fields even if additional external noise is superimposed using a force field on their already-noisy movement (29). Thus, the internal model formation algorithm appears robust to at least some degree of external and internal, trial-to-trial noise.

Robot experiments indicate that the nervous system uses impedance control along with internal models in noisy and unstable force fields. Subjects increased their arm impedance so that variations in the field strength produced less variation in trajectory error, and aftereffects were diminished following exposure to the noisy force field (12). Aftereffects were absent following adaptation to a destabilizing force field that amplified trajectory errors (an unstable spring in the direction perpendicular to movement) (32). Measurements of limb impedance during adaptation indicated that arm stiffness increased only in the direction necessary to stabilize the arm. These results suggest that directionally specific impedance control is combined with varying amounts of internal model-based control for noisy or unstable environments.

Kinematic Versus Dynamic Optimization

That the nervous system optimizes movements by either a kinematic criterion, such as trajectory error or smoothness, or a dynamic criterion, such as force or effort, is an appealing idea. Scheidt et al. (33) applied a viscous force field perpendicular to the reaching direction to investigate this question, then monitored deadaptation

when kinematic errors were either allowed to occur following removal of the field or prevented from occurring by imposing a virtual channel that restricted movement in the perpendicular direction. When kinematic errors were prevented from occurring, subjects persisted in generating corrective forces that were unnecessary to generate an accurate reach. However, the magnitude of these forces decayed slowly over time, with a time constant approximately 15 times longer than when kinematic errors were allowed. This experiment suggests that kinematic and dynamic criteria were optimized simultaneously but at different timescales. The nervous system responded quickly to correct trajectory errors but more slowly optimized muscle force given an acceptable level of trajectory error. Thus, the nervous system may do the same task the next time with less effort, provided it succeeds by a kinematic criterion in the previous attempt.

Multiple Internal Models, Retention, and Interference

The nervous system presumably stores an internal model for each dynamic object with which it knows how to interact, switching between the models based on visual or other sensory clues (e.g., envision switching between a hammer, nail, and board). Several studies have investigated the development and switching of multiple internal models.

Brashers-Krug et al. (34) demonstrated that an internal model learned in the robotic force-field paradigm could be retained over time. When subjects learned to reach in a force field, then rested or even left the robot for a period, their next attempt at reaching in the field was straighter than their first attempt, although not as straight as their last attempt; this finding indicates partial retention of the learned model. Retention was observed after delays of up to five months (35). When subjects learned a second, conflicting field immediately after learning the first, retention of the first was decreased, a phenomenon called interference. The amount of interference depended on the temporal separation between the two conflicting force fields. A delay of five hours between two fields was sufficient for maximal retention, apparently owing to consolidation from short- to long-term memory.

The null field itself is an interfering field, as subjects who practiced reaching in the null field following adaptation to a force field showed little or no retention when experiencing the field a second time (29). However, as described above, subjects who walk away from the robot and move their arms in a null field at home (i.e., not attached to the robot) retain their robot model at a subsequent visit (34). These observations are consistent with the idea that the nervous system associates internal models with objects: We expect a tool (e.g., the robot arm) to behave as it did the last time we used it. When we are not using the tool, we apparently do not use the model associated with it to move our arm.

Several studies illustrate the difficulty in learning two different force fields presented in close opposition by one tool (i.e., the robot). Subjects were unable to predict two viscous force fields presented in alternating groups associated with colored lights or thumb posture (20). However, they predicted the fields with

extended practice when the fields were associated with different handgrips. Thus, a single model may have been formed that predicted the different fields on the basis of the different arm/hand states, or two models may have been formed and switched between on the basis of the grip context. In either case, an intrinsic cue, related to joint posture, was apparently required to predict the two fields. This was somewhat surprising, given that we switch easily between internal models using visual cues in everyday life. Subjects could not predict two viscous force fields that were simply alternated reach-by-reach over four days, which suggests that temporal sequence was insufficient to learn and switch between two models (19).

However, Wada et al. (36) recently showed that subjects ultimately learned to predict randomly presented unstable and stable viscous force fields for a single DOF elbow movement, given days of practice and colors that signaled the field type. Thus, a conflicting force field presented in close temporal succession does not necessarily cause catastrophic interference, and an intrinsic contextual clue is not necessarily needed for switching. Rather, the readiness with which multiple internal models are formed may depend on both the effectiveness of the contextual clues and the similarity of the force fields (36). For example, learning to switch between a robot-applied force field and a glass of water may be straightforward because of the different fields and contexts. Switching between two similar force fields on the robot, or between racquetball and tennis, may be more difficult because of the similarity of both the context and fields.

Forward and Inverse Models

Forward models predict movement on the basis of a motor command, whereas inverse models predict the motor command needed to achieve a desired movement. Learning to cancel a force field ultimately requires an inverse dynamic computation of some form, whether implemented by an explicit inverse model, a neural network, or a feedback controller. Forward models, which are more difficult to isolate (37, 38), could be useful in motor learning for selecting inverse models and as state estimators for use in control. For example, the nervous system could use predictions from a forward model, compared to actual performance, to decide to switch between internal inverse models (39). Forward models could also be used to predict and cancel the sensory consequences of motor commands (40). A control architecture using both forward and inverse models best predicted reaching trajectories during force-field adaptation (41). Saccadic eye movements that track the hidden hand during reaching are controlled by a forward model that predicts the state of the arm about 200 ms in advance and takes into account the dynamics of the arm and its environment (42).

Computational Models of Internal Model Formation

The evolution of movement error during application of a force field can be described with a simple finite difference equation (24, 31, 43):

$$e_i = a_1 e_{i-1} + b_0 B_i + b_1 B_{i-1}, \quad (1)$$

where e_i is movement error on the i^{th} trial, B_i is field strength on the i^{th} trial, and a_1 , b_0 , b_1 are regression coefficients.

This equation suggests that the nervous system updates its currently selected internal model on the basis of sensory information from only one previous trial and an internal state variable, performing a sort of moving average. If it is assumed that the measure of movement performance x_i is related to a motor command u_i and field strength B_i by a static function that can be linearized as

$$x_i = f(B_i, u_i) = c_i B_i + d_i u_i, \quad (2)$$

where u_i is motor command on the i^{th} trial and c_i , d_i are linearization coefficients, then the following simple, motor command update law produces Equation 1:

$$u_i = u_{i-1} + G e_{i-1}. \quad (3)$$

Thus, in this formulation, the nervous system calculates the next motor command by adjusting the previous command on the basis of the last error. In a related formulation, the desired trajectory for a feedback controller could be adjusted on a trial-by-trial basis using performance error, effectively producing the same sort of iterative, inverse computation but without an explicit internal model (44). By vectorizing such a finite difference equation to account for movement error in multiple directions, and by allowing an error in one direction to affect commands in other directions with a Gaussian weighting, error evolution for multi-target reaching can be more accurately modeled (24).

Another way to view the inverse model computation is as a function approximation problem, where the function that must be approximated is the applied force-field equation. Thoroughman & Shadmehr (24) suggested that the function may be approximated by a weighted sum of broadly overlapping Gaussians. In their paradigm, the Gaussian weights were incremented on the basis of force errors. Such a scheme predicted the curvature of reaches in a force field and poor compensation for a force field with high spatial frequency content. Other modeling studies of robotic force-field adaptation can be found in References 45 through 47.

Relationship to Kinematic Models

The nervous system is also capable of forming an internal model of its kinematic environment, defining the relationship between perceived and actual motion. Krakauer et al. (48) suggested that internal models for kinematic and dynamic perturbations form independently because no interference occurred when subjects learned a dynamic perturbation (inertial load) shortly after a kinematic one (rotated spatial reference frame). However, when subjects first adapted to a position-dependent visuomotor rotation and then to a position-dependent rotary force field, the learning of visuomotor rotation was impaired, indicating

interference (49). Thus, internal models of kinematic and dynamic perturbations are not independent when they rely on the same kinematic variable. The nervous system can combine and decompose kinematic and dynamic models. For example, reaching errors for the kinematic perturbations were smaller if subjects had first learned the combined transformation (50).

Other Limb Systems

Investigators have applied velocity-dependent force fields to the leg during the swing phase of treadmill locomotion using a novel backdriveable robotic device (51, 52). Subjects adapted to the field and exhibited aftereffects, indicating formation of an internal model. Studies have also applied force fields to spinal transected rats stepping bipedally on a treadmill during the stance (53) and swing (54) phases of locomotion. The rats adapted to the force field by altering step timing and muscle activity, although with different timescales than in intact human adaptation with the arm and without clear evidence of aftereffects. Subjects exhibited aftereffects when robotic coupling of the hands was unexpectedly broken in a bimanual unloading task (55).

Developmental Studies

Children ages 4 to 18 formed internal models of force fields produced by robotic devices (29, 56, 57). The accuracy of the model was comparable to that of adults, although the time required for adaptation or deadaptation was longer. Children also exhibited more trial-to-trial variability in their movements, both before and after adaptation (29). The youngest children, ages 5 to 7, more quickly reduced their variability with practice, giving the appearance of rapid learning even though their final variability levels were still higher than those in adults. Internal models formed in one workspace region transferred to an untrained region (56).

Force-Field Adaptation after Neurologic Injury

Hemiparetic stroke patients with full reaching range of motion, but who were weakened by ~60%, still adapted to a mild perturbing force field by forming an internal model (58). However, more severely impaired stroke patients, with reduced reaching range of motion and weakness of more than 70%, showed no aftereffects and a continual reliance on feedback control to correct for the perturbation. This finding suggests that severe hemiparesis impairs either the ability to form or implement internal models. For example, destruction of brain areas responsible for internal model formation may impair feedforward control. Alternately, an inability to produce enough force, or perhaps force at a high-enough rate, may render feedforward control ineffective. Subjects with Parkinson's disease adapted to a force field but had decreased learning rates when adapting to a second, opposite curl field after learning the first (59).

Neural Substrates

A number of studies have examined the brain structures in which activity changes in relation to motor learning during robot-applied force fields. Shadmehr & Holcomb (60) used positron emission tomography (PET) scanning to measure cerebral blood flow (CBF) at various phases of motor adaptation. Subjects learned to use their right arm to move a robotic arm in a viscous force field. Early during the learning process, motor output correlated with activation in bilateral sensorimotor cortices and the right striatum. This early learning, when compared to motor performance in an unlearnable random robotic force-field condition, was associated with relatively greater brain activation in areas such as the pulvinar nucleus and the right dorsolateral prefrontal cortex. When PET scans taken at the end of the learning phase were contrasted with scans taken 5.5 h later, however, the location of activation increases during motor task performance showed a relative shift to left posterior parietal cortex, left dorsal premotor cortex, and right cerebellum. This shift over time was not associated with a change in the quality of motor performance but may indicate the substrate underlying consolidation, or stabilization, of motor learning in this model. A later study by these authors (61) used a model of motor learning based on learning two different motor tasks separated either by a short time interval, making them compete for motor learning resources, or by a long time interval. This study suggested that the early phase of motor adaptation is associated with increased activity in the left putamen and bilateral dorsolateral prefrontal cortex. As motor performance reached a plateau, putaminal activation decreased.

Krebs et al. (62) studied various phases of motor learning by acquiring serial PET scans during adaptation to a force field imposed upon the right arm by a robot. Images taken early during the process of motor learning were contrasted with images taken during arm movement in the absence of a force field. The resulting images described brain activation during early motor learning, with increased activation in such areas as the right striatum (at a site more anteromedial than that in Reference 60), the left primary sensory cortex, and the bilateral parietal association areas. Images acquired as motor performance improved found that activation shifted to areas including the left motor and premotor cortices plus the right cerebellum. The role of the right striatum in motor learning, suggested in this study, is further supported by reports of poor motor learning in a patient with ischemic injury to this brain area (62).

Nezefat et al. (63) used PET to study CBF in cerebellum as subjects learned to use the right arm to control force-field changes introduced by a robot handle. In the right cerebellar hemisphere, posterior cortical activation increased during learning then declined as performance improved, whereas a reverse pattern was seen in the deep nuclei. Over the ensuing four weeks, during which motor performance remained stable, serial PET studies found a decrease in anterior cerebellar cortex activation. The results support a role for the cerebellum in the acquisition and retention of motor memories. Imamizu et al. (64) and Flament et al. (65), using

fMRI, further supported changes in cerebellar activation in relation to motor adaptation. These findings are consistent with the observed motor learning deficiencies described in patients with cerebellar damage (63).

Donchin et al. (66) studied the influence of four pharmacological agents on acquisition and recall of new motor memories related to forces imposed by a robot arm. Lorazepam, a GABA-receptor agonist, and dextromethorphan, an NMDA-receptor antagonist, each impeded new motor learning, whereas lamotrigine, a sodium and calcium channel blocker, and scopolamine, a muscarinic-receptor antagonist, had no effect on learning. None of the four agents influenced motor memory recall. The findings support hypothesized relationships between synaptic plasticity and memory, and were novel in extending these relationships to memory in the motor system. Other models have found that lorazepam and dextromethorphan impair use-dependent plasticity in motor cortex (7). In addition, the results are important because they emphasize the presence of distinct neurobiological mechanisms for the processes of motor memory acquisition and recall.

Studies in primates agree with the above human brain mapping investigations. Gandolfo et al. (67) studied neuronal activity in primary motor cortex of two macaques as they learned to perform reaching movements in the presence of interfering external forces. A number of neuronal populations were described in relation to the arm movements. Activity in some cells was related to the direction of arm movement. Some of these cells changed their directional tuning during introduction of the force field, and a subset of these retained these changes. A large number of neurons changed directional tuning properties during adaptation to the force field. These changes in cell firing rate were not related to changes in muscle activity, which led the authors of this study to hypothesize that the neuronal changes were instead related to formation of an internal model within primary motor cortex. Li et al. (68) also found that some cells in primary motor cortex change their preferred direction of movement as a force field is learned.

Therefore, motor adaptation to force fields arises from brain areas that overlap incompletely with those areas related to motor skill acquisition. Early in motor adaptation, activation is increased relatively in cortico-striatal circuits, whereas later, performance is related to cortico-cerebellar circuits (4). Many of the substrates related to robot-mediated motor adaptation overlap with brain areas related to motor recovery after a CNS injury such as stroke (69, 70). This provides a theoretical framework for a possible clinical benefit of robot-related interventions in patients with stroke and other CNS insults. Note that the neurobiological substrate underlying motor adaptation may differ in several ways from that related to motor learning in other contexts such as motor sequence learning (4).

Functional Relevance

Whether the knowledge gained from robotic force-field experiments can be expected to produce practical applications is an important question for biomedical engineering. For example, does the paradigm capture a fundamental-enough motor

situation to provide general insight in a broad range of motor activities? Internal models are used pervasively throughout the day as we interact with tools and the environment, and indeed, every time we move our limbs, because our limbs themselves are dynamic objects. Internal models also may have several functional benefits. They allow movements to be made accurately in a more energy-efficient way, at least for predictable, stable environments. They may provide the mean for adjusting to morphological growth and tissue changes associated with development and aging, although the timescale of internal model formation seems much faster than what is necessary to keep up with such changes. They help us learn new tasks and tools and move in new environments, in a graceful, knowing way. We likely could get along without internal models, but our movements would be slower, less coordinated, less efficient, and more dependent on vision or feel. Therefore, the basic scientific knowledge gained with the robotic force-field paradigm most likely will lead to practical enhancements in motor learning, provided such enhancements are indeed possible.

For example, a thorough understanding of the error signals that drive adaptation may allow them to be amplified or filtered, thus accelerating learning. An understanding of the nature of generalization should facilitate the design of practice regimens for learning a new skill with the greatest generality and least amount of practice. Identifying factors that slow or interfere with learning, retention, or multiple model formation may suggest ways to minimize those factors. Finally, a thorough understanding of internal model formation, and the neural substrates for internal models, may lead to improved rehabilitation or neuroregeneration therapies for people with neurologic injuries. To define the relative role of, and optimal treatments for, different deficits of control, planning, sensing, and outflow pathways on the basis of the pattern of neurologic damage will be a key goal.

ROBOT-ASSISTED MOTOR REHABILITATION

Motivation for Robotic Therapy

Central nervous system diseases characterized by persistent motor deficits are common, a major source of disability, and expensive. Examples include stroke, multiple sclerosis, traumatic brain injury, Parkinson's disease, and spinal cord injury. For example, in patients with stroke a motor deficit is present in approximately 80% of patients early on, and in 50% at chronic time points, so that approximately two million stroke survivors in the United States have chronic arm impairment (71).

Two forces in rehabilitation medicine drove the development of robotic therapy devices, or rehabilitators (see Figure 2), for patients with CNS diseases in the last decade. First, evidence increased that the injured motor system can reorganize in the setting of motor practice. However, the optimal training techniques for facilitating reorganization remained unclear, in part because of difficulties quantifying dose, type, and consistency of rehabilitation therapy. Robotic devices were seen as a possible way to precisely control and measure therapy.

Second, because of increasing pressure on the U.S. health care system, including the aging of baby boomers, patients began receiving less therapy following neurologic injuries such as stroke, even though studies suggested that more therapy was better. Robotic devices were seen as a possible way to automate labor-intensive training techniques, providing new tools for therapists and improved access to therapy for patients.

Four randomized, controlled studies of robotic therapy have been published: three for the upper extremity therapy after stroke (72–74) and one for gait training after stroke (75). Several robotic therapy studies have used chronic stroke or spinal cord–injured patients as their own baseline control (76–79). Other reviews of robotic therapy can be found in References 80 through 84.

Robotic Therapy Algorithm Selection

Several modes of robot-assisted movement have been developed, including passive (72, 73, 75), active-constrained (73), counterpoise control (85), resistive (76), error-amplifying (86), and bimanual modes (73, 75, 87, 88). However, the primary therapy paradigm tested so far is active assistance (72–78), a clinical term that refers to exercises in which the patient attempts a movement (active) and in which a therapist manually helps complete the movement if the patient is unable (assistance). For example, a patient may try to reach to a target, and the therapist may guide the arm, if necessary. Such active assistance may improve recovery by enhancing proprioceptive input, reducing spasticity, restoring soft tissue suppleness, improving self-confidence, or by simply making exercise psychologically more tolerable, but it is labor intensive and has not been validated in controlled trials. It was a logical target when engineers and clinicians were presented with weak patients and force-generating robots.

Using devices to provide active assistance, however, is not new. For arm therapy, mobile arm supports, arm skateboards, and overhead slings are sometimes used in clinics to provide support against gravity, a passive form of active-assist exercise. For gait training, parallel bars, walkers, and overhead weight support systems are used to assist patients in standing and walking. Robotic devices, however, can provide programmable levels of assistance, do work against gravity, and automatically modify their output based on sensing.

Robotic Therapy Devices for the Upper Extremity: First Results

The first robotic system to receive extensive clinical testing was MIT-MANUS, a two DOF backdriveable robot manipulator, similar to the one used by Shadmehr & Mussa-Ivaldi (9) in their original experiment. In a first report, 20 stroke patients received 4 to 5 1-h sessions a week for up to 9 weeks with MIT-MANUS, beginning on average 3 weeks after a single stroke (89). The device assisted planar pointing and drawing movements with an impedance controller. A control group received 1 h of sham therapy a week, in which they used the less-impaired limb

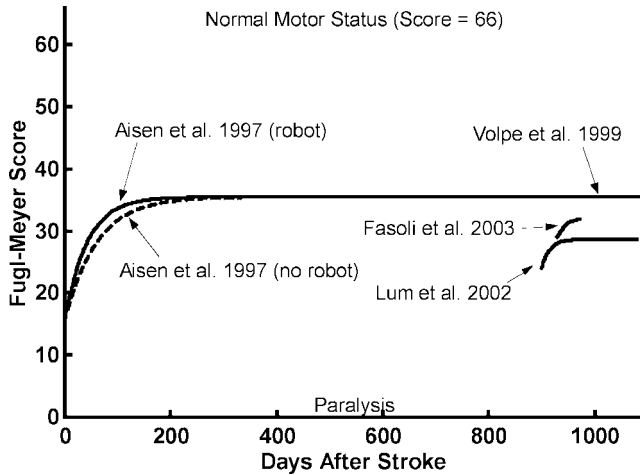


Figure 3 Perspective on the magnitude of recovery of the upper extremity following stroke with robotic therapy. Plot summarizes data from four studies. The long solid curve (robot therapy) and dashed curve (no robot therapy) represent recovery reported in References 90 and 129. The two short curves represent data from References 76 (*upper curve*) and 73 (*lower curve*). All studies used the Fugl-Meyer upper extremity scale, which scores a series of movements 0, 1, or 2, then adds the individual movement scores to obtain the total score.

in the robot, or the robot interacted passively with the more-affected limb. When compared to the control group, the patients who received robotic therapy had reduced motor impairment of the shoulder and elbow according to the motor status score. The groups were still statistically different in terms of motor impairment at a three-year follow-up (90). These findings were confirmed with larger samples of 56 and 96 patients (72). Chronic stroke subjects who performed assistive and resistive exercises with MIT-MANUS also improved arm movement ability (76) (Figure 3).

This pioneering work suggests that supplemental robotic therapy can improve recovery in acute and now chronic stroke patients. However, these studies do not address whether robotic treatment offered unique advantages to conventional therapy or what the key components of the robotic therapy were (e.g., mechanical assistance by the robot versus an increased amount of sheer repetitive effort by the patient).

The MIME (mirror image movement enhancer) is a six-DOF, industrial robot manipulator (Puma 560) that applies forces to the paretic limb through a customized forearm splint. The robot can move the forearm through a large range of positions and orientations in three-dimensional space. A six-axis sensor measures the forces and torques between the robot and the paretic limb. Several modes of robot-assisted movement have been implemented with MIME, including passive, active-assisted,

active-constrained, and bimanual modes, in which MIME copies the mirror image of the movement of a stroke subject's unimpaired limb, measured with a digitizing linkage.

The initial clinical testing of MIME compared the effectiveness of robotic therapy with an equally intensive program of conventional therapy (73). Twenty-seven chronic stroke subjects received 24 1-h sessions over 2 months. Subjects in the robot group practiced shoulder and elbow movements assisted by MIME in all four of its modes. Subjects in the control group received conventional treatment and five minutes of exposure to the robot in each session. The robot group had statistically larger improvements in the Fugl-Meyer score, a common clinical motor-impairment scale. The robot group also had larger gains in strength and reach extent. At the six-month follow-up, the groups were no longer different in terms of the Fugl-Meyer scale; however, the robot group had larger improvements in a scale that measured functional independence in activities of daily living (functional independence measure). These results suggest that robot-assisted therapy can be comparable, or perhaps even more effective, than conventional therapy.

A third device, the assisted rehabilitation and measurement (ARM) guide was designed to mechanically assist in reaching movements (91). Because reaching movements typically follow straight-line trajectories, the device uses a linear bearing to guide reaches by the subject. The linear bearing can be oriented at different yaw and pitch angles to allow subjects to reach to different workspace regions. Like MIT-MANUS and MIME, the device can assist or resist in movement and can measure hand movement and force generation. The device is statically counterbalanced so it does not gravitationally load the arm.

The goal of the initial clinical testing of the ARM guide was to identify the role of mechanical assistance in stimulating movement recovery, as opposed to unassisted, repetitive effort. Nineteen chronic stroke subjects received 24 therapy sessions over 2 months. Subjects in the robot group ($n = 10$) received mechanically assisted reaching exercise with the ARM guide. For this group, the subject initiated movement, and the ARM guide completed the movement along a smooth trajectory through the arm's full passive range if the subject was unable. Subjects in the free reaching group ($n = 9$) performed unassisted, repetitive reaching exercises, matched in the number of repetitions and target locations with the robot group. All subjects were evaluated using a set of clinical and biomechanical measures of arm movement. The subjects who received therapy with the ARM guide showed significant improvement in the time to complete functional tasks and in supported reaching range and velocity (92, 93). However, the amount of improvement in the free reaching group was not significantly different from the robot group and was, in fact, comparable in magnitude.

One interpretation of these results is that the action of repeatedly attempting to move, rather than the mechanical assistance provided by the ARM guide, was the primary stimulus to arm movement recovery for the subjects. This hypothesis is consistent with other repetitive-movement exercise paradigms that improve upper extremity movement ability following brain injury (e.g., 94–96). In addition, it is

consistent with the observation that passive exercise engaged different brain areas and produced less motor learning when compared to active exercise in unimpaired subjects (97). Another possible explanation is that the particular movements (linear reaches) or form of robotic assistance provided by the ARM guide were suboptimal and that a higher DOF device with improved therapy algorithms may demonstrate a benefit over unassisted exercise.

Hesse et al. (77) developed a robotic device for the passive and active practice of bilateral forearm (supination/pronation) and wrist (flexion/extension) movements. Twelve chronic stroke subjects used the trainer for 15 min per day for 3 weeks. The subjects reported a reduction in spasticity, easier hand hygiene, and pain relief. A significant decrease in the modified ashworth score of wrist and finger spasticity was observed. No functional improvements were observed. Investigators have proposed or are developing other devices for arm and hand therapy (87, 88, 98–101), including vertical motion and wrist modules for MIT-MANUS (102, 103) and web-based teletherapy systems (104), but these devices have not undergone extensive clinical testing.

Robotic Therapy Devices for Gait Training

Gait training with body weight support and manual assistance of the legs and pelvis is a promising new therapy technique that may manipulate spinal plasticity (8, 105–109), but it is labor intensive, requiring two to three therapists to assist the patient's legs and torso during each training session. In addition, the assistance provided, and thus the pattern of sensory input to the nervous system, can vary greatly between trainers and sessions. Recognizing this need, several research groups and a major U.S. healthcare provider (HealthSouth) are developing robotic devices for automating locomotor training in humans. The first device to undergo a controlled clinical trial was the mechanized gait trainer (MGT), a singly actuated mechanism that drives the feet through a gait-like trajectory using a doubled crank and rocker system (79).

The MGT was used in a crossover design to train subacute stroke patients to walk (75). A robot training group ($n = 15$) received two weeks of robotic gait training (A), followed by two weeks of human-assisted treadmill therapy (B), followed by two more weeks of robotic gait training (A). A control group ($n = 15$) received B-A-B. The patients were not significantly different before therapy in their overground walking ability but were after therapy, with the robot group performing better. Walking ability improved more rapidly for subjects in both groups during the robot-assisted training. Differences were not significant at a six-month follow-up. These results suggest that robot-assisted gait training can be as effective as conventional training, providing a significant reduction in manual labor.

Other devices for gait training are being developed, but they have not undergone extensive clinical testing yet. The Lokomat is a motorized exoskeleton worn by the patients during weight-supported stepping on a treadmill (78, 110). It drives

hip and knee flexion/extension for each leg using precision ball screws connected to DC motors. The device was able to drive gait-like movement patterns in spinal cord-injured patients, reducing the labor burden on therapists who were assisting in step training. The Lokomat has been installed in dozens of research labs and clinics worldwide, and clinical testing results are forthcoming. ARTHuR (51) and PAM (111) are highly backdriveable robotic devices for measuring and manipulating stepping and pelvic motion, respectively. Small robots for training stepping by rats and mice have been developed to allow investigators to better study the neuromuscular plasticity that underlies step training (112). A new version of the MGT with more degrees of freedom is being developed (113).

Robotic Assessment

Robotic devices provide a means to quantify sensory motor impairment, in addition to providing a means to implement and test specific forms of therapy. Backdriveable devices can act as motion capture devices and measure kinematic features of movements. Smoothness data from MIT-MANUS were used to develop the hypothesis that the nervous system has difficulty assembling movement primitives followings stroke (114). Directional error data gathered with a haptic robotic were used to support the hypothesis that increased variability in reaching after stroke is due to population coding, cosine tuning, neural firing rate noise, and cell death (115).

Nonbackdriveable robots can also quantify movement properties. For example, the pattern of forces reacted in high-impedance directions correlates with clinical measures of abnormal coordination (116, 117).

The active properties of robots can also be used to provide insight into sensorimotor impairment. Brisk stretches applied during reaching with the ARM guide illustrated that the presence of clinically observed spasticity does not necessarily mean an increase in arm stiffness during reaching (91, 118). Lateral forces applied during reaching can increase or decrease reaching range depending on their direction, which illustrates the coupled nature of directional force generation following stroke (58). Experiments have been performed with the Lokomat to identify the role of somatosensory input in gait generation following spinal cord injury (119). Asymptomatic carriers of the Huntington's disease gene had difficulty compensating for brief force pulses provided at the beginning of reaching movements, which suggests that feedback mechanisms are impaired by early damage to the basal ganglia and that robotic measures may provide a sensitive measure of disease onset (120). As reviewed in the previous section, investigators have noted an impaired ability to adapt to force fields after stroke (58) and Parkinson's disease (59).

Functional Relevance

The first clinical studies of robotic therapy suggest that additional therapy provided by a robotic device can improve motor recovery and that robotic therapy is at least as effective as training with therapists alone in restoring arm function and gait after

stroke. Investigators have not yet demonstrated conclusively that motorized therapy is superior to otherwise equivalent, nonmotorized therapy. The incremental improvements in clinical scales seen following intensive robotic therapy are statistically significant but small (Figure 3). They are arguably functionally insignificant from a third-party payer's point of view, although they are certainly meaningful to patients. The fate of robot therapy will be decided as the optimal components of therapy are defined. Robotic assessment techniques will play an important role in this process. In addition, there is a vast frontier that is virtually untouched in designing optimal rehabilitation therapies for specific patterns of neural damage, an important endeavor given the heterogeneity of stroke.

ROBOT-ENHANCED MOTOR LEARNING AND RECOVERY

Could robotic devices enhance motor learning in health and injury beyond what is currently possible with conventional training techniques? Put another way, can the application of force to limbs in clever ways improve motor learning? To address this question, we first review a simple mathematical model of rehabilitation training that suggests conditions under which active assistance may be effective in promoting neurologic recovery. We then review experiments that suggest how three robotic training approaches may be more effective than unassisted, repetitive practice in promoting motor learning under certain conditions.

A Mathematical Rationale for Active Assistance

Figure 4 shows a simple adaptive Markov model of sensory motor control that predicts the best movement recovery when an external trainer intervenes to correct errant movements on an as-needed basis, compared to no assistance or continual assistance (121). The basic assumptions of the model are, first, that the CNS probabilistically interprets somatosensory information in real time to generate motor output. To place this abstraction into a specific context, consider, for example, that changes in load-related afferent information during gait training cause functionally appropriate levels of limb extensor muscle activity to support the body (122). However, inherent variability exists in this response. Second, sensorimotor pathways become more reliable with repetitive activation in a sort of Hebbian learning. In other words, each time a sensorimotor transition is crossed, the probability associated with it is incremented, and competing pathways are decremented. Third, normal sensory input sometimes elicits abnormal motor output following neurologic injury owing to disrupted neural organization. Fourth, the external trainer generates a novel sensory state when it assists.

Given these assumptions, the model makes three intuitively appealing predictions (121). First, recovery can be enhanced by a trainer who actively assists abnormal movements, if the patient's sensorimotor impairment is not too severe. This

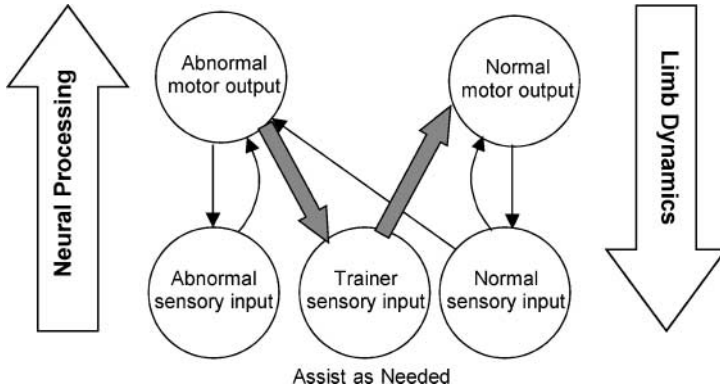


Figure 4 Computational model of sensorimotor control. The model assumes that the nervous system interprets somatosensory information to create motor output and that motor output, in turn, creates sensory input. Motor and sensory states are abstracted into normal and abnormal states. The transitions between sensory and motor states are probabilistic, and the probabilities are modified with use in a Hebbian manner, resulting in an adaptive, Markov model. An external trainer (a therapist or robot) intervenes by recognizing abnormal motor output, assisting the limb and thereby creating a novel sensory state, which leads to a normal motor output (*large transition arrows*).

prediction corresponds well to the robotic studies reviewed above that have successfully used external mechanical assistance to retrain arm or locomotor ability after stroke.

Second, blindly assisting every movement of a patient is never beneficial compared to no assistance or assistance as needed, although it is equivalent in some situations. This prediction corresponds to the intuition that a therapist or robotic device that does not grade the level of assistance they provide will not be as effective as one that does.

Third, active assistance is unnecessary when sensory input is not directly coupled to motor output. Specifically, for a system in which abnormal sensory input does not always cause abnormal motor output, recovery does not require external assistance. This prediction suggests that there may be a fundamental difference in the optimal therapy approach for different sensorimotor systems. For example, attempts to retrain locomotion after spinal cord injury may benefit from active assistance because of the relatively tight coupling of somatosensory input and motor output in spinal-injured locomotion (123). In contrast, attempts to retrain arm movement after stroke may benefit less from active assistance because feed-forward mechanisms appear largely sufficient for controlling arm movements, in the sense that sensory feedback is not required to trigger the next arm movement. Note, the model predicts that external assistance is not detrimental for uncoupled systems, but that its incorporation is simply unnecessary because unassisted, repetitive movement practice produces an equivalent result.

Robot-Guided Training of Complex Trajectories

Feygin et al. (124) investigated the use of a robotic device to teach complex spatiotemporal trajectories to unimpaired subjects. Subjects learned the trajectory by holding a robot that moved along the trajectory (haptic learning), with or without vision, or by simply watching the robot move along the trajectory. Performance in replicating the trajectory was measured with and without vision and quantified using measures of spatial and temporal accuracy. Haptic learning with vision produced the best learning performance. Haptic learning without vision produced better learning of temporal features of the trajectory than vision alone. These results suggest that robotic devices may help therapists or coaches teach tasks of complex temporal patterning.

Using Robot Force Fields to Teach Movement

Patton & Mussa-Ivaldi (125) are exploring the possibility of teaching desired movements using aftereffects from adaptation to robot-applied force fields. Different aftereffect trajectories were generated by shaping the force field, which demonstrates that movement kinematics can be sculpted by relying on implicit, subconscious motor adaptation. Determining how long the aftereffects persist, whether the aftereffect persists when the subject leaves the context of the robot, and whether learning a movement in this fashion is faster than learning it by simply being shown it and practicing are important questions for practical application.

Interesting preliminary data shows that stroke subjects can be taught to correct for systematic errors in directional control rather quickly using appropriately designed robotic force fields (86, 126). Specifically, if a force field is applied that amplifies a repeatable directional error (i.e., pushes the hand even further away from the target), then some subjects can adapt to the force field across tens of movements and return to their previous directional error levels. When the field is unexpectedly removed, the subject then moves more directly to the target (i.e., a beneficial aftereffect occurs that reduces the original directional error). The beneficial aftereffect may persist for some subjects. Thus, the neural processes associated with implicit motor adaptation may reshape sensorimotor mappings altered by stroke that cannot be altered simply by practicing movement.

Guided Force Training

Recently, in comparing the results of the MIME and ARM guide studies of robotic therapy, Kahn et al. (127) observed a striking difference in a shared outcome measure (127). Despite similar therapy duration, therapy dosage, and subject characteristics, subjects who received therapy from the MIME device improved their active range of motion of free reaching by over 9 cm on average, whereas subjects who received therapy from the ARM guide device did not increase their active range of motion of free reaching. The control subjects from the studies who performed

unassisted reaching therapy, or who received conventional therapy, also did not increase their active range of motion of free reaching.

MIME may have allowed a broader range of natural movements, perhaps enhancing functional retraining. Alternately, the bimanual training mode may have provided a unique stimulus for recovery of bilateral or ipsilesional neuromotor pathways. However, Kahn et al. (127) suggest that the MIME mode called active-constrained mode may be responsible. In active-constrained mode, the robot halted the subjects' movements when incorrect movement patterns were sensed, forcing subjects to learn how to generate the correct pattern at each troublesome workspace position. Active-constrained mode may thus be an effective way to functionally strengthen a weakened arm and to teach new muscle activation patterns necessary for coordinated movement.

CONCLUSION

Robotic devices are helping us to understand the human motor controller and particularly the structure of feedforward control processes and their relationship to impedance and feedback control. Robotic devices are also helping us to understand how external force and movement practice influence motor recovery. New physical training modes, impossible with human teachers, are possible with robots. Elucidating how training can best manipulate physiology, and thus rationally defining the range of effective applications for robot trainers, is a key goal for future work. For example, clinical studies examining effectiveness of robotic training will need to devote increased attention to patient selection and the specific pattern of

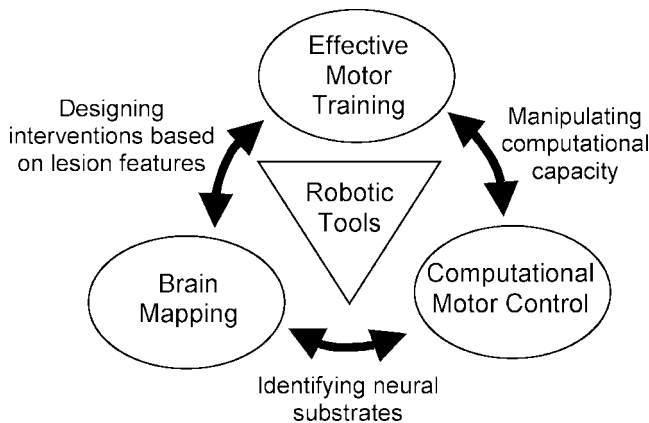


Figure 5 Robots are facilitating an emerging synergy in which an improved understanding of the computational mechanisms and neural substrates of motor learning will drive improvements in motor rehabilitation.

neuropathology to be treated (128). We see the possibility of a new synergy facilitated by robotics, in which choice of patients and training techniques will arise logically from computational motor learning and brain mapping studies (Figure 5).

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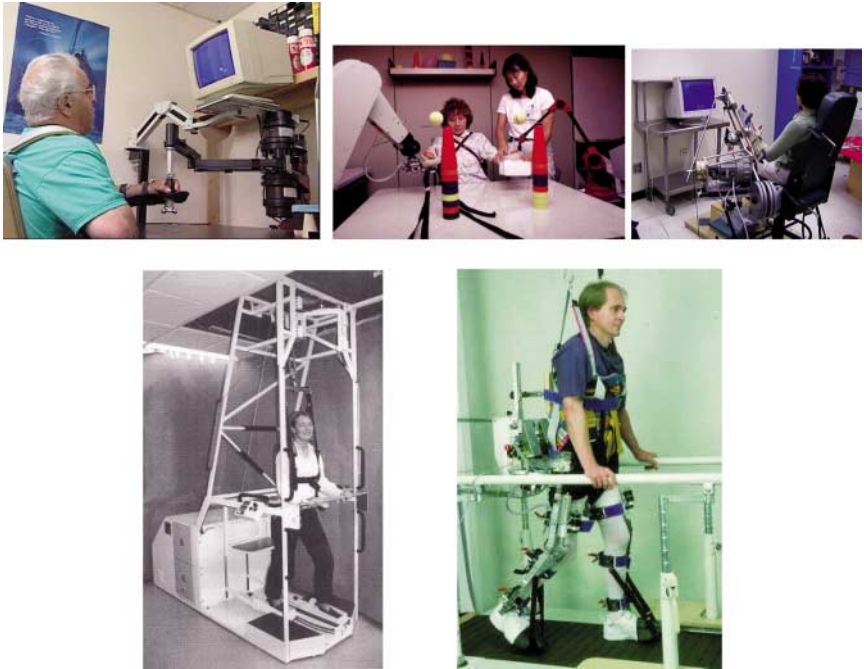


Figure 2 Examples of robotic therapy devices (*clockwise from upper left*): MIT-MANUS allows horizontal planar motion of the arm using a two DOF robot (89); MIME uses a six DOF industrial robot arm to control arm motion and can be used in a bimanual mode in which the unimpaired arm of a stroke patient specifies the desired movement of the robot-controlled, impaired arm (73); the ARM Guide is a trombone-like, three DOF robot with one actuated DOF—the linear slide—which can be used to assist in reaching movements across the arm’s workspace (91); the Lokomat drives hip and knee flexion and extension using ball-screw actuators attached to an exoskeleton (110); and the mechanized gait trainer uses a rock and cranker mechanism to drive the feet through a gait-like pattern (79). Figures reprinted with permission from the *Journal of Rehabilitation Research and Development*.

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