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**Robotic assessment and rehabilitation of
rhythmic upper-limb
movement primitives after stroke**

PhD Thesis presented by

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Abstract

Stroke is an attack during which some brain regions are deprived from oxygen and begin to die. When this affects the sensorimotor neural pathways, motor disorders may occur. Stroke patients may suffer from a loss of motor control, muscle weakness, or spasticity of mainly one side of the body. Consequently, two fundamental upper-limb motor primitives are potentially impaired after stroke, i.e. rhythmic and discrete movements.

Discrete movements consist of movements between a succession of postures with zero velocity and acceleration while rhythmic movements capture periodic movements like cycling. These primitives, which have been thoroughly studied in healthy subjects, are at least partially controlled by different neural pathways. Indeed, rhythmic movements require less cortical activity than discrete ones, and few to no learning transfer is observed between both movements.

In this thesis, both primitives were compared in the upper-limbs of cortical and subcortical stroke patients. In particular, we tested the hypothesis that rhythmic movements are less affected than discrete ones. Consequently, the *first objective* of this thesis was to assess the kinematic performance of both primitives with stroke patients and with healthy subjects as a control group.

After stroke, it is recommended to train functional movements with a high intensity. Since rhythmic and discrete movements are governed by different neural pathways, they might deserve specific and differentiated training to permit the recovery of the complete motor repertoire. However, functional movements of the upper-limb mainly consist of discrete movements. Therefore, our *second objective* was to design a purely unilateral rhythmic movement therapy that could complement existing rehab protocols.

Rehabilitation robotics are useful tools to boost the effectiveness of such a therapy. In order to optimize motor learning, it has been showed that patients should be assisted only "as-needed". In other words, the haptic assistance given to the patient

should be as low as possible, but sufficient so that the exercises can be completed with no drop of motivation. The rhythmic movement therapy that we designed precisely relied on such a performance-based assistance: the amount of assistance given to the patient was adapted in real-time as a function of his/her performance.

Finally, the *last objective* of this thesis was to study the effect of this rhythmic training on the general motor performance on a larger stroke population. Thirteen chronic stroke patients participated in a longitudinal study during which they performed 12 rhythmic therapy sessions of active training. Patients were assessed twice before and twice after the therapy in order to confirm their chronic stage and to establish the short- and long-term effects of the therapy. We observed motor improvements both in rhythmic movements, and, more surprisingly, some in specific features of discrete movements.

The thesis offers thus a better understanding of the mechanisms governing fundamental motor primitives, and provides some guidelines to improve existing rehab protocols.

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General introduction

1

With stroke being the second cause of permanent motor disorders in adults, there is a need to improve and optimize post-stroke recovery [15,75,97,175]. In this thesis two particular types of movements were studied in post-stroke survivors, i.e. rhythmic and discrete movements. The overarching objective was to question some hypotheses about motor control and how they can be used to leverage post-stroke recovery in the upper limb.

Recent literature established that rhythmic and discrete movement primitives are controlled by different neural networks, at least partially. Rhythmic movements require, inter alia, less cortical activity than discrete ones [145]. Until now, these movements have mainly been compared in animals and healthy subjects but never in stroke patients. Therefore, the *first objective* of this thesis is to establish whether rhythmic movements are differently impaired after stroke. Next, if rhythmic movements are lower in the hierarchy of motor control, they might be interesting to train in order to recover the complete motor repertoire after stroke. In order to address this hypothesis, the *second objective* is to develop a unilateral robotic upper-limb therapy with appropriate robotic assistance in order to study the effect of such a therapy on stroke survivors. This is the *third objective* of this thesis.

The general introduction is structured as follows: The first section (i) is about stroke. It overviews the stroke pathology, its prevalence, the recovery process and upper-limb rehabilitation process. Next, (ii) the concept of motor primitives is introduced and a state of the art about rhythmic and discrete motor primitives is provided. Thereafter, (iii) upper-limb rehabilitation robotics are presented with their effectiveness in the stroke recovery process, their ideal features and how they will be used during this thesis. Finally, the general objectives of the thesis are summarized and the publications from this thesis are listed.

1.1 Stroke

1.1.1 Pathology and impairments

Stroke is a "brain attack" which can happen at any time [15]. Parts of the brain are deprived from oxygen and begin to die. Of all strokes, 87% are ischemic, i.e. a blood clot blocks the blood flow to some brain areas (Figure 1.1), 10% are due to an intracerebral hemorrhage (Figure 1.2), and 3% are subarachnoid (space between the pia mater and arachnoid mater - Figure 1.3) hemorrhage strokes [140]. Depending on the size and the region that has been damaged, several impairments can occur. The most common impairments are (i) *motor impairments* such as reduced muscle power or tone on one side of the body (hemiparesis), spasticity, reduced coordination [35], joint stability and joint mobility, balance impairment and an altered gait pattern, (ii) *cognitive disorders* such as altered consciousness, attention or alertness, reduced energy and motivation, changes in temperament or personality and cognitive decline, (iii) *sensitive disorders* with altered sensation and proprioception, (iv) *language disorders* such as dysphonia¹, dysarthria² and dysphasia³, (v) *visual impairments* with a loss of visual acuity or field deficits and *perceptual disorders* including agnosia, apraxia and neglect [15]. From those impairments, motor impairments have the highest prevalence, affecting about 80% of the survivors [97].

The multi-tiered effects of stroke on the patient implies that the disease is classified within the World Health Organization's International Classification of Functioning, Disability and Health (ICF) framework. This classification provides a framework for the effects of stroke on the individual in terms of pathology (disease or diagnosis), impairment (symptoms and signs), activity limitations (disability), and participation restriction (handicap) (see Figure 1 in [96]). Indeed, due to the post-stroke impairments, stroke will induce disability (limitations of activities) and handicap. Up to 74% of stroke survivors require assistance from caregivers for their basic activities of daily living (ADL) [126].

1.1.2 Prevalence

Every 40 seconds someone over the world suffers a stroke [140]. Two third of stroke survivors will display some type of disability, so that stroke is the leading cause of adult disability in developed countries [140]. It represents the largest single cause of long-term adult disability in Europe [166]. Stroke is therefore a very expensive disease for the society [15]. As an illustration, in 2003 the medical and non-medical costs of caring for a typical Dutch stroke patient during the first six months after the attack were approximately 16000 EUR per patient [3]. More than 3% of the Dutch

¹Dysfunction of the voice

²Motor speech disorder

³Or aphasia, which refers to the full or partial loss of verbal communication skills

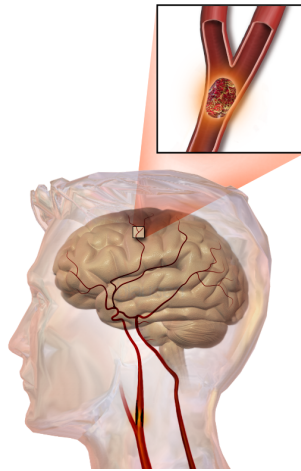


Fig. 1.1: An ischemic stroke is caused by a blood clot, depriving parts of the brain from oxygen. Figure obtained with permission by Blausen Medical Communications, Inc. (Donated via OTRS, see ticket for details) [CC BY 3.0 (<http://creativecommons.org/licenses/by/3.0>)], via Wikimedia Commons.

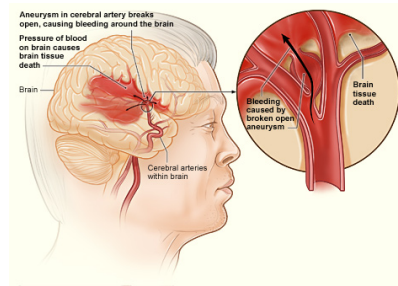


Fig. 1.2: Hemorrhagic stroke is due to a rupture or a leak of a blood vessel in the brain. Figure obtained with permission by National Heart Lung and Blood Institute (NIH) (National Heart Lung and Blood Institute (NIH)) [Public domain], via Wikimedia Commons.

National Health Service in 1994 and more than 4% of the National Health Service of the UK in 2000 was spent on stroke services [3]. These numbers are moreover tending to increase since the population in developed countries is getting older [15].

1.1.3 Risk factors

Some risk factors such as the age (older people are at higher risk), the gender (men are at higher risk), heredity and race of the patient cannot be modified. However, a particularity of stroke is that many risk factors can be changed, treated or controlled: i.e. high blood pressure, smoking, type 2 diabetes, artery disease, atrial fibrillation and other heart diseases, high blood cholesterol, poor diet, lack of physical activity and obesity [2, 142]. Therefore, improving the population lifestyle, and implement preventive strategies could limit the impact of stroke on our society [142].

After a stroke, the delay between the brain attack and the admission to the hospital can also be considered as a risk factor regarding the level of impairments [125]. Indeed, if the patient is quickly admitted to the hospital (less than 4.5 hours after the first symptoms), drugs may, under certain circumstances, be administered early

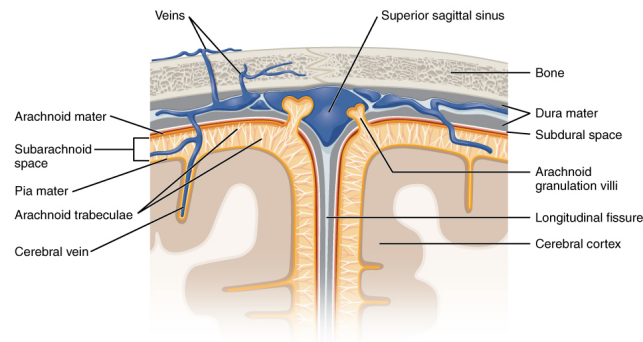


Fig. 1.3: Section across the top of the skull. The subarachnoid space is the space between the pia mater and arachnoid mater. Figure obtained by OpenStax [CC BY 4.0 (<http://creativecommons.org/licenses/by/4.0>)], via Wikimedia Commons.

and may minimize or eliminate post-stroke disabilities [125]. Therefore, teaching the first symptoms of the pathology to the population can limit the consequences of the brain attack: if a person suddenly presents face drooping, arm or leg weakness or difficulties to speak, it is time to call an ambulance.

1.1.4 Recovery

Recovery, as defined by [126], implies improvement of impairments in any level of the ICF thanks to either restitution or compensation. Restitution means the restitution of normative biological structures and function, while compensation is the use of biological structures and/or function different from those originally used before the injury. A straightforward example of compensation is the use of the non-paretic limb to execute a task which would have been executed with the affected limb before the injury.

After the brain attack, almost all patients show some spontaneous neurological recovery, following a natural logarithmic pattern (Figure 1.4) [96]. Indeed, in the first months after stroke, the recovery rate is the highest, while it reaches a plateau afterwards [92, 97].

During the first 3 months after stroke, spontaneous recovery involve both reduction of the ischemic penumbra and brain reorganization [117]. During this phase, brain plasticity is promoted because of injury-induced changes in the potential for neuronal plasticity [22]. For instance, researchers found that there is a deployment of new connections in the brain and spinal cord after stroke which is called "post-stroke axonal sprouting" [22]. In rodents, it is established that behavioral activity patterns can modify this axonal sprouting response. Therefore, during this phase, intensive motor training revealed its interest for optimizing plasticity of both

surviving and new neural networks, resulting in large recovery of motor performances. This recovery is thus more related to restitution of normative biological structures and function than compensation [22, 126]. In sum early mobilisation and motor rehabilitation is therefore recommended after stroke [103, 175, 181]. Note however that intensive very early mobilisation (less than 24h post-stroke) was associated with a reduction in the odds of favourable outcome at 3 months [11]. Presently, studies suggest that 33% to 66% of stroke patients with a paretic upper limb do not show any recovery in upper limb function 6 months after stroke [126]. Improving the rehabilitation protocols and increase the intensity of the therapies might however improve this outcome.

During the chronic phase, i.e. 6 months post-stroke, motor learning can still occur, although the learning curve is less steep. During this phase, new motor skills will be acquired in a similar way healthy subject can learn new motor skills. These recovery are mainly due to compensation rather than restitution [126]. The anatomy of the damage, however, sets a limit on how much impairments can be reduced. Generally speaking, improvements during this phase will remain modest [126].

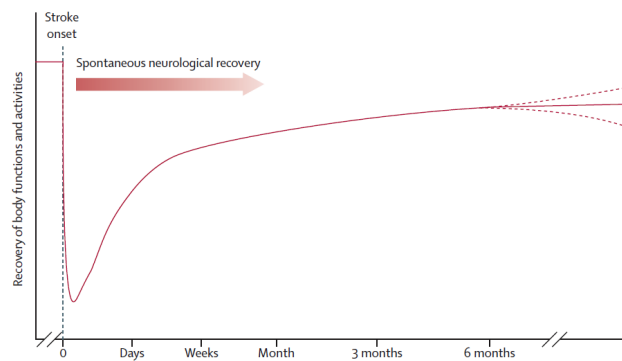


Fig. 1.4: Hypothetical pattern of recovery after stroke (adapted from [96], with permission from Elsevier)

Predictive recovery

In order to bring the recovery at a higher level, rehabilitation is recommended. Researchers work on computational neurorehabilitation models to get a better understanding of the neurorehabilitation process and to increase the predictions of recovery [15, 126]. These models try to capture spontaneous biological recovery and activity-dependent plasticity related to motor learning in order to describe and predict patient's behavioral outcomes. They aim at aiding to design new clinical experiments in a less expensive and more effective way than by trial-and-error fashion by simulating the effect of variations in rehabilitation parameters. In a next step,

these models could also optimize therapy towards a more patient-centred approach in terms of dosage, timing, scheduling and content. In this line, a recent study showed that predicting the recovery potential for individual stroke patients could indeed increase rehabilitation efficiency [157].

For example, a first model shows that if finger extension and shoulder abduction could be performed within 72h after stroke, there is 98% probability of recovering some manual dexterity within the subsequent 6 months [118]. In such patients, promoting manual dexterity early on could improve general outcome in manipulation.

Another model presumes that when patients reach a sufficient level of autonomy in a given skill, they will probably continue using it and they will probably continue improving this skill without further intensive rehabilitation [60]. However, when patients do not reach this level of autonomy, they will probably not rely on that skill during daily live activity, which will lead to a "learned non-use" once the intensive rehabilitation protocols are stopped. The objective is thus to bring the patients above these thresholds.

This thesis focuses on the upper extremity motricity of stroke patients, which brings us to the presentation of the actual upper-limb rehabilitation protocols and some new rehabilitation paradigms related to motor learning principles.

1.1.5 Upper-limb rehabilitation

Defining the optimal therapy after a stroke is still nowadays a real medical and societal challenge. Indeed, three quarter of of stroke survivors will be dependent for a number of daily life activities. This is mainly due to a lack of abilities for using their paretic upper limb [113].

Current upper-limb rehabilitation recommendations

Obviously, the final objective of the rehabilitation therapies is to bring the patient at the highest level of autonomy he/she could get in order reduce stroke-related disability.

To achieve this objective, the actual recommendations for upper extremity rehabilitation are the following [181]: (i) task-specific training in which the tasks are graded to challenge individual capabilities, practised repeatedly and progressed in difficulty on a frequent basis; (ii) daily live activity training tailored to individual needs and eventual discharge setting; (iii) constrained induced movement therapy (CIMT), when possible; (iv) robotic therapy is relevant to be considered to deliver more intensive practice for individuals with moderate to severe upper limb paresis; (v) mental practice, strengthening, virtual reality, bilateral training may be considered as adjuncts to functional task practice.

Motor learning principles

Motor learning relies on the ability to find appropriate motor commands that will lead to desired task outcome. Mechanisms governing motor learning were first extensively studied on healthy subjects, and these gave rise to several (sometimes contradictory) motor learning theories. However, it is only recently that these theories were studied and tested in post-stroke rehabilitation protocols [72].

Motor learning is a fuzzy concept. It encompasses motor adaptation, skill acquisition and decision making [72]. According to [85, 86] different types of motor learning components can play a role in post-stroke recovery. (i) *Instruction* plays an important role in selecting task-appropriate actions while these have not been often emphasized in motor learning literature. (ii) In *reinforcement learning*, also called unsupervised learning, actions are selected based on rewards and punishments. These can be extrinsic or intrinsic. Extrinsic rewards can be provided by loss or gain in points or praise, intrinsic rewards are based on self-perceived success or failure. In the latter form, there is a risk to stick on an adoption of habitual "just good enough" actions acquired prematurely. The patient could do better but is not reinforced to do so. CIMIT, for example, tries to prevent this adoption of bad habits by restricting the use of the non-paretic limb. (iii) *Sensorimotor adaptation*, also called supervised or error-based learning, refers to the reduction of errors in response to a perturbation. This has been extensively studied experimentally and computationally modeled with healthy subjects. An example of motor adaptation is when a subject learns a task in a perturbed force field. When the force field is removed, after effects exist. (iv) Recently the term "*motor acuity*" was introduced for the component of motor skill by which movement variability and smoothness improve with practice. This kind of learning probably occurs in the same cortical areas as the ones responsible for the motor commands themselves.

Two major modalities for implementing neurorehabilitation of the upper limb in chronic stroke based on motor-learning principles are CIMIT and robotics. In robotics, assistance can be considered as reinforcement learning, but also as motor acuity learning. If applied in an appropriate way (see Section 1.4.5), they can induce small but lasting effects [86]. Error-augmentation, which is an error-based learning during which the errors of the patients are emphasized, can also easily be provided with rehabilitation robots. This technique gives impressive corrective after effects but they have unfortunately short-lived retentions [122, 128].

These motor learning paradigms brought the community to the development of new rehabilitation protocols. Improving our understanding on how an intact and damaged brain code for motricity helps to build new effective rehabilitation protocols (e.g. CIMIT). In this thesis, two particular types of motor primitives are studied in stroke patients. By understanding how they are governed in the brain and

how they are impaired after stroke, new rehabilitation protocols could be built and tested. They could also in the future supply neurorehabilitation models.

1.2 Motor primitives

Motor primitives have been studied since several decades both in animals and humans [12, 46]. They can be defined in many different ways. First, a general definition will be given, and next rhythmic and discrete motor primitives will be more precisely discussed.

1.2.1 General definition

Humans are able to execute a high amount of gestures with ease and precision. They have the abilities to adapt movements to unexpected situations without having to think about it, in a robust and seemingly effortless way. To explain both adaptivity and robustness, the concept of motor primitives is attractive, since they allow to reduce the dimensionality of the problem and consequently simplifies the control of physical interactions [32].

A lot of types of motor primitives can be found in the literature. The general idea behind them is that complex motor behavior can be decomposed into simpler building blocks. Primitives can be found at behavioral level, muscle level and neural level [46].

At the behavioral level, movements are thought to be composed of simple building blocks such as a minimum-jerk submovements. This was highlighted from the kinematic decomposition of perturbed movements by healthy subjects or after a stroke [46, 132]. As such, even complex and visually continuous movement appear to be constructed by individual segments blended together [46, 133].

At the muscular level, motor primitives are also called synergies. These are the co-activation of several muscles that produce a torque about a joint or a force in a particular direction [30, 46, 164]. Complex motor behaviors can in this sense be described by a superposition of such muscle synergies. For example human locomotion muscle patterns can be decomposed into a finite set of synergies [76].

Finally, at the neural level, motor primitives are considered as networks of spinal neurons that activate a set of muscles (synergies) in a coordinated way in order to execute a specific movement. In animals, strong evidences support their existence. For example, central pattern generators (CPGs) and force fields have been highlighted in both vertebrates and invertebrates (for more details about CPGs, see next section) [12, 32, 46].

In this thesis, two specific high-level primitives were investigated, i.e. rhythmic

and discrete primitives. These two building blocks can be described in the three above mentioned levels and seem to be governed by two different neural systems, at least partially.

1.2.2 Rhythmic and discrete primitives

First of all, a clear definition of rhythmic and discrete movements must be provided. A simplistic way to define both movements is that rhythmic movements are movements being periodically repeated and discrete movements are movements between two postures. Walking is therefore a rhythmic movement and reaching is a discrete movement. However, successive discrete reaching movements between two targets can also be considered as rhythmic. And vice versa, a rhythmic movement that starts in one posture and after a few cycles stops in another posture, can also be considered as discrete. Accordingly, Hogan and Sternad defined a mathematical framework to differentiate both movement types [67]. However, for this thesis, we will stick to a simpler definition.

In this thesis, the discrete movements that were studied are straight reaching movements with a period of zero acceleration (i.e. posture) between each individual movement. They can however be repeated over time. Rhythmic movements on the other hand are (quasi-) sinusoidal movements. The initiation and termination phases of these movements are in the gray zone [172], and were not considered in our analyses.

Historically, rhythmic and discrete movements have mainly been studied separately in motor control [32]. For example, locomotion have mainly been studied relying on central pattern generators. In discrete reaching movements however, the impact the motor cortical function was the main focus.

Since the last two decades, research efforts intensified to study the differences and synergies between both movements. The researchers' objective was to establish how both movements are being managed by the motor system. Consequently, they have been studied in humans through analysis of the kinematics, motor learning paradigms, muscular activation, and brain imaging, but also in animals through more invasive techniques. A central question was to establish whether both movements are sharing the same neural processes with (i) rhythmic movements being repeated discrete movements (concatenation hypothesis) or (ii) discrete movements being interrupted cyclic movements (half-cycle hypothesis) or (iii) if both movements result from different neural processes (two primitives hypothesis) [145, 172]. These research efforts are overviewed in the paragraphs below.

Spinal level

The spinal level of the central nervous system is considered to govern motor generation [81]. At this level, CPGs and force fields have been highlighted in invertebrates such as salamanders and frogs, and vertebrates such as cats and monkeys [12, 16, 32, 73]. CPGs are spinal networks producing rhythmic muscle activities while being stimulated by monotonic (i.e. non rhythmic) excitation without any sensory input. In animals, strong evidences for their existence exist since rhythmic patterns of activation were observed both in decerebrated and in deafferented animals [17, 73, 109, 147]. However, proving their existence in humans is more difficult since influences from higher cortical areas and from sensory pathways can hardly be excluded. However, indirect evidences suggest that CPGs may also exist in humans [26, 27, 37, 41, 82, 115, 161]. In sum, spinal CPGs might play a significant role as a source of rhythmicity for rhythmic movements.

In parallel, Bizzi and colleagues came with the concept of force fields [12]. They showed that when stimulating specific inter-neuronal areas of the frogs' spinal cord, the limb moved in the direction of a target position (equilibrium point), independent of the initial position of the limb. Other researchers showed that CPG networks could be activated by stimulating particular area of the spinal cord. Interestingly the different orientations of oscillation were very close to the direction of the force fields for discrete movements found with the same method. However, it is not known if the concept of force fields can be applied in higher vertebrates.

Motor cortex

The motor cortex is believed to govern the definition of the motor task [81]. It can be divided into two areas, i.e. the primary motor cortex and the premotor cortex. The latter is involved in learning sequences of movements, in timing in processing of sensorimotor information, as well as in the selection of actions. The former is involved in the control of movement parameters.

Haiss and Schwarz found that rhythmic and non rhythmic movements can be evoked through two different areas of the primary motor cortex in rats [59]. They found that both movements, although performed by the same set of muscles, were elicited by different (but adjacent) regions of the primary motor cortex. Simultaneous activation of both areas resulted in a shift of the offset of the oscillatory movements which is a combination of both movements. Other researchers suggested that the primary motor cortex encode behavior and that some primary motor cortical neurons are connected in a one-to-one relationship with spinal motor synergies [32].

In humans, brain activity was measured while performing similar rhythmic and discrete wrist movements [145]. Healthy subjects were asked to execute simple flex-

ion and extension movements of the wrist in discrete and rhythmic ways under fMRI¹. Even in such simple tasks, large differences in brain activities could be observed. Discrete movements activated much broader cortical areas than rhythmic movements. Therefore, this result falsifies the concatenation hypothesis, i.e. rhythmic movements are not repeated discrete movements.

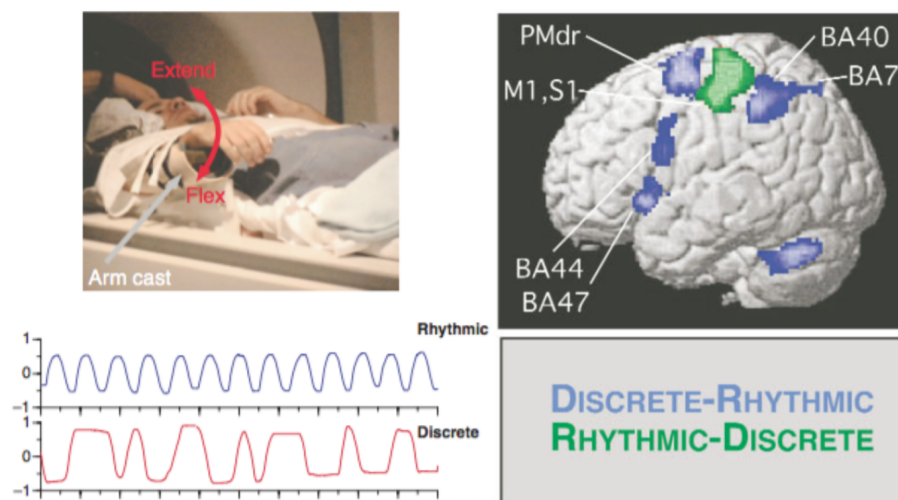


Fig. 1.5: Researchers studied the brain areas being active during rhythmic and discrete wrist movements. They reported that rhythmic wrist movements required less cortical activity than discrete movements (adapted from [145]. Reprinted by permission from Macmillan Publishers).

Kinematics and motor learning

Several researches studied the kinematic properties of rhythmic and discrete movements in healthy subjects [18, 57, 172]. They came to the conclusion that cyclical movements differed markedly from discrete movements as well as from the first and last half-cycles of cyclical movements. Those researchers weakened also the hypothesis that rhythmic movements are assembled as a string of discrete movements.

Other researchers looked at the learning transfer between both movements. They state that if both movements share the same neural process, it would be expected that discrete tasks would completely transfer to the same task performed in a rhythmic way, and vice versa. Ikegami and colleagues asked healthy subject to per-

¹Functional magnetic resonance imagery (fMRI) is a functional neuroimaging procedure using MRI technology that measures brain activity by detecting changes associated with blood flow. This technique relies on the fact that cerebral blood flow and neuronal activation are coupled. When an area of the brain is in use, blood flow to that region also increases. [4]

form back-and-forth upper limb movements with visual distortion (Figure 1.6) [74]. Howard and colleagues, on the other hand, asked healthy subjects to perform circular arm movements while they were exposed to a velocity-dependent force-field perturbation. The former showed that almost no transfer occurred from rhythmic to discrete movements and transfer from discrete to rhythmic was only partial. This last result was attributed to the fact that the first cycle of a rhythmic movement actually recruits the discrete primitive [71,74]. The latter showed that subjects could co-represent two force-field perturbations only when each force-field was associated to one movement type (rhythmic or discrete). Both of these results suggest that different neural resources are employed for the two movement types. This provides evidences that rhythmic and discrete movements employ at least partially separate control mechanisms in the motor system.

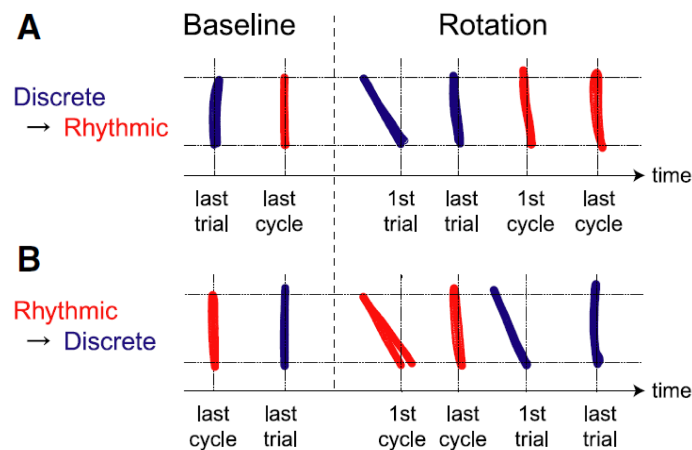


Fig. 1.6: Ikegami et al. studied the learning transfer from rhythmic to discrete movements and vice versa in healthy subjects. They asked subjects to practice back-and-forth upper-limb movements with distorted visual feedback. The actual movements were displayed with an angular distortion. They established that no learning transfer occurred from rhythmic to discrete movements. From discrete to rhythmic movements, only few learning transfer occurred [74] (Republished with permission from Society of Neuroscience).

In stroke survivors

Upper-limb rhythmic and discrete movements have been distinctly studied in stroke survivors, revealing that both movements may be impaired after stroke. Discrete movements display inadequate recruitment of agonist muscles [56] and stereotyped sub-movements in the velocity profiles. Said differently, they are performed in a jerky way [38,51,56,68,88,132]. Early after stroke, a lot of submovements are ty-

pically identified in the velocity profiles. Over time, movements become smoother since submovements progressively blend together, which is associated to stroke recovery [38, 88, 132].

Rhythmic upper-limb movement are less studied in the stroke population, and results tended to show that amplitude and rhythmicity may be altered in stroke survivors [148, 186]. However, according to [186], the rhythmic patterning of arm muscle activation and neural control of spinal cord excitability appears to be preserved in chronic stroke even if they show a somewhat "blunted" effect. This probably means that the putative spinal contributions to rhythmic arm movements - possibly governed by CPGs - remain accessible after stroke.

Rhythmic and discrete movements have however never been compared in stroke survivors. This brings us to the first objective of this thesis. Since stroke impacts mainly the brain and since discrete movements require more cortical activity than rhythmic movements, it was expected that rhythmic movements would be less impaired than discrete ones. Therefore, in Chapter 2, both rhythmic and discrete movements were compared side-by-side in a stroke population. This has been achieved by measuring the kinematics of both movements through a rehabilitation robot (see Section 1.4).

1.3 Rhythmic movement training after stroke

Since both, rhythmic and discrete movements are impaired after stroke and since both movements likely rely on different motor primitives, the second line of research in this thesis was to explore whether rhythmic movement training could have some benefits in post-stroke rehabilitation. During post-stroke rehabilitation, physical therapists are recommended to train intensive functional movements. Functional upper limb movements are however mainly composed of discrete movements. Therefore, the motor repertoire might not be entirely covered by these exercises. Researchers already put to test rhythmic movement trainings. They showed positive results of these therapies in terms of arm strength, amplitude and general motricity [39, 64, 104, 178, 179]. However, these rhythmic trainings were always combined with other stimuli such as auditory cueing, bilateral training and specific level of intensity, which makes it impossible to determine the exact effect of pure rhythmic movement training on upper limb motor control.

Therefore, during this thesis, a pure unilateral rhythmic movement training was developed for chronic stroke patients in order to establish which movement features are being improved by rhythmic movement therapy (objective 2 and 3 of this thesis).

With this rhythmic movement training, the learning transfer from rhythmic to discrete movements was studied in a stroke population. In healthy subjects, no lear-

ning transfer was highlighted from rhythmic to discrete movements. However these observation were only made on error-based metrics. In stroke patients, motor acuity learning also plays an important role in motor recovery. We question thus whether learning transfer occurs in post-stroke rehab context. This rehabilitation protocol was also performed by using a rehabilitation robot.

1.4 Rehabilitation robotics for the upper-limb

In order to achieve its objectives, this thesis strongly relied on the use of a rehabilitation robot. In this section, some key elements related to these machines is briefly presented.

Robotic neurorehabilitation is attractive because of its applicability across of a wide range of motor impairments, its abilities to offer high intensity, goal directed training and its high measurement reliability [72, 113]. Beside their applicability to rehabilitation, they can also be used to study motor learning (in healthy subjects but also in stroke survivors) and assess motor recovery. The first robots developed for neurorehabilitation date back from the 1980s.

1.4.1 Types of robots

Broadly speaking, two classes of upper-limb robots were developed by rehabilitation engineers: end-effector robots and exoskeletons. In the former, the subject is attached to the robot through a single actuated point. These robots are easy to install and require only few adjustments before the therapy can start (Figure 1.7). In the latter case, every joint of the arm is actuated by a multi-body actuated structure. These types of robot allow to deliver individual assistance to each join, but their drawback is the longer time of installation of the patient in the robot (Figure 1.8).

1.4.2 Effectiveness

The most recent Cochrane review about "Electromechanical and robot-assisted arm training [...] after stroke" (2015) states that *"Electromechanical and robot-assisted arm and hand training improved activities of daily living in people after stroke and function and muscle strength of the affected arm. As adverse events such as injuries and pain were seldom described, these devices can be applied as a rehabilitation tool, but we still do not know when or how often they should be used."* [113].

The effectiveness of robotic rehabilitation is related to a lot of factors. The target group for a specific robotic therapy [75] but also to the type of assistance, the feedback given to the patients, the type of exercises,... are all parameters that can affect the effectiveness of a given training program. This is not taken into account in the Cochrane reviews, which considers all clinical studies as a whole. One therapy with

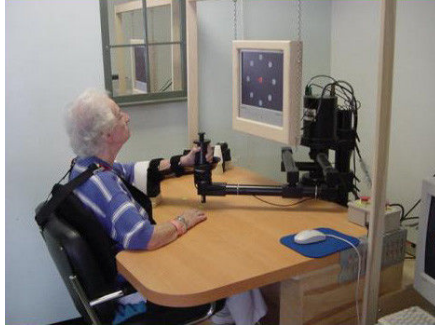


Fig. 1.7: End-effector MIT-Manus (Reproduced with permission from [87])



Fig. 1.8: Exoskeleton Armeo Power by Hocoma (courtesy of Hocoma AG)

a specific robot can be inefficient because it assists the patients in a way that they are almost passive in the device or because the provided feedback is not appropriated [28, 124]. Another therapy with the same robot, on the other hand, could be effective if it properly reacts to the patient's performances and provides challenging feedback [28, 124]. Interestingly, note that a similar phenomenon can exist between human therapists. One therapist who gives appropriate exercises to a patient will get better results than another therapist who does not motivate the patient to work actively, as suggested by the stroke rehabilitation guidelines.

1.4.3 Cost-effectiveness

Although not central for the present thesis, cost-effectiveness of rehabilitation robots is often presented in the literature as a strong incentive for their development. In brief, cost-effective robots should help in maintaining the quality of care with controlled costs. However, cost-effectiveness of robotic upper-limb rehabilitation strongly depends on how and when robotic therapy is being used. For highly impaired patients, robots are valuable at early stage of recovery [112]. They can help to increase the intensity of the therapy through a recreational approach without the need of a physical therapist next to every patient [102]. The robot can help the patient to fulfil movements which can maintain his/her motivation. Also, they can increase the level of autonomy of the patients. In this sense, this can lead to a reduction of the costs related to the assistance of chronic post-stroke during daily live activities.

In less impaired patients, they can be interesting for the same reason. However, for these patients, actual review of the literature shows that other cheaper solutions

exist to intensively train the patients and reach the same level of recovery [175, 181].

1.4.4 Ideal features

Robotics, in contrast to human therapists, have the advantage to offer assistance in a measurable and repeatable way. As stated above, the effectiveness of a therapy partly depends on the assistance or resistance given to the patient during the exercises. Too much assistance lead to slack, not enough leads to frustrations.

The actual recommendation regarding the ideal features of neurorehabilitation robotics (for upper- and lower-limbs) are the following [9, 75, 116, 182]: (i) high mechanical compliance, (ii) ability to assist patients in completing desired movements, (iii) minimum assistance level, (iv) large range of forces, soft haptic interaction for proprioceptive awareness, (v) adaptive assistance properties, (vi) high repeatability, (vii) increased training motivation through use of interactive (bio)feedback, (viii) precisely controllable assistance or resistance during movements, (ix) objective and quantifiable measures of subject performance, (x) standardized training sessions, (xi) intensive training and (xii) relieving therapists from physically demanding work.

1.4.5 Assist-as-needed principle

When a subject is learning a new movement, several learning strategies can be deployed (See Section 1.1.5 - Motor learning principles). Reinforcement learning is one of them and can be applied by assisting the movements with the minimal amount of assistance, for instance through proprioceptive haptic feedback. However, the level of assistance has to remain as low as possible in order to prevent slacking behavior to occur. Slacking may indeed have adverse effects on recovery, since subjects will rely too much to execute their movements while commit themselves to execute them on their own [9, 43, 183]. This type of assistance is called "assist-as-needed".

In order to be successfully implemented, an "assistive-as-needed" strategy should be more lazy than the patient. The device will help the patient to fulfil the task only if he/she is not able to do so by oneself, and fade away if the patient can do it [43, 126]. In sum, if the patient is able to perform the desired task, he/she will receive no or at least less and less assistance. In this sense, many methods were proposed to determine the necessary amount of assistance: (i) Impedance controllers comparing the position and velocity of the robot to a desired reference trajectory that provide restoring forces proportional to the distance from the path [143], (ii) controllers that specify both a desired trajectory and a desired completion time, adding assistance in moving along the trajectory toward the target [13], (iii) controllers that do not need a predefined track allowing the subjects to choose their own trajectory while assisting movement toward the target [114], (iv) controllers that adapt the amount of assistance according to some performance metrics [13]. All these controllers gave

promising results in clinical trials. However, in most of the cases, a tendency for users to rely on the assistive force is still observed. To counteract this effect, forgetting terms are sometimes included in the controller, which decreases the amount of assistance after successful trials, encouraging more active participation by the subjects [13, 23, 58, 183].

The vast majority of these assist-as-needed controllers assist discrete point-to-point movements [13]. In contrast, few rhythmic assistances for the upper-limb are described such as in [153] in which assistance for small-amplitude oscillation of the wrist is offered; or in [176] where a continuous eight-shaped trajectory is proposed. In the latter, the amount of assistance is tuned according to the performance made along fixed segments.

In this thesis, we developed a framework in which, rhythmic movement assistance exploits the cyclic nature of the movement to anticipate the future trajectory based on previous cycles. More precisely, the second objective of this thesis was to develop a rhythmic performance-based assist-as-needed algorithm, in order to offer assistance-as-needed during a rhythmic movement therapy (see Section 1.3).

1.4.6 Robot used in this thesis

In this thesis, the end-effector robot REAplan, developed within our university, was used. This robot mobilizes the upper limb of a patient along a horizontal plane through an actuated handle whose patient's hand is attached to. The handle is equipped with force sensors so that force and/or impedance control can be implemented.

This robot was especially developed for post-stroke rehab, with the ability to assist all types of patients as needed. One of the main feature of this robot is its large workspace allowing to work the full upper-limb extension. Before this thesis, this robot had already been used in assessment [50, 51] and in rehabilitation studies [52]. A more in-depth description of the general architecture and controller of the REAplan robot can be found in Appendix A.

1.5 Thesis objectives

In summary, the objectives of this thesis were the following :

1. Improve our understanding on how stroke patients perform upper-limb movements, and more specifically on how two motor primitives (rhythmic versus discrete) are impaired after stroke. Such a better understanding can significantly influence the recommendations given for stroke rehabilitation.
2. Design and assess a robotic rehabilitation protocol in order to train rhythmic movements after stroke.

3. Investigate how such rhythmic movement training can improve motor performances after stroke, both regarding rhythmic movements themselves, and a possible transfer to discrete ones.

The thesis is articulated around these three objectives. Each of them was investigated in a separate chapter, also corresponding to a journal publication (first two are published, third one is in preparation). Chapter 2 of this manuscript establishes that rhythmic arm movements are less affected than discrete ones after a stroke. Chapter 3 develops the performance-based robotic assistance during rhythmic arm exercises; and Chapter 4 unveils that rhythmic upper-limb movement training enhances motor skills of both rhythmic and discrete movements after stroke through a longitudinal study.

At the end of the manuscript, the main results and perspectives of the thesis are wrapped up and discussed.

1.6 Publication from this thesis

- P. Leconte, R. Ronsse, Rhythmic movements are smoother than discrete movements after stroke, *Altacro symposium 2013*
- P. Leconte, R. Ronsse, Rhythmic movements are smoother than discrete movements after stroke, *In proceedings NCM 2014*
- Patricia Leconte, Jean-Jacques Obran de Xivry, Gaëtan Stoquart, Thierry Lejeune & Renaud Ronsse, Rhythmic arm movements are less affected than discrete ones after a stroke *Exp. Brain Res.* Jun;234(6):1403-17, 2016 [98]
- Patricia Leconte & Renaud Ronsse - Performance-based robotic assistance during rhythmic arm exercises *In proceedings BIOROB 2016*
- Patricia Leconte & Renaud Ronsse - Performance-based robotic assistance during rhythmic arm exercises *J. NeuroEng Rehabil.* Sep 13;13(1):82, 2016 [99]
- Patricia Leconte, Gaëtan Stoquart, Thierry Lejeune & Renaud Ronsse, Rhythmic upper-limb movement training enhances motor skills of both rhythmic and discrete movements after stroke - A longitudinal study, In preparation

Rhythmic arm movements are less affected than discrete ones after a stroke

2

Exp. Brain Res., 234(6):1403-17; 2016

Patricia Leconte, Jean-Jacques Obran de Xivry,
Gaëtan Stoquart, Thierry Lejeune & Renaud Ronsse

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2.1 Introduction

Daily life motions of the upper limb are composed of complex combinations of rhythmic and discrete movements, e.g., wiping a table or playing the piano [154]. Discrete movements are defined as movements between a succession of postures with zero velocity and acceleration, while rhythmic movements are periodic and display an acceleration peak at the zero-velocity movement reversal [55,67]. The literature reached a consensus stating that rhythmic and discrete movements form two different motor primitives [18,31,53,57,67,69–71,74,100,144,145,149,150,155,172]. In summary, discrete movements are not made of truncated rhythmic movements, and rhythmic movements do not consist of concatenated discrete movements.

Schaal et al. (2004) investigated the brain areas involved in producing simple discrete and rhythmic movements of the wrist via fMRI. They observed that discrete movements activated a variety of contralateral areas, such as BA7, BA40, BA44, BA47, PMdr, and RCZa, known to be involved in high-level computational processes, e.g., planning. Rhythmic movements, on the other hand, activated only a small number of unilateral sensorimotor areas (M1, S1, PMdc, SMA, pre-SMA, CCZ, RCZp, and cerebellum), most of which being also recruited in producing discrete

movements. After a stroke, both discrete and rhythmic movements are potentially affected [38, 50, 51, 56, 68, 88, 133, 148, 186]. However, to the best of our knowledge, no study has compared the levels of impairment between both movements in the same patients.

Consequently, in this chapter, we tested the hypothesis that stroke would affect rhythmic task motor performance less than discrete task motor performance. Indeed, the stroke insult significantly impacts cortical areas, and the cortical network recruited in producing discrete movements is larger than for rhythmic movements. In addition, we tested the existence of a hierarchy in the levels of impairments after a stroke: patients with impaired rhythmic movements should have impaired discrete movements, but not vice versa. Indeed, if the cortical network activated in producing discrete movements is larger than the one for rhythmic movements [145], some patients could be affected only in the production of discrete movements, if the circuitries governing rhythmic movements are left intact. The reverse picture is more unlikely, since impairment in producing rhythmic movements would reveal a disorder in the recruitment of unilateral sensorimotor areas being active during the production of both movement types. The main goal of the present chapter is thus to compare the levels of impairment between discrete and rhythmic movements in the same post-stroke patients. To this end, stroke patients and healthy subjects were asked to perform simple back-and-forth movements with their upper limbs between two visual targets, once in a discrete way and once in a rhythmic way.

Finally, a third movement type was added, i.e., a non-visually guided rhythmic task where participants were asked to make rhythmic movements without receiving visual targets. Our objective was to test whether this task would be differently affected than the one with visual targets. Indeed, the presence of visual targets requires more planning and leads to possible movement corrections by the visuomotor pathways [5, 33, 54, 61], hence reinforcing the dependence on cortical networks. Therefore, removing the visual targets should facilitate the task and further isolate possible subcortical and/or spinal contributions.

In sum, the present chapter aims to establish whether there exists a hierarchy of impairment in different motor tasks after a stroke by comparing the levels of impairment of (1) non-visually guided rhythmic movements, (2) visually guided rhythmic movements, and (3) visually guided discrete movements between stroke patients and healthy controls.

2.2 Materials and Methods

2.2.1 Participants

Eleven stroke patients and eleven age-matched control subjects were included in this study. Stroke patients were ineligible for this study if they suffered from: (i) any other disorder affecting the upper limb; (ii) severe visual impairments or severe neuropsychological impairments like aphasia, attention deficit disorder, or neglect; (iii) a cerebellar stroke; or (iv) an active elbow range of motion smaller than 20°. To assess the sensorimotor function of the upper limb, stroke patients were evaluated with the Fugl-Meyer Assessment of the upper extremity (FMA-UE) [48]; this scale quantifies the level of impairment, with an index ranging from 0 to 66 points. The FMA-UE score and other relevant characteristics of the patients and control participants are presented in Table 2.1.

Table 2.1: Main characteristics of the patients and control subjects

Patient	Gender	Age	Months post-stroke	Dominant hand	Paretic side	Type, location of lesion	FMA/66	Force elbow flexion/5	Ashworth elbow flexors/4	Box and block test (healthy side/paretic side)
1	F	41	60	R	R	N/A	41	4	2	61/6
2	M	50	4	R	L	Hemorrhagic, sub-cortical	12	1+	1+	54/1
3	M	54	12	R	L	N/A	61	5	0	59/36
4	F	57	22	R	L	Ischemic, cortical	41	4	1	N/A
5	F	58	11	R	L	Hemorrhagic, sub-cortical	22	4	2	64/10
6	M	39	36	R	R	N/A	66	5	0	N/A
7	M	63	3	R	L	Ischemic, cortical and sub-cortical	47	5	0	36/0
8	F	57	8	R	R	Ischemic, cortical	57	2	1+	27/0
9	M	53	3	L	L	Ischemic, cortical and sub-cortical	21	4	1+	32/0
10	M	56	3	L	L	Ischemic, cortical and sub-cortical	6	0	0	42/0
11	M	58	10	R	R	Ischemic, cortical	52	4+	1+	N/A
Stroke							Control			
Amount of subjects							11			
Gender (male/female)							7/4			
Age (SD)							53.3 (7.4) years			
Dominant hand (left/right)							2/9			
							11			
							3/8			
							55 (12.2) years			
							2/9			

Force: Clinical assessment of the muscular force following the British Medical Research Council System; the best note is 5 (normal muscle force capacity) and the worst is 0 (no muscular contraction). Ashworth: modified Ashworth scale capturing muscle spasticity; the best note is 0 (no increase in tone) and the worst is 4 (rigidity in flexion or extension)

FMA Fugl-Meyer assessment, SD standard deviation, N/A information not available

Before beginning the experiment, all participants gave their written informed consent to participate to the study, which was approved by the scientific and ethical committees of the Université catholique de Louvain.

2.2.2 Measurement device

The experiments were performed by using the REAplan, an upper-limb end-effector research prototype robot developed within our university. The REAplan was initially designed to quantify the upper limb impairments of disabled patients [50, 51] and to provide robot-assisted therapies to the same populations [52].

The robot is composed of (i) a height-adjustable, horizontal table, (ii) a handle equipped with force sensors that are held by the participant, (iii) two motors actuating the handle along the orthogonal directions in the horizontal plane, (iv) a flat screen and loudspeakers in front of the participant, which can provide visual feedback of the position of the handle and any other visual or auditory information, and (v) an interface for the therapist. Components i-iv can be seen in Figure 2.1(top). During the tasks, data were recorded at 125Hz for off-line analyses.

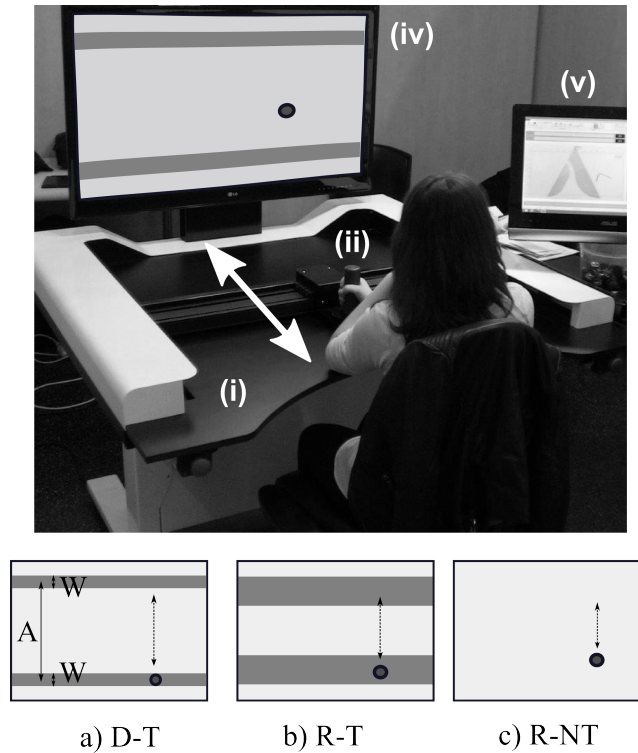


Fig. 2.1: Top: the REAplan robot, which was used as a measurement device. The white arrow denotes the movement direction that was studied in this experiment, i.e. forward-backward in the sagittal plane. Bottom: graphical interface (iv) shown to the patients when performing, with the right arm, (a) the discrete task with small targets (D-T), (b) the rhythmic task with large targets (R-T), and (c) the rhythmic task without targets (R-NT).

2.2.3 Experimental procedure

Participants were seated on a chair or their own wheelchair in front of the device. The height of the REAplan was adjusted such that the elbow formed a right angle and the arm was in a neutral position along the trunk when the participant held the handle in its initial position. Seven patients were strapped to the handle when performing the task with their paretic arm because their hand was too weak to hold it. For seven patients, their trunks were strapped to the chair because they made compensatory movements during the training phase.

All participants performed three tasks with each of their arms. All tasks consisted of performing back-and-forth movements restricted to a straight trajectory in the forward-backward direction of motion (sagittal plane). Lateral movements were thus prohibited by implementing stiff virtual walls with the device, while the direction of motion was controlled under a "free-mode" (or transparent) admittance controller.

Each task consisted of the achievement of three trials of fifteen back-and-forth movements at self-selected speed, i.e., forty-five back-and-forth movements per task per arm. Two patients out of eleven (patients 2 and 10) were too weak to fulfill three trials with their paretic arm and thus only performed two trials. Participants received visual feedback that mapped the position of the handle on the screen during all tasks.

The first two tasks consisted of making back-and-forth movements between two green rectangular targets (Figure 2.1, a and b), with the instruction to make the movement reversal (i.e., to reach zero velocity) inside the target. Once the handle reached the target, it turned red and a beep was delivered; this gave visual and auditory feedback for reversing the movement direction. The only differences between the first two tasks were the width and distance between the targets, determined according to the so-called "index of difficulty" (ID) [18, 57], based on Fitts' law [45]:

$$ID = \log_2(2A/W) ,$$

where A denotes the movement amplitude and W is the target's width (Figure 2.1a). This index thus captures that it is more difficult to make longer movements and aim at smaller targets. Researchers [18, 57] showed that healthy participants perform kinematically discrete movements with zero acceleration at the movement reversal when the ID is large. When the ID is smaller, the same authors further showed that healthy participants perform kinematically rhythmic movements, with maximal acceleration (in absolute value) at the movement reversal.

In the present study, the movement amplitude A was set to 12.5 cm and the target width W was set to 0.7 cm for the first task ($ID = 5.16$; pilot tests showed this ID was large enough to induce discrete movements with the present task). For the second task, A was set to 10.5 cm and W was set to 3.5 cm ($ID = 2.58$). The position cursor,

provided as visual feedback, had a diameter of 0.5 cm. All patients had active ranges of motion larger than these amplitudes.

During the third task, no rectangular target was visible on the screen, and the participants were instructed to make movements of similar amplitudes as during the other tasks. They were instructed to imagine that they were sawing wood to induce kinematically rhythmic movements; no auditory feedback was delivered during this last task. The three tasks were thus "discrete with targets" (D-T), "rhythmic with targets" (R-T), and "rhythmic with no target" (R-NT); see Figure 2.1.

Before starting each block of trials, participants were trained for each task for approximately one minute, until obtaining consistent movements. The first six subjects and patients performed the tasks in the following order: R-T, R-NT, and D-T, first with their right or healthy arm and then with their left or paretic arm. The remaining five subjects and patients performed the tasks in the reverse order: D-T, R-NT, and R-T, with their left or paretic arm first.

2.2.4 Data processing and kinematic indices

The raw position trajectories of the handle were filtered using a forward and backward second-order Butterworth filter with a cut-off frequency of 6 Hz. Thereafter, the velocity, acceleration, and jerk (third derivative) of the handle were obtained by successive numerical differentiation of the position profile.

All trials were then cut into individual movements between the locations of the zero velocity points at the movement reversal. Each movement thus corresponded to an individual discrete movement or to a half-cycle of a rhythmic movement.

General performances of the tasks, i.e., mean velocity (v_{mean}), movement amplitude (A), and precision at the movement reversals, were computed. The precision at the movement reversal was computed as 1 standard deviation of the distribution of the absolute error between the handle position at movement reversal and the location of the target center. This metric thus captures the distribution of reversal points around their average and was computed only for the D-T and R-T conditions, where visual targets were displayed.

Next, dwell time in individual movements was computed to assess the kinematic difference between discrete and rhythmic movements. Dwell time was introduced in the literature as a specific landmark of discrete movements [18, 67, 156]; it corresponds to the duration around movement reversal between the first time the velocity gets below 5% of the velocity peak of the preceding movement and the first time it gets above 5% of the velocity peak of the following movement (Figure 2.2). Note that, with this definition, an ideal sinusoidal movement displays a dwell time of about 3.2% of the cycle duration.

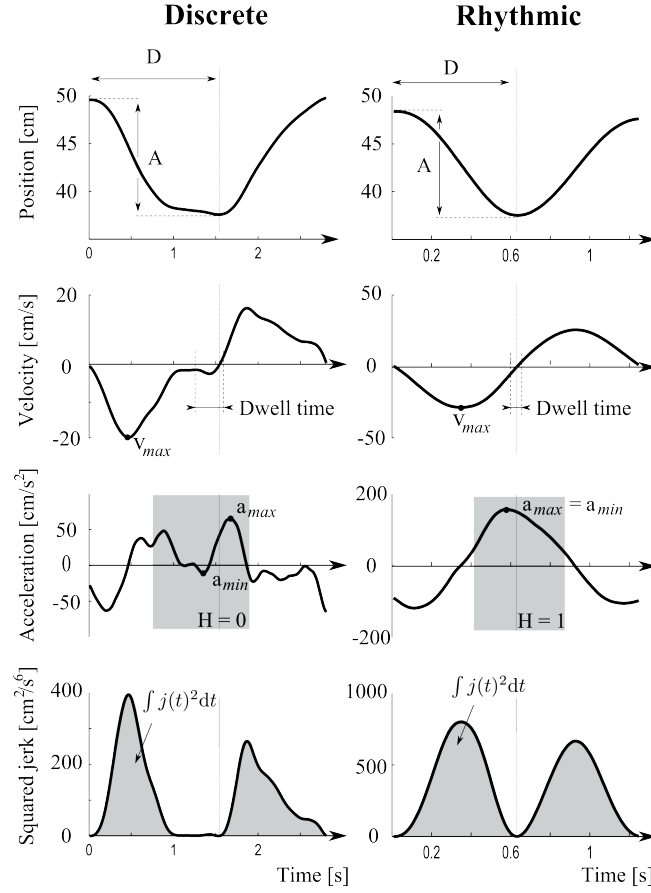


Fig. 2.2: Illustration of the reported metrics during the production of discrete (left) and rhythmic (right) movements. One period or two submovements are displayed. Top: the position profile is displayed with the amplitude (A) and duration (D) of the first movement. Bottom: the velocity profile is displayed with the mean velocity, the number of peaks in the velocity profile, and the dwell time. Below, the acceleration profile is displayed with the landmarks used to compute the harmonic index (i.e., a_{min} and a_{max}). The lowest panel displays the squared jerk, which was used to compute the LDJ by normalizing the surface under the squared jerk profile by D^3/v_{mean}^2 .

Finally, the following movement kinematic indices were computed for each individual movement to assess their harmonic nature and smoothness.

- **Harmonicity index H [18, 57]:** This metric captures the movement nature, i.e., whether it is a rhythmic movement (maximal acceleration at the movement reversal) or a discrete movement (zero acceleration at the movement reversal). It is computed by selecting a time window around the movement

reversal, i.e., the second half of the preceding movement (before movement reversal) and the first half of the following movement (after movement reversal). In this time window, the acceleration is extracted and multiplied by the sign of its mean value to force the mean to be positive. Therefore, the maximum acceleration a_{max} (Figure 2) is also positive. If a single peak occurs in this acceleration profile, H is set to 1. If several acceleration peaks occur, H is set to $H = \max(a_{min}/a_{max}, 0)$, where a_{min} is the smallest value in the window between the first and the last acceleration peak (Figure 2). If a_{min} is negative, then H is equal to 0. Since an ideal rhythmic movement is sinusoidal, its acceleration peak occurs at the movement reversal and H is thus equal to 1. An ideal discrete movement has a minimum jerk profile and thus acceleration is equal to zero at movement reversal; the corresponding H is equal to 0. Any post-stroke effect affecting the smoothness of discrete movements will thus be hardly visible with this index, which saturates to 0 for both smooth and non-smooth discrete movements. Consequently, the H index is reported for all tasks, but the statistical analysis mainly focuses on both rhythmic ones.

- **PEAK:** this smoothness metric gives the number of peaks in the movement velocity profile. It was already used by several authors to analyze discrete movements after a stroke [24, 80, 132]. This metric is valuable because it is not sensitive to the movement type; indeed, the number of velocity peaks of both rhythmic and discrete movements is ideally equal to 1 for healthy subjects, disregarding corrective sub-movements which may happen close to movement reversal (Figure 2). Consequently, this metric was independently computed in the zone of movement reversal and in the central phase of the movement. This measure provides an understanding of whether the differences observed between the different movement types and populations (patients vs. control) were due to changes in the final corrective sub-movements or in the central transport phase of the movement. These two zones were separated based on movement amplitude rather than on movement timing: the initial 25% and final 25% of the total movement amplitude were considered as the regions of movement reversal. Therefore, the central phase was taken as the centered 50% of the total movement amplitude (see Figure 2.3 for examples of typical trials).
- **Logarithmic dimensionless jerk (LDJ):** This jerk-based smoothness metric was validated for discrete movements performed by healthy and stroke patients [6]. The main feature of this particular jerk-based smoothness metric is that it is not sensitive to the movement amplitude and duration and does not have a ceiling effect, like the dimensionless jerk [68]:

$$LDJ = \log(D^3/(v_{mean}^2) \int |j(t)|^2 dt),$$

with D being the movement duration and $j(t)$ the movement jerk (Figure 2). The smoother the movement is, the lower the LDJ value. This metric is, nevertheless, sensitive to the movement type. An ideal rhythmic movement corresponds to a portion of the sinus [67], so that the corresponding LDJ should be equal to 4.1. An ideal minimum-jerk discrete movement should have a bell-shaped velocity profile [67] with a LDJ equal to 6. We explored normalizing the LDJ metric according to these expected values (4.1 or 6) to make the metric insensitive to the movement type. We decided to not do this because we observed that this reduces the information that can be retrieved from the LDJ metric. Indeed, reporting a LDJ metric between 4.1 and 6 in a rhythmic task can capture (i) a movement performed with a non-ideal smoothness (i.e., a rhythmic movement with more than one velocity peak) or (ii) a smooth movement performed with a lower harmonicity, i.e., more like a healthy discrete movement. Therefore, the three metrics provide complementary information and must be analyzed in parallel. In particular, the PEAK metric will increase in the case of non-ideal smoothness of movement (particularly during the central movement phase), but not in movements with lower harmonicity.

Importantly, note that both of the smoothness indices we selected (PEAK and LDJ) were developed to measure smoothness without being sensitive to movement speed or amplitude.

All the above computations were performed using Matlab 7.10.0 R2010a (The MathWorks Inc, Natick, MA).

2.2.5 Data Analysis and Statistics

For all trials, the first five movements were excluded from analysis to avoid transient phenomena. In addition, this further excluded the first rhythmic cycles, which might be governed by the discrete primitive (van Mourik and Beek 2004; Howard et al. 2011). Statistics were performed with JMP 10.0.0 software (SAS Institute Inc.).

We first analyzed the learning effect between the three trials for both groups and the lateralization effect between the dominant and non-dominant arms of the control group. Therefore, a mixed model that included the factors "group (patient and control)", "arm (dominant/non-paretic and non-dominant/paretic)", "task (D-T, R-T and R-NT)", "trial", the two-factors interactions and the "participant number" as random effect to take into account the repeated structure of the dataset, was analyzed. The equation of this model is provided in appendix C. It contained 11 variables: the 4 factors, the corresponding 6 two-factors interactions, and the bias. This model was solved using a "Restricted Maximum Likelihood" method to estimate the variance parameters. No learning effect was observed, either in the control or in the patient group, in the sense that no significant effect was found with the factor "trial"

or its interactions in all metrics (all p -values > 0.05). Similarly, no laterality effect was found in the control group, i.e., the interaction "arm - group" was significant in all metrics and the post-hoc Tukey HSD tests did not show a significant difference between the dominant and non-dominant arms in the control group (all p -values > 0.05). Consequently, for the subsequent analyses, the data were simplified by pooling the three trials together, and the dominant and non-dominant arms together in the control group. Therefore, for each task, a single mean value was kept for every metric for the paretic and non-paretic arms in the patient group and only one value per metric and per task in the control group.

We did not perform a 3 (arm) $\times$ 3 (task) analyses on this dataset, as it would have mixed intra- and inter-subject data in the "arm" factor (including the paretic and non-paretic arms of the stroke group, and a single arm from the control group). Therefore, three independent mixed models were performed on the simplified dataset for all the above-mentioned metrics over (i) the paretic side vs. control data, (ii) the non-paretic side vs. control data, and (iii) the paretic side vs. non-paretic side. Each model contained the following effects: the task (D-T, R-T, R-NT), the arm (two among paretic, non-paretic, and control), their interaction, and the participant number that was used as a random effect. Note that the degrees of freedom were different in models (i) and (ii) vs. model (iii) since the later was an intra-subject analysis while the formers were inter-subject analyses. The models were solved using a "Restricted Maximum Likelihood" method to estimate the variance parameters. Post-hoc Tukey HSD test was used to compare the modalities of significant factors. In order to account for the potential increase in type I error due to the multiplicity of tests, the significance level was adjusted with a Bonferroni correction to $p=0.017$ [29].

Classification of the smoothness impairment of patients

To further classify the patients, the movement smoothness performed by the paretic arm of each patient was compared to the healthy control group. The PEAK and LDJ metrics were selected for this analysis. For both metrics, a patient was considered affected for a particular task if the corresponding metric value was above the mean value of the control group plus x standard deviation(s) of the control group value for the same metric. To test sensitivity effects with respect to the threshold being used, x was varied from 0.5 to 2. As such, patients could be classified into several groups according to two different metrics, i.e., patients affected in the R-T task, patients affected in the R-NT task, and patients affected in the D-T task. This analysis was performed first in the PEAK metric computed over the total movement duration, and then in the same metric restricted to the central movement phase. This permitted us to exclude possible sub-movements in the target reaching phase and focus on possible impairments restricted to the central transportation phase, which should be similar across movement types.

2.3 Results

2.3.1 Typical traces and general performances

Figure 2.3 shows typical traces of a healthy subject on the left and a stroke patient on the right for a rhythmic task (R-T, upper row) and for a discrete task (D-T, lower row). The healthy control subject (left column of Figure 2.3) displayed the expected acceleration peak at the movement reversal of rhythmic movements and zero acceleration at the movement reversal during the discrete task; both the rhythmic and discrete movements of the stroke patient were affected (right column of Figure 2.3). However, observing the velocity profiles reveals a fundamental difference in the way the hemiparesis affected rhythmic and discrete movements: while this patient displayed more than one velocity peak per discrete movement, he managed to keep a single peak for the rhythmic movements.

Figure 2.4 (four upper panels) shows the general performances during the three tasks at the population level. In both healthy subjects and patients, discrete movements were performed with a lower velocity than rhythmic movements (task effect paretic vs. control: $F(2,40)=65.5$; paretic vs non-paretic: $F(2,50)=66.7$; and control vs non-paretic: $F(2,40)=120.5$ where all p 's < 0.0001 , and Tukey HSD, $R-T > R-T > D-T$ with all p 's < 0.0001); this is consistent with Fitt's law [18, 57, 156]. The mean amplitudes were 12.7 (SD 0.6) cm in the D-T task, 10.4 cm (SD 1.1) in the R-T task, and 13.4 cm (SD 2.9) during the R-NT task, with no significant differences between the groups (paretic vs non-paretic: $F(1,50)=0.85$, $p=0.35$; paretic vs control: $F(1,20)=0.49$, $p=0.49$; and control vs non-paretic: $F(1,20)=2.9$, $p=0.1$). As expected, dwell times were significantly higher during the discrete task than during both rhythmic tasks (exercise effect in control vs. non-paretic arms ($F(2,40)=58.1$, in paretic vs. control $F(2,40)=13.8$, and paretic vs. non-paretic $F(2,50)=6$ with all p 's < 0.0001 and Tukey HSD $R-T$ vs $D-T$: $p < 0.0001$ and Tukey HSD $R-NT$ vs $D-T$: $p < 0.0001$), which confirms that the tasks were executed as expected, i.e., with longer dwell times during the discrete task. Moreover, the reported dwell time in both rhythmic tasks was around 40ms, i.e. about 3% of the total movement duration, corresponding thus to an ideal sinusoidal movement (see methods).

The D-T task was performed with significantly longer dwell times by the patients with their paretic arm, as compared to their non-paretic arm or to the healthy group (all p 's < 0.0001). This was not observed in the R-T and R-NT tasks.

Furthermore, the D-T task was performed with lower precision by the patients with their paretic arm, as compared to their non-paretic arm or to the healthy group (all p 's < 0.0001). This was again not observed in the R-T task, while this metric was not computed for the R-NT task due to the absence of visual targets (see methods). Note finally that the level of precision was better for the discrete than the rhythmic task in both the control group and the non-paretic arm of patients. The decrease of

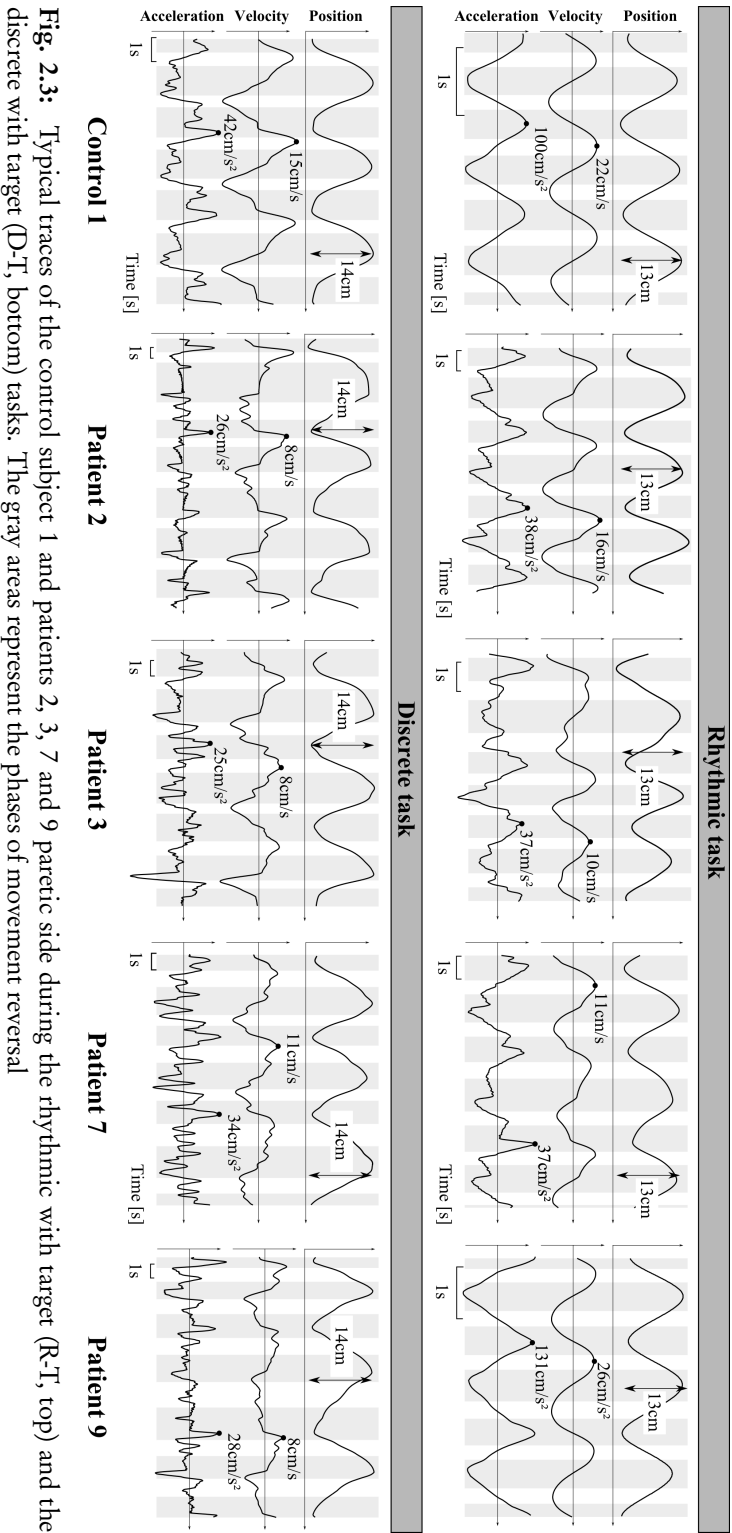


Fig. 2.3: Typical traces of the control subject 1 and patients 2, 3, 7 and 9 paretic side during the rhythmic with target (R-T, top) and the discrete with target (D-T, bottom) tasks. The gray areas represent the phases of movement reversal

precision in the D-T task reported for the patients' paretic arm brought it to the level of performance of the control group in the R-T task, i.e. about 0.7cm.

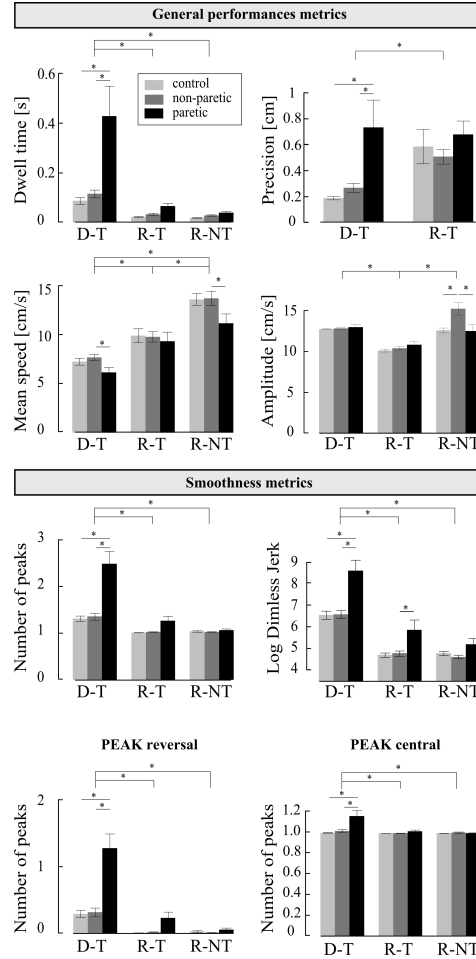


Fig. 2.4: *Top* general performance metrics, i.e., dwell time, precision, mean velocity and movement amplitude. *Bottom* smoothness metrics, i.e., number of peaks, LDJ during the complete movement and number of peaks during the movement reversal and during the central phase of the movement only. These results are reported at the population level for the paretic arms (*black*), the non-paretic arms (*dark gray*) and the control arms (*light gray*) during the three tasks (except for the precision which cannot be computed during the R-NT task since no target was displayed). The *error bars* represent 1 standard error of the mean. The task-specific *horizontal lines with an asterisk* symbol show the cases for which the paretic arm is significantly different from the control and the non-paretic arms. The *upper horizontal lines with an asterisk* highlight when the metrics are significantly different from each other

2.3.2 Stroke spares the smoothness of rhythmic movements

The observation reported above for a single patient - that rhythmic and discrete movements are differentially affected - is confirmed at the population level for both smoothness metrics (Figure 2.4, bottom). First of all, for both measures of smoothness (LDJ and PEAK), movement smoothness was lower for the paretic arm of patients compared to their non-paretic arm and to the arms of age-matched healthy controls. This difference was stronger for discrete movements than for rhythmic movements (interaction between group and tasks, see Table 2.2). In all cases, this interaction indicated that the effect of group was higher in the discrete task than in any of the two rhythmic tasks (Table 2.2). In contrast, movement smoothness of the non-paretic arm appeared to be preserved in stroke patients in all tasks (interaction between group and tasks: PEAK: $F(2,40) = 0.28$, $p = 0.76$; and LDJ: $F(2,40) = 0.69$, $p = 0.51$).

Table 2.2: Group-arm interaction and Tukey HSD of the paretic versus control arms and of the paretic versus non-paretic arms in the PEAK and LDJ metric over the total movement and in both phases of the movement (central and reversal phase)

	Paretic versus control		Paretic versus non-paretic	
	Interaction group-task	Tukey	Interaction group-task	Tukey
PEAK total	$F_{(2,40)} = 17.5$, $p < 0.0001$	D-T: $p < 0.0001$ R-T: $p = 0.68$ R-NT: $p = 1$	$F_{(2,50)} = 14.3$, $p < 0.0001$	D-T: $p < 0.0001$ R-T: $p = 0.63$ R-NT: $p = 0.998$
LDJ total	$F_{(2,40)} = 13.0$, $p < 0.0001$	D-T: $p = 0.0008$ R-T: $p = 0.11$ R-NT: $p = 0.93$	$F_{(2,50)} = 0.69$, $p = 0.006$	D-T: $p < 0.0001$ R-T: $p = 0.01$ R-NT: $p = 0.45$
PEAK central	$F_{(2,40)} = 9.6$, $p = 0.0004$	D-T: $p < 0.0001$ R-T: $p = 0.99$ R-NT: $p = 1$	$F_{(2,50)} = 7.13$, $p = 0.0019$	D-T: $p = 0.0002$ R-T: $p = 0.99$ R-NT: $p = 1$
PEAK reversal	$F_{(2,40)} = 18.3$, $p < 0.0001$	D-T: $p < 0.0001$ R-T: $p = 0.6$ R-NT: $p = 1$	$F_{(2,50)} = 15.1$, $p < 0.0001$	D-T: $p < 0.0001$ R-T: $p = 0.32$ R-NT: $p = 1$

We further investigated whether the above-mentioned effects were due to movement changes during the central part of the movement - which is supposed to be very similar across conditions - or during the reversal phase, i.e., where rhythmic and discrete movements are intrinsically different due to the need for stopping in discrete movements. Consequently, the velocity peak metric was independently computed during the central and reversal phases of the movement (Figure 2.4). As expected, results show that, for the control group, the central phase of the movements was characterized by a single velocity peak. In contrast, the smoothness of the movements during the reversal phase differed as a function of the movement type: virtually no corrective sub-movement was performed during the rhythmic conditions, while about one corrective sub-movement was performed for every three discrete movements. Results further show that the movement smoothness of the patients' paretic arm was altered in both phases of the movement: more than one velocity

peak was often observed during the central movement phase, while some extra velocity peaks were often observed during the reversal phase. Again, the difference in movement smoothness, compared to the healthy and non-paretic arm groups, was larger in the discrete task (statistics are given in Table 2.2). Finally, no difference was found between the non-paretic arm group and the control group, either in the central phase of the movement (factor arm non-paretic vs. control group: PEAK: $F(1,20) = 2.7$, $p = 0.12$) or in the movement reversal phase (factor arm non-paretic vs. control group: PEAK: $F(1,20) = 0.03$, $p = 0.87$). In sum, during discrete movements, the smoothness during both the central and reversal phases of the movements was affected by stroke.

2.3.3 Stroke affects the harmonicity of rhythmic movements

The harmonicity metric measures the movement continuity at movement reversal. If the subject stops, this index is equal to zero while perfect (sinusoidal) reversal would be associated with an index of 1. In agreement with the existing literature [57, 109], our healthy control group showed an harmonicity index close to 1 in both rhythmic tasks and a harmonicity index close to zero in the discrete task (Figure 2.5).

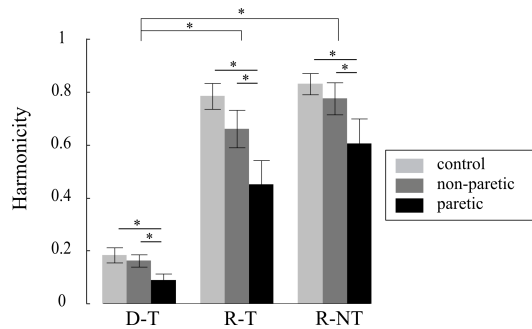


Fig. 2.5: Harmonicity index H of the paretic arms (*black*), the nonparetic arms (*dark gray*) and the control arms (*light gray*) during the three tasks. The error bars represent 1 standard error of the mean. The task-specific horizontal lines with an asterisk symbol show the cases for which the paretic arm is significantly different from the control and the non-paretic arms. The upper horizontal lines with an asterisk highlight when the tasks are significantly different from each other

The trace of patient 7 in Figure 2.3 shows that the rhythmic movements were not continuous (i.e. the harmonicity index during the rhythmic task was reduced); this observation can also be extended to the population level. In both rhythmic tasks, the paretic arm of the patients had a lower harmonicity index than in the control and non-paretic arm groups, although harmonicity index was higher in the R-NT task than in the R-T task. Both factors, task and group, had a significant ef-

fect (control vs. paretic: factor "task": $F(2,40)=100.1$, $p<0.0001$, factor "group": $F(1,20)=9.6$, $p=0.0057$ and no interaction: $F(2,40)=3.7$, $p=0.034$; paretic vs. non-paretic: factor "task" : $F(2,50)=72$, $p<0.0001$ with $R-NT > R-T$, $p=0.02$, $R-T > D-T$, $p<0.0001$; factor "group": $F(1,50)=14.4$, $p=0.0004$ and no interaction: $F(2,50)=1$, $p=0.37$). Again, the non-paretic and healthy arms exhibited similar harmonicity index in both rhythmic tasks (factor "task": $F(2,40) = 142.3$, $p<0.0001$; factor "group": $F(1,20) = 1.80$, $p=0.19$, interaction: $F(2,40) = 0.8$, $p=0.44$).

2.3.4 Absence of visual cueing induces better performances in rhythmic movements

We already illustrated that a lack of visual targets led to a less-degraded harmonicity index (Figure 2.5). Namely, the harmonicity index of the paretic arm was lower than the non-paretic and healthy arms in both rhythmic tasks, but the harmonicity index was higher in the R-NT task than in the R-T task. Moreover, the LDJ metric revealed that the smoothness was not different between the paretic and non-paretic arm in the R-NT task (see LDJ row of Table 2.2), but well in the R-T task. This confirms that rhythmic movements of the paretic arm were less affected when no visual guidance was given to the patient. A similar observation can be reported when comparing the paretic vs. control group, although in this case the significance threshold was not reached in any of the rhythmic tasks.

2.3.5 Hierarchy in the motor impairments

Our data suggest that a discrete task was more affected than a rhythmic task after stroke and also that a visually guided rhythmic movement was more impaired than a non-visually guided rhythmic one. In this section, we report a final analysis on the PEAK and LDJ metrics, which was conducted to classify the patients into groups in order to identify a possible hierarchy in the impairments. To establish this classification, a patient was considered "impaired" in a specific task and according to a given metric if it was larger than 'x' standard deviation(s) above the mean value from the control group (Figure 2.6). The classification displayed in Figure 2.6 (a, c, and e) was built with $x=1$. This analysis highlights the existence of a hierarchy: a patient who was impaired in the R-NT task was also impaired in the R-T and D-T tasks, and a patient who was impaired in an R-T task was also impaired in the D-T task. No patient was only affected in a rhythmic exercise and nobody was only affected in the R-T or R-NT tasks. Finally, some patients were affected in none of the tasks, according to our metrics. These are the patients being displayed out of the Venn diagram (two in Figure 2.6a and c, and three in Figure 2.6e).

To analyze the sensitivity of this hierarchy to the SD threshold (parameter x), this threshold was varied from 0.5 to 2 times the standard deviation (SD) of the control group (Figure 2.6b, d, and f). This analysis revealed that the identification of

the hierarchy was insensitive to the threshold being used. Finally, this analysis was refined by keeping only the number of peaks in the central phase of the movement (Figure 2.6, e and f), which is ideally made of a single velocity peak and disregards all corrective sub-movements close to the reversal zones; similar results were obtained. In this case, eight patients were identified as affected in the D-T task, among which only one was affected in the R-NT task.

2.4 Discussion

The objective of the present study was to quantify the level of impairment in producing visually guided discrete, visually guided rhythmic, and non-visually guided rhythmic movements with the upper limbs after a stroke. We found that: (i) stroke preferentially affects the smoothness of discrete movements, not rhythmic movements; (ii) stroke affects the harmonicity of rhythmic movements; and (iii) patients who were affected in producing rhythmic movements were all affected in producing discrete movements, but not the other way around, i.e., there was a hierarchy of impairment: a patient affected in a rhythmic task was always affected in the discrete task, and a patient affected in a non-visually guided rhythmic movement was always affected in the visually guided rhythmic movement.

2.4.1 Both rhythmic and discrete movements are affected by stroke, but not to the same extent

Results showed that the movement smoothness of the patients' paretic arm was altered for both rhythmic and discrete movement production. However, the difference in movement smoothness compared to the healthy and non-paretic arm was larger in the discrete task than in the rhythmic one. This was, for instance, quantified with the LDJ metric. This metric was reported to be insensitive to the movement amplitude or timing, but sensitive to the movement type: a perfect rhythmic movement should have a sinusoidal profile with a LDJ of 4.1, and a perfect discrete movement should display a bell-shaped velocity profile with a LDJ of 6. This is critical for the performance analysis during the rhythmic task. Indeed, as explained in the methods, a LDJ metric between 4.1 and 6 during the production of rhythmic movements can be due either to a decreased smoothness or to a lower harmonicity (i.e., a movement with longer dwell-time, like a discrete one). This last case was observed for the paretic arm in both rhythmic conditions, where the amount of velocity peaks was not different across the groups in both the central and reversal portions of movements. Therefore, the reported increased LDJ value in the paretic arms during both rhythmic tasks (reaching significance only for the R-T task) can only be due to a lower harmonicity and not to a decreased smoothness. This result was confirmed by the analysis of the harmonicity index: rhythmic movements with the paretic arm were produced with

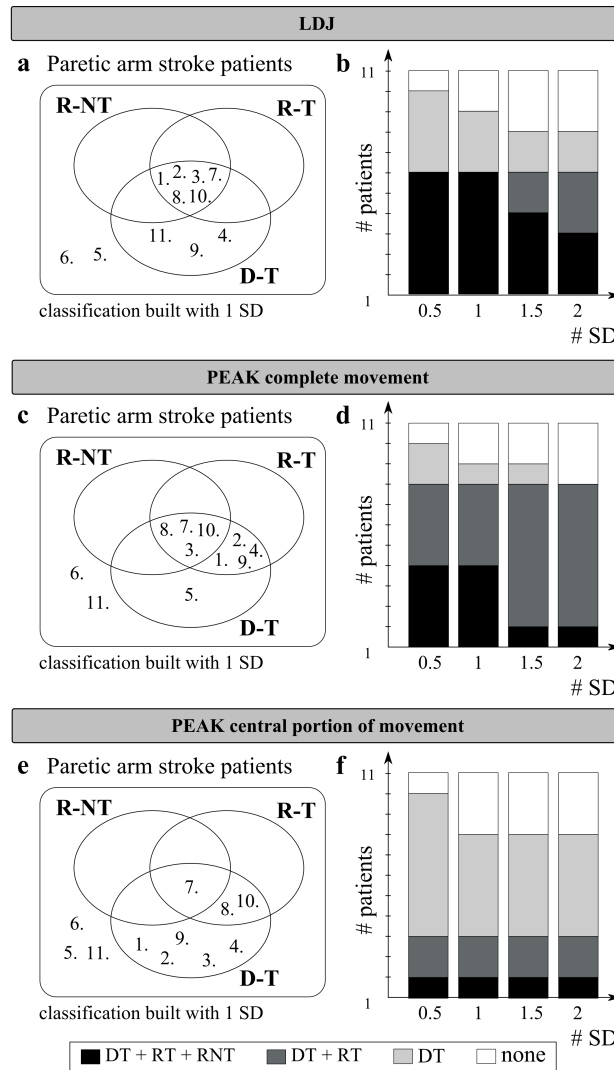


Fig. 2.6: Classification of the patients according to their impairments in the R-NT, R-T and D-T task computed from the LDJ and PEAK metric during the complete movement (a-d) and during the central phase of the movement only (e and f). Panels "a", "c" and "e" show a Venn diagram of the classification with a threshold set to 1 SD of the control group. Panels "b", "d" and "f" show the same patient distribution by varying the classification threshold from 0.5 to 2 SD

a decreased harmonicity with respect to the control group. In sum, discrete movements were affected in the sense that the patients performed them in a less smooth way, i.e. with more velocity peaks, while rhythmic movements were affected in the sense that the patients performed them in a less harmonic way, i.e., resembling the

discrete movements of the control group.

2.4.2 Post-stroke behavior suggests that discrete and rhythmic movements form two different primitives

We reported an impairment hierarchy, namely that the rhythmic task was not affected for some patients being affected in the discrete task, and that this impairment was visible in both the central transportation and reversal phases of the movement. This is in line with the theory postulating that rhythmic and discrete movements are, at least partially, controlled by distinct neural circuitries [18, 31, 53, 57, 67, 69–71, 74, 100, 144, 145, 149, 150, 155, 172]. A discrete movement is not a truncated rhythmic movement, i.e., discrete movements are not based on the use of the rhythmic movement primitive. Moreover, if rhythmic movements were based on a concatenation of discrete movements, rhythmic movements should be affected in the central phase of the movement, similar to the discrete task. Indeed, if both movements shared the same neural representation, both movements should be equally affected [119]. This suggests that discrete and rhythmic movements form two different primitives, despite the identified hierarchy in post-stroke performance.

The degradation hierarchy in performing discrete and rhythmic movements is not unique to stroke patients. For instance, cerebellar patients are impaired in producing discrete movements but not rhythmic movements [150]. This demonstrates the prominent role of the cerebellum in representing the temporal goal of discrete movements [150, 151]. The temporal properties of rhythmic movements are, however, supposed to be emergent. Once the rhythmic movement is initiated, the performance is probably controlled by other parameters governing other movement constraints, such as minimizing the jerk or spatial noise.

Together, these results support the results showing that discrete and rhythmic movements recruit different cortical and cerebellar networks during their execution [145]. This reinforces the consensus claiming that rhythmic and discrete movements form two fundamental and distinct motor primitives.

On top of that, planning is an important step in goal-oriented movements, both discrete and rhythmic. Planning precedes execution, and requires the assessment of the movement (energetic) cost in order to select an appropriate control policy [146]. This process likely takes place - at least partly - in the basal ganglia, an area being severely degraded in Parkinson's disease [111]. Patients suffering from Parkinson's disease display impairments in intensive and inter-segment coordinative aspects of both discrete and rhythmic movements, leading respectively to e.g. lower velocity peaks and decreased accuracy [101]. This shows that, despite they form different motor primitives, discrete and rhythmic movements might also recruit similar mechanisms, for instance associated to movement planning.

2.4.3 Non-visually guided rhythmic movements are less affected than visually guided rhythmic movements

The non-visually guided rhythmic movements were less affected than the visually guided ones, so that the non-visually guided condition was the least affected among the three conditions tested. Although the number of velocity peaks was not significantly different between the paretic arms of the patients and the arms of control subjects in both rhythmic conditions, we observed a higher harmonicity of the paretic arm during the R-NT task than during the R-T task. Moreover, all patients but one (patient 7) who were affected in the R-T and/or D-T tasks performed the R-NT task like the healthy control group, at least regarding the PEAK metric during the central phase of the movement.

Executing a rhythmic movement under visual guidance recruits an extended visuomotor cortical network [5, 33, 34, 54, 61], while this activation decreases when visual feedback is removed [136]. Any potential damage in this pathway seems to preserve the capacity to execute non-visually guided rhythmic movement with limited kinematic impairments.

2.4.4 Impairment hierarchy shows a possible role for spinal oscillators in rhythmic upper limb movements

The observation that rhythmic arm movements recruit fewer cortical areas could be connected with the principle of central pattern generators (CPGs). CPGs were identified as neural oscillators capable of producing a periodic output while receiving no periodic input [17, 73, 109, 147]. Locomotor CPGs are located - at least partly - at the spinal level, as revealed by studies in nonprimates and humans [26, 27, 37, 41, 82, 161]. More recently, the concept of CPGs has also been extended to rhythmic movements in the upper extremities [36, 137, 180, 184, 185], suggesting the presence of similar lower-level, i.e., spinal, circuitries for voluntary rhythmic arm movements.

Our data revealed that the smoothness of rhythmic movements is preserved to a larger extent than discrete movements after a stroke, possibly associated with the fact that rhythmic arm movements might be partly governed by low-level CPGs. As the spinal contribution to rhythmic arm movement would remain accessible after a stroke [186], smooth rhythmic movements - once initiated - could be performed mainly by relying on those undamaged low-level circuitries. In contrast, discrete movements require the recruitment of a broad cortical and cerebellar network, spanning over areas silent during rhythmic movement production [145].

This hierarchy of impairment could also account for the reported findings on asymmetric transfer between rhythmic and discrete movements [74]. In a motor learning task, these authors reported that rhythmic movements training do not transfer to discrete movements, while in contrast discrete movements training does transfer,

as least partially. Again, this suggests that the cortical substrate involved in discrete motor learning includes the one recruited during rhythmic movements, but not the other way around.

2.4.5 Limitations

In this study, we compared two naturally-induced movement types (rhythmic vs. discrete movements) by asking subjects to perform the same task but with different IDs. In particular, the discrete movement was induced by making the task "more difficult," i.e., forcing the subject to stop on the targets, although this was not explicitly requested.

The main limitation of this study is, consequently, that we did not add an additional discrete task with the same ID as during the rhythmic task, i.e. by explicitly asking the participants to stop on the targets. Our intention was rather to induce rhythmic and discrete movements in an "ecological" (or implicit) way, as happens in daily life contexts. Participants produced rhythmic and discrete movements, although they received the exact same instructions for both tasks. Forcing discrete movements in a task having an ID calling for rhythmic movements would have broken this implicit context and strongly impacted the instructions to be delivered. In particular, we did not have to ask the participants to spend a specific duration on the targets (the so-called dwell time): this was, again, naturally happening due to the movement strategy they selected.

Interestingly, we reported an impairment in the D-T task in both the central and reversal phases of the movement; this suggests that this type of movement requires a planning step that embraces the whole movement duration [5, 54], and that this whole planning process is affected by a stroke insult. However, whether these results would be observed with discrete movements produced with the explicit instruction to stop on the targets (i.e., potentially with the same ID as our rhythmic movements) or without visual targets is still an open question.

Finally, our protocol was made so that there were two simultaneous changes in the design of sequences: half of the participants performed the sequence with the reversed order of conditions and arms with respect to the other half. It would have been preferable to fully randomize the sequence of conditions and arms for each participant. Indeed, with this sequencing, neither the arm sequence effect nor the condition order effect can be studied, as they may cancel each other out.

2.4.6 Potential therapeutic interest

Currently, classical upper-limb therapy focuses on intensive, task-specific, and context-specific movement training, which is composed of mainly discrete movements [96].

Our data confirms that these movements are the most affected ones and confirms the importance of intensively training these movements after stroke.

However, if rhythmic movements are affected by a stroke - as we report in the present study for a majority of our patients - they should also be included in the post-stroke therapy, in order to reach proper motor recovery of rhythmic movements themselves. Several complex daily life movements are based on the combination of rhythmic and discrete movements, like handwriting, scrabbling, hammering, knitting, sweeping a table, and playing the piano [154]. Recovering such coordinated movements after a stroke would require the recovery of the combined execution of the independent motor primitives. Indeed, since rhythmic and discrete movements are - at least partially - controlled by independent neural circuitries and form two different primitives, both need to be trained to recover a complete motor repertoire [59, 71, 74, 145, 154].

Moreover, assuming that rhythmic movements are less affected than discrete ones, a progression in the exercises could be proposed from rhythmic to discrete movements. It might be feasible to build on the fact that rhythmic movements are lower in hierarchy and hence are more frequently intact. If so, discrete elements could be combined with rhythmic movements, leveraging the execution of movements with a higher degree of impairment to those which are performed more stably. Experimental paradigms including both movement types, like those performed by Sternad et al. (2000) for single-joint movements or Sternad and Dean (2003) for two-joint movements, are viable candidates [154, 155].

Finally, several previous studies showed that rhythmic arm cycling reduces spasticity and improves the range of motion and strength [8, 39, 188, 189]. Moreover, bilateral arm training with rhythmic auditory cueing [104, 178] was shown to improve motor functions beyond those being trained, as captured by the improvement of several functional post-stroke assessment scales (FMA, Wolf Motor Function Test, daily live function, strength, and range of motion). This tends to suggest that performing unilateral rhythmic movements improves the general upper-limb performances after stroke.

In conclusion, the present chapter studied rhythmic versus discrete movements in stroke patients to provide new insights on the neural organization of those two fundamental movements. These findings further suggest training rhythmic movements in addition to discrete movements during therapy to maximize post-stroke motor recovery.

Performance-based robotic assistance during rhythmic arm exercises

3

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Article in open Access distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>) [99].

In the previous chapter, we came to the conclusion that rhythmic movement training might be interesting to offer to stroke patients. This chapter presents a new robotic assistance to specifically train rhythmic movements. Thanks to the periodic nature of these movements, quasi real-time performance-based assistance can be provided to the patients. This means that when the patient improves his/her performances, the assistance will automatically decrease and vice versa.

3.1 Background

Rhythmic and discrete movements have recently been recognized as two of the most fundamental units of the upper- [69] and lower-limb [70] motor repertoire. Rhythmic movements capture periodic movements like hammering or scratching, while discrete movements capture movements between a succession of postures with zero velocity and acceleration, like reaching and pointing [55, 67]. These two fundamental motor primitives are controlled by distinct neural circuitries, at least partially [18, 31, 57, 67, 71, 74, 145, 149, 154, 156, 172]. For example, previous research with healthy subjects showed that (i) discrete movements require more cortical activity than rhythmic ones [145], and (ii) no learning transfer occurs from rhythmic

to discrete movements and only a little transfer occurs from discrete to rhythmic movements when they are executed in altered visual or haptic conditions [71, 74].

After a stroke, both rhythmic and discrete movements can be impaired [38, 50, 52, 56, 68, 88, 132, 148, 185]. Recently, we compared the performance in executing both movements in the same stroke population. As a main conclusion, we found that rhythmic arm movements are less affected than discrete ones. In particular, stroke preserved the smoothness of rhythmic movements so that fewer submovements were identified than in the discrete counterparts [98]. However, rhythmic movements were impaired compared to healthy subjects. Stroke patients decelerated more than healthy subjects at the movement reversal, and some patients displayed a larger amount of submovements.

If rhythmic and discrete movements are two distinct primitives, they deserve specific and differentiated training to permit the full recovery of the complete motor repertoire. This is a necessary condition to recover autonomy life activities requiring a combination of rhythmic and discrete movements (such as wiping a table or playing the piano [156]).

Most post-stroke therapies tend to focus on functional and thus mainly discrete movements [91, 93, 173], although some previous contributions did focus on upper-limb rhythmic movement training. Interestingly, they all tended to display an improvement in motor skills [20, 39, 65, 104, 158, 178, 179]. For instance, [65] and [20] highlighted that the intensity of the training is critical to enhance motor skills. In [179], the authors compared bilateral arm training with auditory cueing (BATRAC) to dose-matched therapeutic exercises and concluded that none was superior to the other, although the adaptations in brain activation were greater after BATRAC. Whether this result is due to the rhythmic nature of the movement, its bimanual nature, the auditory cueing, or a combination of these features, is however difficult to establish, since these are closely intertwined in BATRAC.

The current state-of-art of rhythmic upper-limb movement therapy calls thus for the development of post-stroke therapies tailored to unilateral rhythmic movement training, in order to study their exact effect on motor skills. The development of such a therapy is presented in this chapter.

Robotic devices are particularly suited for implementing post-stroke therapies, with a specific focus on movement intensity. Rehabilitation robots enable patients to practice well-specified motor actions and can deliver an appropriate amount of assistance to help patients in improving their motor behavior [19, 78, 88, 94, 105, 106, 108, 177, 183]. Motor performance can be computed in real-time by the robot controller, allowing for continuous adaptation of the type and amount of assistance. The patient only receives the necessary support and is prevented from slacking [127,

183]. In the literature, this is often referred to as the "slacking hypothesis," which suggests that too much assistance will cause a progressive decrease in patient effort to accomplish a desired task and reduce motor recovery. This assistance principle is also called "assistance as needed" and has progressively emerged as a hallmark of successful robot-assisted therapies [8, 108, 127, 183]. This principle lies also at the core of the present contribution.

Most upper-limb robot-assisted therapies are designed for discrete movement training and implement the assist-as-needed principle through different strategies. One type of strategy delivers assistance proportional to the trajectory error with respect to a predefined trajectory [47, 49, 58, 89, 106, 107, 141]. Another assistance approach relies on dynamical systems and adapts the assistance parameters as a function of the patient performance [89]. Other approaches tune the amount of assistance across sessions as a function of the performance during the preceding session [79, 89]. Another method [58] performs an online adaptation of the amount of support depending on the activity (for a survey, see [13, 108]).

In contrast with these approaches, a rhythmic movement therapy should exploit the cyclic nature of the movement to anticipate the future trajectory based on previous cycles. This can be achieved by using adaptive oscillators [130]. These mathematical tools are particularly suited to track the main features of a typical rhythmic movement (like amplitude and frequency). This continuous assessment allows the robot to constantly seek to improve movement features with the appropriate amount and type of assistance. Moreover, this approach naturally allows for trajectory-free assistance algorithms so that the therapist does not have to specify an arbitrary target trajectory for the patient to follow. The patient receives assistance to improve the impacted movement features, but is left free to produce any rhythmic trajectory.

Our previous work already paved the way in using adaptive oscillators to deliver trajectory-free assistance for upper- [139] and lower-limb [44, 135] rhythmic movements. These contributions focused on movement assistance for healthy subjects, showing evidence of decreases in metabolic consumption when the assistance was switched on. The present study is the first to propose a metric-based assistance method for patients with motor disorders, with emphasis on the potential to assist different rhythmic movement features as a function of the patient needs.

This chapter outlines the performance-based assistance method and its mathematical foundations in details. The method was validated with data from simulations and a pilot study with two stroke patients with upper-limb impairments is also reported. The proposed performance-based assistance method can (i) enhance motor-performance, (ii) give appropriate assistance according to patient performance, and (iii) maintain active patient participation in the task so that no slacking effect occurs.

3.2 Methods

The main interest of the developed method is that it can independently assist different movement features, only if needed. In particular, the method implements parallel strategies to assist the patient in improving performance regarding movement smoothness, velocity, and amplitude. Therefore, the method requires measuring (Figure 3.1-A) and quantifying (Figure 3.1-B) the amplitude, velocity, and smoothness features of patient movement in real-time in order to assess the corresponding performance. The method must also compute and deliver the appropriate amount of assistance in amplitude, velocity, and/or smoothness as a function of the performance (Figure 3.1-C).

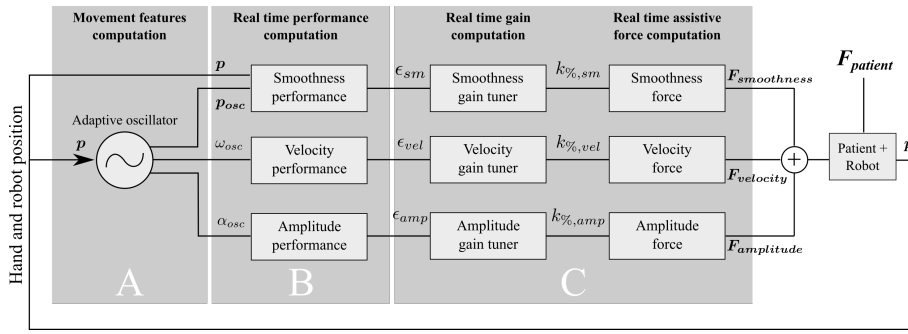


Fig. 3.1: Methodology. Outline of the overall control strategy of the performance-based assistance. First, the movement features are computed by the adaptive oscillator (a) and serve as input to compute the real-time performance in smoothness, velocity, and amplitude (b). These features are then used to compute the gains to tune the level of the assistance forces in smoothness, velocity, and amplitude (c). These three forces are eventually summed up and delivered to the patient

The most comprehensible way to develop the proposed assistance method requires focusing on a simple rhythmic movement. This movement is a rhythmic circular trajectory executed with the upper-limb. It advantageously combines different desirable features: it is harmonic by essence, involves no contact with the environment, and requires the coordination of several degrees of freedom. The parameters shaping this movement are the amplitude, offset (i.e. position of the circle center), and rotational frequency. The desired movement kinematics are characterized by the vectorial position and velocity in Cartesian space, as a function of time:

$$\mathbf{p}_d = \begin{pmatrix} x_d \\ y_d \end{pmatrix} = \begin{pmatrix} \varphi_{x,d} + \alpha_d \sin \omega_d t \\ \varphi_{y,d} - \alpha_d \cos \omega_d t \end{pmatrix} \quad (3.1)$$

$$\dot{\mathbf{p}}_d = \begin{pmatrix} \dot{x}_d \\ \dot{y}_d \end{pmatrix} = \begin{pmatrix} \alpha_d \omega_d \cos \omega_d t \\ \alpha_d \omega_d \sin \omega_d t \end{pmatrix} \quad (3.2)$$

where α_d is the movement amplitude, ω_d is the angular frequency and $\varphi_{x,d}$ and $\varphi_{y,d}$ are the offsets along the x - and y -axes, respectively.

3.2.1 Real-time measurement of the movement features

Adaptive oscillators are particularly suited for estimating the real-time movement parameters of a rhythmic movement [130, 131, 134, 138]. From the ideal movement in (1), an adaptive oscillator can learn an equivalent movement captured by the following model:

$$\mathbf{p}_{osc} = \begin{pmatrix} x_{osc} \\ y_{osc} \end{pmatrix} = \begin{pmatrix} \varphi_{x,osc} + \alpha_{osc} \sin \phi_{osc} \\ \varphi_{y,osc} - \alpha_{osc} \cos \phi_{osc} \end{pmatrix} \quad (3.3)$$

where α_{osc} is the learned amplitude, ϕ_{osc} is the learned phase (the time integral of the learned angular velocity ω_{osc}), and $\varphi_{x,osc}$ and $\varphi_{y,osc}$ are the learned offsets.

These variables are the state variables of the adaptive oscillator. Their learning dynamics are governed by:

$$\dot{\phi}_{osc} = \omega_{osc} + \nu_\phi \left(F_x \frac{\cos \phi_{osc}}{\alpha_{osc}} + F_y \frac{\sin \phi_{osc}}{\alpha_{osc}} \right) \quad (3.4)$$

$$\dot{\omega}_{osc} = \nu_\omega \left(F_x \frac{\cos \phi_{osc}}{\alpha_{osc}} + F_y \frac{\sin \phi_{osc}}{\alpha_{osc}} \right) \quad (3.5)$$

$$\dot{\alpha}_{osc} = \eta_\varphi (F_x \sin \phi_{osc} - F_y \cos \phi_{osc}) \quad (3.6)$$

$$\dot{\varphi}_{osc,x} = \eta_\varphi F_x \quad (3.7)$$

$$\dot{\varphi}_{osc,y} = \eta_\varphi F_y \quad (3.8)$$

where $F_x = x - x_{osc}$ and $F_y = y - y_{osc}$ are the error signals that capture the difference between the oscillator input (x and y , i.e. either the simulated or real 2D hand position reported in the experiments) and the estimated position output.

By properly tuning the learning gains ν_ϕ , ν_ω , and η_φ , the output signal will synchronize with the input signal after only a few cycles while learning the actual input features in the internal state variables. The learning dynamics can be finely tuned by adapting the learning gains [134]. If the input signal contains higher harmonics in its frequency spectrum, the oscillator output can be considered as a "smoothed"

or filtered version of the input, although both will be phase-synched on average. In sum, this adaptive oscillator provides real-time estimates of the parameters of a time-varying periodic signal while filtering this signal in its output.

The method can also provide a smooth estimate of the signal derivatives [134]. For instance, the estimate of the signal's first derivative is obtained by analytical time-differentiation of the augmented phase oscillator (3.3):

$$\dot{\mathbf{p}}_{osc} = \begin{pmatrix} \dot{x}_{osc} \\ \dot{y}_{osc} \end{pmatrix} = \begin{pmatrix} \alpha_{osc}\omega_{osc} \cos \phi_{osc} \\ \alpha_{osc}\omega_{osc} \sin \phi_{osc} \end{pmatrix} \quad (3.9)$$

More details about the mathematical foundations of these adaptive oscillators can be found elsewhere [44, 130].

The adaptive oscillator is used for two different purposes throughout the proposed therapy: for measuring the initial abilities of the patient through an initialization phase and for measuring the real-time performance (smoothness, velocity, and amplitude) of the patient during the robot-assisted rhythmic exercises (Figure 3.1-A). The second item is further detailed in the next section.

3.2.2 Real-time performance computation

Real-time smoothness metric

Assessing the smoothness of a discrete movement after completion (off-line) has been the topic of many former studies. The challenge lies in determining a dimensionless metric that is independent of the movement amplitude and duration while having a univocal response to the motion characteristics: the smoothness has to monotonically decrease when the amount of submovements and the inter-submovement duration decrease [6, 7]. Several metrics were proposed and analyzed to quantify the movement smoothness after the completion of the whole movement, such that the normalized mean absolute jerk, number of peaks in the velocity profile, logarithmic dimensionless jerk, spectral arc length, and speed arc length [6, 68, 132, 133].

Real-time measurement of rhythmic movement smoothness is required to continuously adapt the assistance. The metrics mentioned above are thus ineligible since they can only provide a smoothness estimate after the completion of one or several movement cycles. Hence, we propose measuring the smoothness performance in continuous-time by comparing the actual velocity of the patient, $\dot{x}_{pat}$ and $\dot{y}_{pat}$, with the desired velocity computed by the adaptive oscillator (3.9); i.e., the filtered version of the patient actual velocity. This error is normalized with respect to the angular velocity (the product of ω_{osc} and α_{osc}) to obtain a dimensionless metric:

$$\eta = \frac{\sqrt{(\dot{x}_{osc} - \dot{x}_{pat})^2 + (\dot{y}_{osc} - \dot{y}_{pat})^2}}{\omega_{osc}\alpha_{osc}} \quad (3.10)$$

Next, we compute the numerical differentiation of this velocity error signal and normalize it again with the angular velocity:

$$\xi = \frac{d\eta}{dt} \frac{1}{\omega_{osc}} \quad (3.11)$$

Consequently, if a patient smoothly accelerates or decelerates, this dimensionless differentiated velocity error ξ will stay bounded. Finally, the absolute value of ξ is low-pass filtered to obtain a quasi-real-time smoothness measurement. The time constant (and bandwidth) of this filter is proportional to ω_{osc} , which normalizes the filter response with respect to the movement frequency:

$$\dot{\epsilon}_{sm} = a\omega_{osc}(|\xi| - \epsilon_{sm}) \quad (3.12)$$

In (3.12), a is a constant gain that tunes the frequency-dependent time constant of the filter. If the movement is performed as an ideal circle of constant tangential velocity, η , ξ , and thus ϵ_{sm} will converge towards 0. Moreover, a circular movement performed with a constant acceleration will cause ϵ_{sm} to converge towards 0 since the velocity error η will reach a plateau. The more fluctuations there are in the velocity error, the higher ϵ_{sm} is.

Real-time velocity error

The real-time velocity error is simply obtained from the difference between the desired movement frequency and the actual one estimated by the adaptive oscillator:

$$\epsilon_{vel} = \omega_d - \omega_{osc} \quad (3.13)$$

Real-time amplitude error

Similarly to the real-time velocity error, the real-time amplitude error is the difference between the estimated amplitude of the circles drawn by the patient, α_{osc} , and the desired amplitude, α_d :

$$\epsilon_{amp} = \alpha_d - \alpha_{osc} \quad (3.14)$$

3.2.3 Performance-based assistance forces

The estimates of different movement features allow for three types of assist-as-needed forces to be delivered to the patient. "Smoothness assistance" is delivered if the per-

formed movements are detected to be jerky and deviate too much from the ideal movement given by (3.1). "Velocity assistance" is delivered if the performed movements are too slow, which is determined by the detected movement tangential velocity (the product of the movement frequency ω_{osc} and amplitude α_{osc}) being too far below the desired one $\alpha_d \omega_d$. "Amplitude assistance" is delivered if the performed movements are too small with detected movement amplitude α_{osc} too far below the desired one α_d . Since the types of assistance are managed by parallel algorithms, they can occur simultaneously (Figure 3.1-C):

$$\mathbf{F}_{robot} = \mathbf{F}_{smoothness} + \mathbf{F}_{velocity} + \mathbf{F}_{amplitude} \quad (3.15)$$

where $\mathbf{F}_{robot}$ is the total assistance force being delivered by the robot.

Smoothness assistance

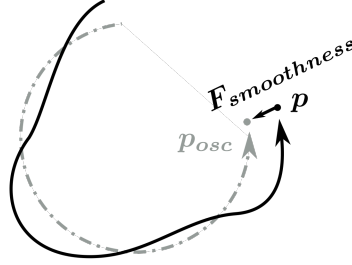
Smoothness assistance is provided by a virtual damped spring between the current estimated position provided by the adaptive oscillator and the actual position of the patient (Figure 3.2-A). This type of assistance guides the patient hand to a "smoothed version" of its own movement since the adaptive oscillator synchronizes to the input while filtering out the frequency content from its main harmonic. The oscillator neither lags behind nor leads the patient hand on average since it is phase-synched to it. Accordingly, the force applied to the patient hand ($\mathbf{F}_{smoothness}$) is equal to:

$$\mathbf{F}_{smoothness} = k_{sm}(\mathbf{p}_{osc} - \mathbf{p}_{pat}) + c(\dot{\mathbf{p}}_{osc} - \dot{\mathbf{p}}_{pat}) \quad (3.16)$$

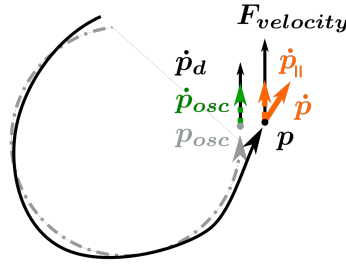
where k_{sm} is the adaptive stiffness of the spring and c is the damping coefficient. To render the behavior of a spring with critical damping, $c = 2\sqrt{mk_{sm}}$ (where m is the equivalent virtual mass of the robot, see Section 'Validation with experimental data'). In (B.7), $\mathbf{p}_{pat}$ and $\dot{\mathbf{p}}_{pat}$ denote the measured vectorial position and velocity of the patient hand, respectively.

Due to the adaptive nature of the oscillator used to compute the movement features, $\mathbf{p}_{osc}$ and $\dot{\mathbf{p}}_{osc}$ constantly adapt to the movement being performed by the patient. Therefore, the smoothness assistance should equally accelerate and decelerate the patient hand during steady-state behavior. Said differently, it should provide no positive mechanical work to the patient on average. In sum, the smoothness assistance helps in making a smoother movement but does not directly make it larger or faster.

A. Smoothness assistance



B. Velocity assistance



C. Amplitude assistance

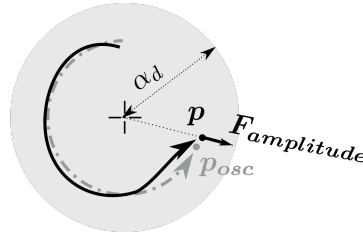


Fig. 3.2: Assistance forces. The three assistance forces that can be provided to the patient to enhance the movement features are presented in the three panels. **a** The smoothness assistance attracts the patient to the smooth position produced by the adaptive oscillator, **b** the velocity assistance tangentially supports the patient to reach the desired velocity, and **c** the amplitude assistance is a radial force towards the desired amplitude

Velocity assistance

If the patient is not able to perform the desired movement at the desired frequency, velocity assistance can be provided. This assistance is implemented through a force that is tangential to the desired velocity profile:

$$\mathbf{F}_{velocity} = k_{vel}(\dot{\mathbf{p}}_{d\parallel} - \dot{\mathbf{p}}_{\parallel}) \quad (3.17)$$

if $|\dot{\mathbf{p}}_{d\parallel}| > |\dot{\mathbf{p}}_{\parallel}|$; otherwise, $\mathbf{F}_{velocity} = 0$. k_{vel} denotes the adaptive gain (Figure 3.2-B), $\dot{\mathbf{p}}_{\parallel}$ is the orthogonal projection of $\dot{\mathbf{p}}_{pat}$ on $\dot{\mathbf{p}}_{d\parallel}$, and $\dot{\mathbf{p}}_{d\parallel}$ is the desired velocity vector, which is tangential to the ideal circle being learned by the adaptive oscillator:

$$\dot{\mathbf{p}}_{\parallel} = (\dot{\mathbf{p}}_{pat} \cdot \mathbf{e}_{\parallel}) \cdot \mathbf{e}_{\parallel} \quad (3.18)$$

$$\dot{\mathbf{p}}_{d\parallel} = v_d \mathbf{e}_{\parallel} \quad (3.19)$$

where $v_d = \omega_d \alpha_d$ and

$$\mathbf{e}_{\parallel} = \frac{\dot{\mathbf{p}}_{osc}}{\|\dot{\mathbf{p}}_{osc}\|}. \quad (3.20)$$

In sum, this assistance provides a smooth longitudinal force if the patient's tangential velocity is below a desired threshold.

Amplitude assistance

Finally, if the amplitude of the patient movement (captured by the adaptive oscillator state variable α_{osc}) is below the desired amplitude, a radial force is provided by the robot to encourage larger movements. Therefore, if the actual position of the patient is inside the minimal amplitude circle ($|\alpha_{pat}| < |\alpha_{d\perp}|$), assistance is delivered through a force:

$$\mathbf{F}_{amplitude} = k_{amp}(\alpha_{d\perp} - \alpha_{pat}) \quad (3.21)$$

Otherwise, $\mathbf{F}_{amplitude} = 0$. In (3.21), α_{pat} is the vector between the center of the circle $\varphi_{osc} = (\varphi_{x,osc}, \varphi_{y,osc})$ and the actual position of the patient, $\alpha_{d\perp}$ is the vector from the center of the circle towards the actual position of the adaptive oscillator (with length α_d), and k_{amp} is the adaptive gain (Figure 3.2-C). In mathematical terms,

$$\alpha_{d\perp} = \alpha_d \mathbf{e}_{\perp}, \quad (3.22)$$

$$\alpha_{pat} = (\mathbf{p}_{pat} - \varphi_{osc}) \quad (3.23)$$

and

$$\mathbf{e}_{\perp} = \frac{\mathbf{p}_{pat} - \varphi_{osc}}{\|\mathbf{p}_{pat} - \varphi_{osc}\|}. \quad (3.24)$$

Gain tuners

To prevent the patients from slacking [183] and to mimic the way a physical therapist would help a patient during an exercise, the levels of assistance have to evolve as a function of the real-time patient performance. If a performance metric is low, the gain of the corresponding assistance has to increase. If the performance improves, the gain should decrease in order to encourage the patient to stay active. Three parallel low-pass filters are thus used to tune the three gains of the assistance forces: k_{sm} (3.16), k_{vel} (3.17), and k_{amp} (3.21); see Figure 3.3. They dynamically evolve between 0 (no assistance if the performance is good) and a maximum value (if the performance is poor) through a scaling factor $k_{\%,metric} \in [0, 1]$, such that $k_{metric} = k_{\%,metric} k_{max,metric}$. The input of these three filters are the corresponding ϵ_{metric} : the performance indices ϵ_{sm} (3.12), ϵ_{vel} (3.13), and ϵ_{amp} (3.14). $\epsilon_{min,metric}$ is the minimum error tolerated before $k_{\%,metric}$ increases, and $\epsilon_{max,metric}$ is the maximal error that causes $k_{\%,metric}$ to saturate to 1. The time constant of these filters is set to τ_g seconds.

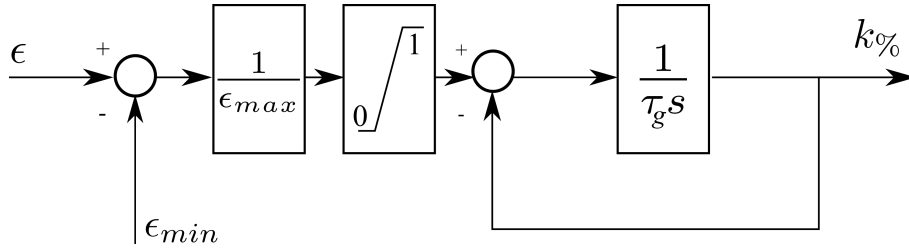


Fig. 3.3: Performance-based gain tuners: Low-pass filters tune the amount of assistance $k_{\%}$ delivered to the patient according to the corresponding performance ϵ with a time constant of τ_g seconds.

3.2.4 Validation with simulated data

Before validating the performance-based assistance with patient data, the adaptive oscillator, smoothness metric, and performance-based assistance were validated with simulated jerky circular movements. These unideal rhythmic signals were generated by augmenting a smooth rhythmic circular movement (similar to (3.1)) with lateral and longitudinal errors of time-varying amplitude and frequency captured by:

$$\alpha_{jerky} = \bar{\alpha}(1 + \delta_{lat} \sin(\omega_{lat}t)), \quad (3.25)$$

$$\omega_{jerky} = \bar{\omega}(1 + \delta_{long} \cos(\omega_{long}t)), \quad (3.26)$$

$$\phi_{jerky} = \int \omega_{jerky} dt \quad (3.27)$$

$\bar{\alpha}$ and $\bar{\omega}$ are the mean amplitude and frequency of the simulated jerky movement, while ω_{lat} and ω_{long} capture the frequency of the lateral errors and longitudinal errors, and δ_{lat} and δ_{long} capture the amplitude of the lateral and longitudinal errors, respectively (Figure 3.6, top).

The longitudinal velocity v_{long} of the simulated jerky movement with longitudinal errors is equal to:

$$v_{long} = \bar{\alpha}\bar{\omega}[1 + \delta_{long} \cos(\omega_{long}t)] \quad (3.28)$$

which is obtained by time-differentiating (3.1) with $\phi_d = \phi_{jerky}$ and $\alpha_d = \alpha_{jerky}$. By varying δ_{long} , the longitudinal velocity error varies proportionally to the mean longitudinal velocity $\bar{\alpha}\bar{\omega}$. These simulated jerky signals were first used to validate the convergence of the adaptive oscillator towards the average amplitude $\bar{\alpha}$ and frequency $\bar{\omega}$. The values of the parameters that were used during the learning phase are shown in Table 3.1 ("Sim. data and learning" column). $\bar{\alpha}$ was set to 5cm and $\bar{\omega}$ to 3.14rad/s.

Table 3.1: List of parameters used to compute the smoothness metric (ϵ_{sm}), output of the adaptive oscillator (AO), and gains of the assistance forces (gain tuner). The column "Sim. data and learning" contains the values of the parameters used in the validation with simulated data and in the learning phase of the patient performance. The second column "Pat. data" shows values used during the assisted trials with the pilot patients. The adaptive oscillator gains were tuned using a published method [134] to obtain fast ($\tau = 3s$) and slow ($\tau = 10s$) learning time constants, respectively for both columns.

	Parameter	Sim. data and learning	Pat. data
ϵ_{sm}	a	0.004	0.004
AO	ν_ϕ	7.33	2.2
	ν_ω	2.22	0.2
	η	0.67	0.2
Gain tuner	τ_g	1	1
	$\epsilon_{min,sm}$	0.0025	0.0025
	$\epsilon_{min,vel}$	0	0
	$\epsilon_{min,amp}$	0	0
	$\epsilon_{max,sm}$	0.009	0.009
	$\epsilon_{max,vel}$	1	1
	$\epsilon_{max,amp}$	1	1

Next, in order to validate the smoothness metric, a variety of simulated movements were computed with different magnitudes of lateral and longitudinal errors. Ideally, the metric should increase when the amplitude (δ_{lat}) or frequency (ω_{lat}) of the lateral error increase, or when δ_{long} or ω_{long} increase for the longitudinal error. Simulations were achieved by testing different sets of parameters ($\delta_{lat} \in [0, 3.75]$ cm, $\omega_{lat} \in [0, 4]\bar{\omega}$, $\delta_{long} \in [0, 3.75]$, and $\omega_{long} \in [0, 3]\bar{\omega}$), as well as for different mo-

vement amplitudes ($\bar{\alpha} \in [4, 10]\text{cm}$) and frequencies ($\bar{\omega} \in [\pi/2, 3\pi]\text{rad/s}$). The other parameters are displayed in Table 3.1 ("Sim. data and learning" column).

Finally, to validate the performance-based assistance, we built a signal composed of different types of errors. This signal was composed of (i) five cycles of unperturbed circular rhythmic movement ($\bar{\alpha} = 5\text{cm}$ and $\bar{\omega} = 3.14\text{rad/s}$, $\delta_{lat} = 0$ and $\delta_{long} = 0$), followed by (ii) five cycles of smaller circular rhythmic movements ($\bar{\alpha} = 3\text{cm}$), (iii) five cycles of slow movements ($\bar{\omega} = 2.09$), (iv) five cycles of jerky movements with lateral errors ($\delta_{lat} = 0.2$, $\omega_{lat} = 4\bar{\omega}$, $\bar{\alpha} = 5\text{cm}$, $\bar{\omega} = 3.14$), and (v) five cycles of jerky movements with longitudinal errors ($\delta_{long} = 0.6$, $\omega_{long} = 4\bar{\omega}$, $\bar{\alpha} = 5\text{cm}$ and $\bar{\omega} = 3.14\text{rad/s}$). These simulated pathological movements were separated from each other by five periods of unperturbed rhythmic circular movements.

This signal was used to compute the real-time performance metrics and evolution of the corresponding gains of the performance-based assistances. The minimum desired amplitude α_d was set to 4cm, and the minimum desired frequency ω_d was 2.8. The values of the parameters used to compute the metrics and gains are displayed in Table 3.1 ("Sim. data and learning" column). In all simulations, no assistive force was actually delivered since the kinematics was prescribed to follow the simulated signals.

3.2.5 Validation with experimental data

Finally, the performance-based assistance was implemented on an end-effector robot, and the protocol was tested with two stroke patients (see Table 3.2). Both patients gave written informed consent to participate in the study, which was approved by the scientific and ethical committees of the Université catholique de Louvain.

Table 3.2: Patients characteristics

	Age	Gender	Time post-stroke	FMA	hemiplegic side
P1	61	Male	4y	23	Left
P2	50	Male	1y	24	Right

Experimental apparatus

The robotic assistance was implemented on an upper-limb end-effector robot, RE-Aplan, which was developed within our university. This device was designed to quantify upper limb impairments of disabled patients [50, 51] and to provide robot-assisted therapies to the same populations [52]. The robot is composed of (i) a height-adjustable horizontal table, (ii) a handle equipped with strain gauges force sensors held by the participant, (iii) two MAXON motors (EC40 170W 42VDC with planetary gearheads GP42C6/1 and encoder HEDL5560 1000imp 2ch) actuating the

handle in the horizontal plane, (iv) a flat screen and loudspeakers in front of the participant, which can provide visual feedback of the position of the handle and any other visual or auditory information, and (v) an interface next to the robot for the therapist. All these components are shown in Figure 3.4.



Fig. 3.4: Planar end-effector robot (REApplan) used to validate the performance-based assistance. The patient is seated in front of the device and holds the handle with the paretic hand.

When controlled to be transparent, i.e. to deliver no force hindering the patient's voluntary movements, the actual robot impedance was identified to be similar to the one of a damped mass. The residual force $\mathbf{F}_{\text{res}}$ thus obeyed a dynamical equation like $\mathbf{F}_{\text{res}} = m\ddot{\mathbf{p}}_{\text{pat}} + b\dot{\mathbf{p}}_{\text{pat}}$. The residual virtual mass of robot was identified to be equal to $m = 0.45\text{kg}$ and the virtual damping factor to $b = 2.26\text{kg/s}$ (see Appendix A).

Patients were too weak to hold the handle by themselves with their paretic hand. Consequently, it was strapped to the handle, and their forearm was supported by a plate rigidly attached to the handle.

Proposed therapy

After seating the patient in front of the robot, his initial abilities were computed. Patients were asked to perform ten rhythmic circular movements at a comfortable speed and amplitude while moving the robot handle with their paretic hand. The robot was configured to be transparent in this case. During this initialization phase, the adaptive oscillator learned the movement features of the patient with dynamics governed by equations 3.3 (see "Sim. data and learning" column in Table 3.1 for the numerical values of the parameters). For the next phase, the therapy itself, the

desired amplitude α_d and tangential velocity $v_d = \omega_d \alpha_d$ were set 10% higher than those obtained after this initialization. This increase was administered in order to make the patient performing close to their maximum capacity.

Next, patients were asked to perform rhythmic circular movements while receiving assistance with the desired movement parameters during half of the trials. The screen displayed a circular path with inner radius set at α_d . The width of this path was set to 4cm. Patients were asked to perform circular movements while staying inside the path. The path was displayed in red if they moved too slowly on average ($\omega_{osc} < \omega_d$), while the path was green if they were going faster than ω_d . The patients were instructed to maintain the green color as much as possible.

This task was continuously performed by the patients during 40 seconds and was repeated ten times, i.e. 10 trials of 40 seconds. They received assistance during half of these trials with random distribution in order to prevent them to display different behaviors in anticipation of a trial with or without assistance. They received at least one minute of rest between two consecutive trials.

The therapist interface served as control unit, i.e. to select if the assistance has to be delivered or not, and to follow the real-time performances of the patient. Importantly, the therapist was instructed not to mention to the patient if he/she was receiving assistance or not, and to deliver no other feedback than what was displayed on his screen.

To validate our approach, we show that the assistance (i) adapts to the real-time motor performance, (ii) enhances the global motor performance, (iii) does not increase with time (no slacking), and that (iv) the smoothness assistance does not provide positive mechanical work on average. The last analysis was performed by computing the mechanical work transferred from the robot to the patient during each cycle:

$$W_{patient,cycle} = \int^{cycle} \mathbf{F}_{patient} dl \quad (3.29)$$

where dl represents the infinitesimal trajectory of the patient hand, and $\mathbf{F}_{patient}$ is the actual force being measured at the interface between the patient and the robot. The numerical parameters used during the therapy are provided in Table 3.1 ("pat. data" column).

Data acquisition

Data were acquired by the robot at a frequency of 250 Hz and exported in a text file with a sample frequency of 125 Hz¹. The handle position and velocity were directly

¹The software of the robotic device runs at 250Hz, however the visual interface receives information at 125Hz. It is through this interface that the text file was provided.

taken from the motor drivers with no extra filtering or signal processing.

3.3 Results and discussion

3.3.1 Validation with simulated data

Adaptive oscillator

Simulation data confirm the capacity of the adaptive oscillator to quickly synchronize to an input rhythmic movement while learning its features in state variables. Figure 3.5 (left) shows an illustration of the adaptive oscillator synchronizing with the simulated data with a mean amplitude of $\bar{\alpha} = 5cm$ and mean angular velocity of $\bar{\omega} = \pi rad/s$. This simulated signal was distorted both with longitudinal ($\delta_{long} = 0.6$ and $\omega_{long} = 4\bar{\omega}$) and lateral errors ($\delta_{lat} = 0.2$ and $\omega_{lat} = 4\bar{\omega}$). The state-variables are also displayed and reach steady-state after about two cycles (3 seconds), which corresponds to the expected settling time (see Table 3.1 and [134]). The oscillator output produces a smooth quasi-sinusoidal version of the distorted input and is fully synchronized after the same amount of time.

This result confirms that the state-variables ω_{osc} and α_{osc} are good candidates for estimating the real-time frequency and amplitude of quasi-harmonic movements performed by the patients. They can also be extracted in real-time during the therapy given the low computational cost of the discrete-time integration of the oscillator state equations. Interestingly, these state variables are also good candidates for assessing the initial ability of the patient to perform circular movements before receiving the therapy (see "Proposed therapy" section).

Validation of the real-time smoothness index

Figure 3.6 shows the impact of longitudinal and lateral errors on the metric quantifying movement smoothness. These graphs were generated by varying both the mean amplitude and angular velocity of the circles and the frequency or amplitude of the longitudinal or lateral error. Longitudinal error mostly impacts the signal temporality, while lateral errors mostly impact the signal spatial distribution.

The figure shows that the smoothness metric is insensitive to the mean movement amplitude and frequency during movements being distorted with lateral errors. This is visible in both left panels of Figure 3.6, which show no variation of the metric with the mentioned parameters (i.e., flat surfaces). This capacity to predict movement smoothness independently of the movement amplitude and frequency is highly desirable. It complies with efforts made to construct a smoothness metric for discrete movements that is dimensionless and independent of the movement amplitude and duration [6, 68, 132]. With longitudinal errors, the smoothness metric is also in-

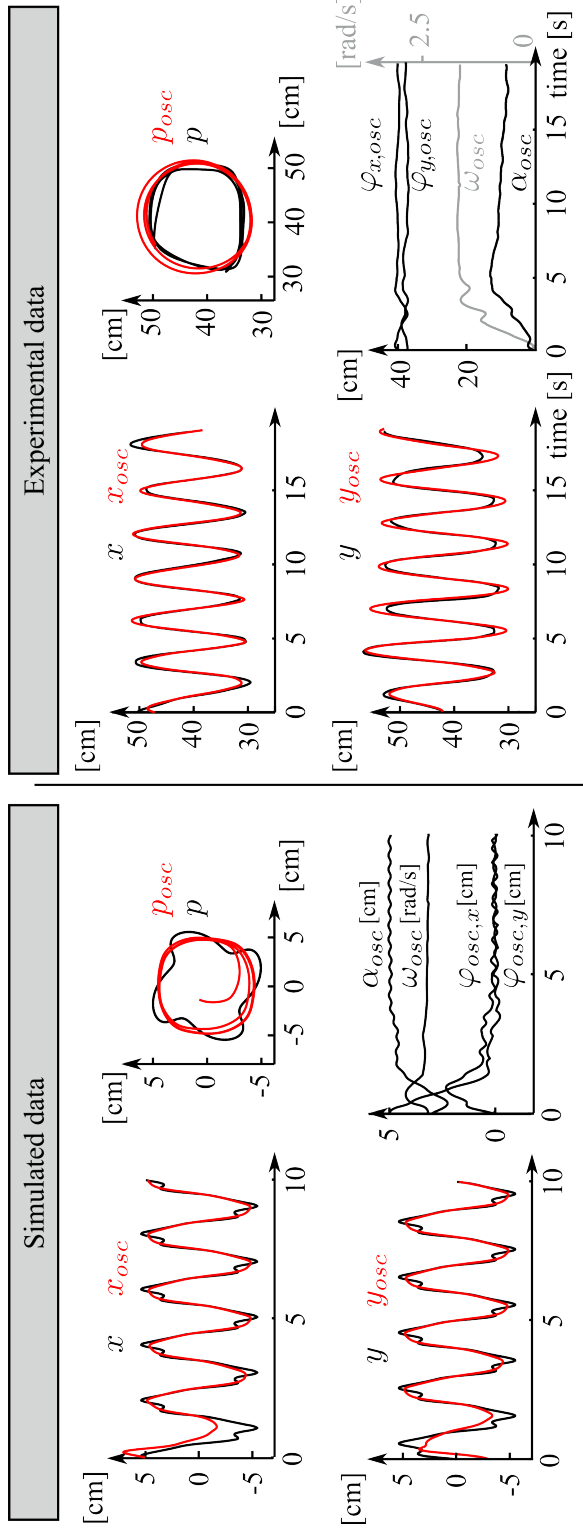


Fig. 3.5: Convergence of the adaptive oscillator with simulated and experimental data: The two left graphs of both panels (simulated data and experimental data) display the oscillator input (left: simulated; right: actual position of the patient; black line) and the learned position by the adaptive oscillator (red line) as x and x_{osc} (top) and y and y_{osc} (bottom) as a function of time. The top right panel displays the actual movement in space (x and y axes) and the trajectory being estimated by the adaptive oscillator during 3 seconds. The bottom right panel displays the adaptive oscillator state variables as a function of time as the offsets $\varphi_{x,osc}$ and $\varphi_{y,osc}$ and the amplitude α_{osc} in [cm], the phase ϕ_{osc} in [rad] and the angular velocity ω_{osc} in [rad/s]. After two cycles, the oscillator synchronizes with the actual signal and gives a smooth version of the input circle (left: simulated; right: drawn by the patient.)

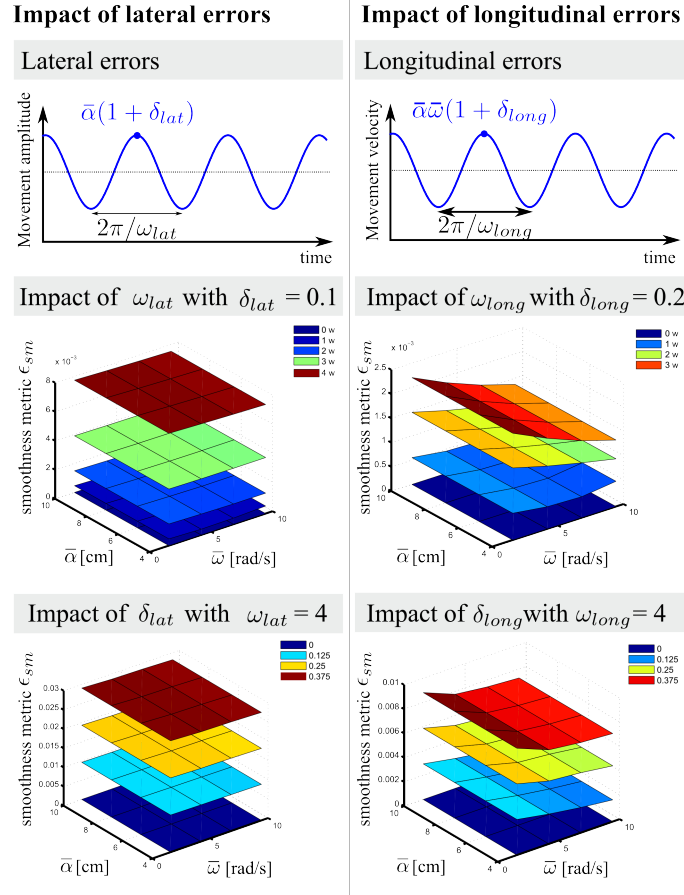


Fig. 3.6: The left panels present the impact on the metric due to lateral errors (errors in amplitude), and the right panels show the impact due to longitudinal errors. The two upper panels display the simulated variation of amplitude and velocity (the product of amplitude and frequency), while the middle panels represent the metric variation as a function of the error frequency (fixed error amplitude), mean signal frequency, and mean signal amplitude, and the bottom panels present the metric variation as a function of the error amplitude (fixed error frequency), mean signal frequency, and mean signal amplitude.

sensitive to the average movement amplitude but displays small sensitivity to the movement frequency (right panels of Figure 3.6). This is due to inherent non-linear dynamic couplings between the state variables of the adaptive oscillator.

Validation of the performance-based assistance

Figure 3.7 shows the evolution of the gains of the three types of assistance as a function of their corresponding errors (smoothness error, velocity error, and am-

plitude error; bottom panel). From top to bottom, the different panels show (i) the position signals, (ii) velocity signals, (iii) absolute error in velocity η , its time derivative ξ , and the smoothness metric ϵ_{sm} (the filtered version of ξ), and (iv) the evolution of α_{osc} and ω_{osc} with respect to the desired amplitude α_d and angular velocity ω_d . The three assistance gains respond as expected. When the error of the corresponding assistance is above ϵ_{min} , the assistance increases. If the error goes above ϵ_{max} , the gain saturates to 1 with a settling time of about 1 second.

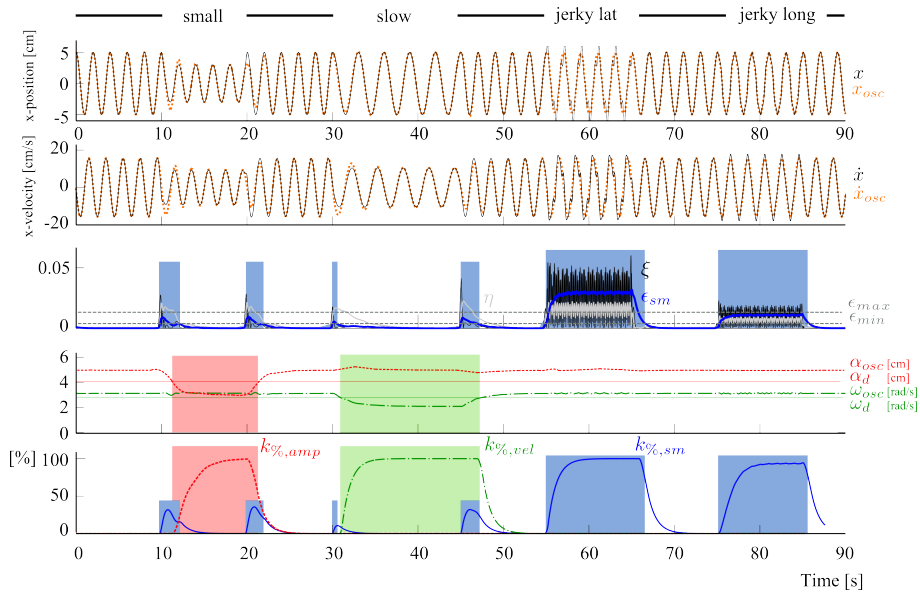


Fig. 3.7: The simulated data is composed of a succession of 5 periods of unperturbed sinusoidal movements and 5 periods of simulated pathological movements. The pathological movements are first small movements, followed by slow movements, jerky movements with lateral errors, and finally jerky movements with longitudinal errors. The upper panel shows the position signal along the x -axis, and the second panel shows the velocity signal along the x -axis. The third and fourth panels display the signals used to assess the motor performance. The third panel shows the signals involved in computing the smoothness metric (η , ξ , ϵ_{sm} and $\epsilon_{sm,min}$), and the bottom panel shows the adaptive oscillator state variables ω_{osc} and α_{osc} together with the corresponding minimum desired values ω_d and α_d . The corresponding assistance gain increases when the performance is lower than the desired threshold, as displayed in the bottom panel. This panel shows the evolution of the three assistance gains $k\%_{sm}$, $k\%_{vel}$, and $k\%_{ampl}$. When the corresponding error is above the threshold, a color background is added (smoothness in blue, velocity in green, and amplitude in red).

3.3.2 Experimental validation with patient data

Initialization

The adaptive oscillator were used to assess the patient abilities at the beginning of the therapy. Patients were asked to execute ten circles with their paretic arm, at comfortable velocity and amplitude while receiving no assistance. Meanwhile, the adaptive oscillator learned the corresponding movement features with a small time constant (see Table 3.1). Figure 3.5 (right) shows a representative result of this adaptation in the form of the adaptive oscillator trajectory, x_{osc} and y_{osc} , synchronizing to the actual position data x and y . For this particular patient and trial, the initialization finished with the oscillator state variable equal to $\alpha_{osc} = 9.1\text{cm}$ and $\omega_{osc} = 1.71\text{rad/s}$. Consequently, setting the target movement amplitude and longitudinal velocity to 10% higher during the therapy is achieved by setting $\alpha_d = 1.1\alpha_{osc} = 10.01\text{cm}$ and $\omega_d = \omega_{osc}$ (remember that the longitudinal velocity is the product of the amplitude α_d and frequency ω_d). The patient initial average longitudinal velocity was thus equal to $v_{osc} = \omega_{osc}\alpha_{osc} = 15.56\text{cm/s}$, while the target velocity used for the therapy was 10% higher: $v_d = \alpha_d\omega_d = 17.1\text{cm/s}$. Consequently, the patient is encouraged to perform both larger and faster movements than those executed during the initialization phase.

Performance-based assistances adapt to real-time motor performance

Figure 3.8 illustrates the evolution of the error signals (ϵ_{sm} , ϵ_{vel} , ϵ_{amp} ; Equations 3.12, 3.13, and 3.14) during a trial without assistance (upper panel) and with assistance (bottom panel). The bottom panel also shows the evolution of the level of smoothness assistance. Both tested patients showed a consistent ability to execute the circular movements at desired amplitude (α_d) and speed (v_d). Only a small amount of amplitude or velocity assistance was provided at the beginning of some trials, but this never lasted longer than 5 seconds. Maybe this reveals that 10% of increase with respect to the natural velocity and amplitude was not high enough to make the movement really challenging. In contrast, the smoothness assistance was active during all trials. The assistance decreased when the smoothness metric ϵ_{sm} was close to 0 and increased when the smoothness metric increased.

Interestingly, the low use of the amplitude and velocity assistance by the patients could also reveal an interaction between the assistance modes. This suggests that providing smoothness assistance also had a positive impact on the steady-state movement amplitude and velocity. However, this observation should be investigated further with a larger population.

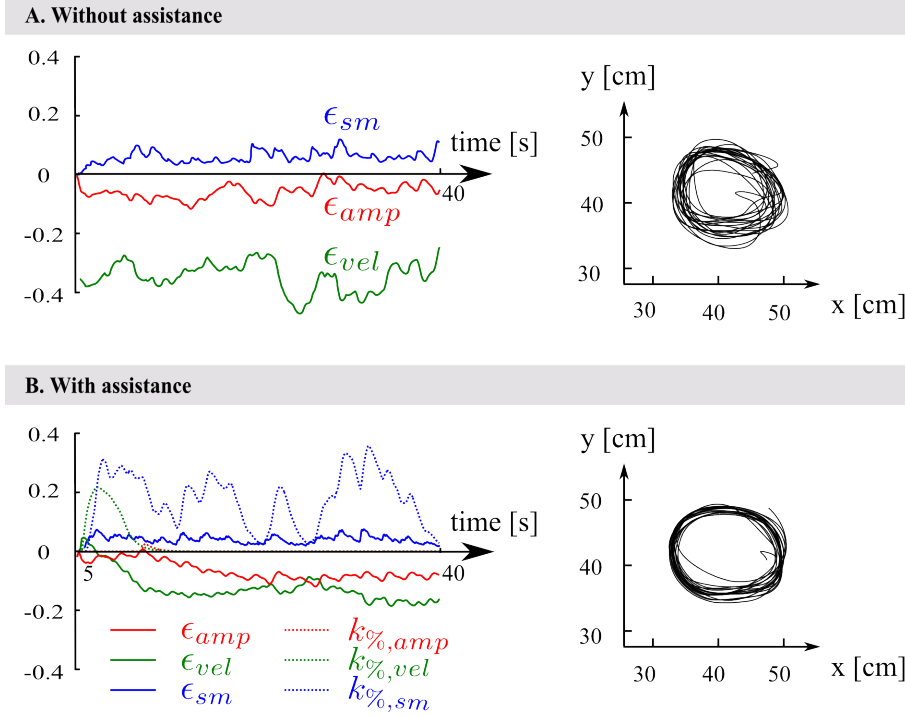


Fig. 3.8: Performance with experimental data: The upper and bottom panels show trials without and with assistance, respectively. The left displays the smoothness, velocity, and amplitude error and gain signals, and the right shows the corresponding 2D hand paths.

Performance-based assistance enhances motor performance during training

On the right side of Figure 3.8, the hand trajectory during a trial with and without assistance is traced. This clearly shows that the hand trajectory was smoother when assistance was provided. This observation can be quantified by measuring the mean smoothness errors during the trials with and without assistance (Figure 3.9). As expected, the error was significantly higher during the trials without assistance than with assistance for both patients (one-way anova, assistance effect: patient 1, $F_{(1,8)} = 9.89$, $p = 0.01$; patient 2, $F_{(1,8)} = 5.96$, $p = 0.04$).

This result shows that the smoothness assistance had the expected impact on motor performances, by improving the smoothness feature of both patients movements.

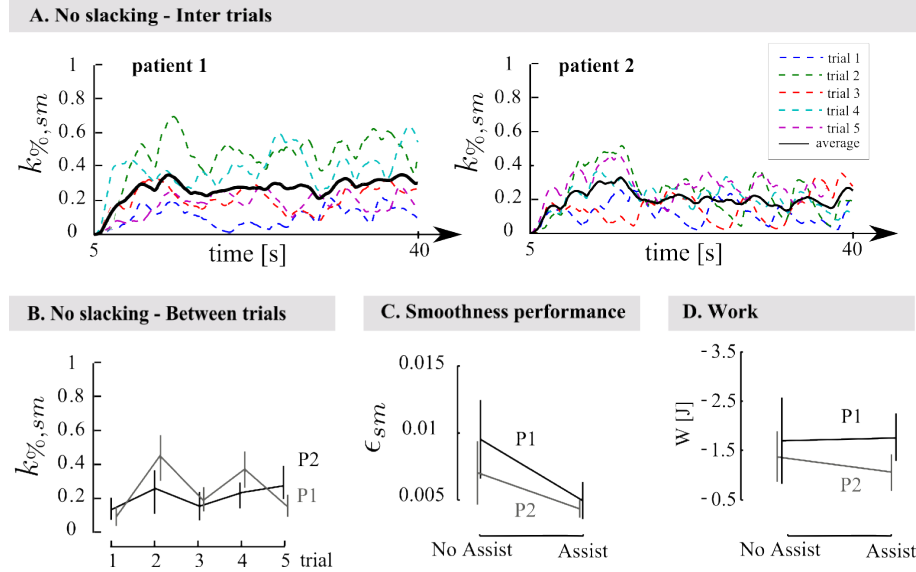


Fig. 3.9: Patient data: A) Evolution of the smoothness gain along the 5 assisted trials for both patients. The averaged evolution over the 5 trials is displayed in black. B) Mean gain for each trial for both patients. C) Mean real-time smoothness metric during the trials with and without assistance for both patients. D) Mean mechanical work provided by the robot to the patient during one cycle with and without assistance for both patients. Vertical lines in panels B, C, and D capture the patient standard deviation across trials.

Performance-based assistances keep the patient active

The slacking hypothesis suggests that when receiving too much assistance, a patient relies on the assistance and stops providing the maximum effort to execute the task alone [183]. This can be observed both within a trial and between trials. If patients display slacking behavior, the amount of assistance should increase over time. The evolution of the smoothness assistance gain is displayed in Figures 3.9-A (inter trials) and B (between trials) for both patients. Figure 3.9-A shows the amount of assistance provided during the five assisted trials for both patients (colored dashed lines) and their average (black solid line). The figure clearly illustrates that the assistance did not increase over time during the trials, except during the initialization phase where the level of assistance reached steady-state. Figure 9-B shows the mean assistance provided during each trial and confirms that the assistance was also not increasing across the 5 trials. These results show that the patient stayed equally active during the successive trials. Indeed, if they would have displayed a slacking behavior, the movement would have been degraded and the assistance gains would have increased accordingly.

Since both patients maintained the desired amplitude and velocity, the amplitude and velocity assistance did not turn on. Therefore, conclusions about a possible slacking behavior with these modes of assistance would require more experiments. Slacking is however unlikely since these assistances are based on same principles as for the smoothness assistance.

Smoothness assistance does not provide positive mechanical work, on average

Figure 3.9-D illustrates the average mechanical work delivered by the robot to the patients during the execution of one movement cycle with assistance and without assistance (see equation 3.29). This mechanical work was negative on average, revealing that the robot was actually dissipating energy in both the transparent mode (no assistance) and when the assistance was switched on. This is due to the residual robot friction b , which was not entirely hidden by the robot force controller (see Appendix B). Patient 1 injected the same amount of energy to the robot to execute the circles with and without assistance (one-way ANOVA; assistance effect: $F_{(1,8)} = 0.13$, $p = 0.73$). Patient 2 delivered slightly less energy with assistance than without, although this did not reach significance ($F_{(1,8)} = 3.54$, $p = 0.09$).

This result suggest that our smoothness assistance obeys passivity-like properties, as the mechanical energy provided to the patient remain bounded (more information can be found in Appendix B). Passivity has recently emerged as a highly desirable feature for rehabilitation robots since it does not compromise the stability of the patient-robot interaction once they are connected to each other [168–171].

3.3.3 Perspectives

The reported data were acquired for the purpose of validating our approach with two representative pilot patients. Consequently, this opens several perspectives for future research. The first is to validate our assistance principle with a larger stroke population, in order to confirm the reported preliminary results. The second is to explore the short- and long-term effects of the suggested unilateral rhythmic movement training on the motor performances of stroke patients. Moreover, possible improvements should also be quantified on other types of movements, like discrete reaching, although the literature established that there is few to no learning transfer from rhythmic to discrete movements in healthy subjects [71,74]. Interestingly, our previous study suggested that stroke patients tend to perform their rhythmic movements kinematically close to discrete movements of healthy subjects [98]. Therefore, investigating possible transfer of learning between rhythmic and discrete movements in a stroke population is of high interest, in particular regarding movement features like smoothness. In sum, our future investigations will aim at establishing which movement features could be improved, both in rhythmic and discrete primate-

ves, after a unimanual rhythmic movement training. The assistance presented in this chapter is proposed as a candidate for implementing such a robot-assisted rhythmic movement training.

In parallel, a progression in the exercises could also be proposed, owing to the fact that our recent findings also revealed smaller impairments of rhythmic movements in a typical stroke population [98]. Discrete elements could be combined with rhythmic movements, supporting the execution of movements with a higher degree of impairment by those that are performed more stably. The combination of rhythmic and discrete movements, like those performed by [155] for single-joint movements or [154] for two-joint movements, are viable candidates for this type of training. Our performance-based assistance could assist the rhythmic component of such movements, although it would have to deal with the reported conflicts between both neural controllers that are being trained. For instance, [154] revealed that the discrete component of a combined rhythmic+discrete movement is systematically triggered during a limited phase window of the rhythmic one.

Finally, the presented performance-based assistance could be extended to more functional rhythmic movements such as wiping a table, brushing teeth or even walking [135]. Indeed, the assistance principle is applicable to any rhythmic movement performed with an end-effector robot, but also with an exoskeleton.

3.4 Conclusion

Rhythmic and discrete movements are considered to be two different motor primitives, and both are affected after stroke. Therefore, both movements should be trained during post-stroke therapies. Currently, mainly functional discrete movements are used during post-stroke therapies, and similarly, the majority of assistance methods being developed for rehabilitation robots target only discrete movement training. To bridge this gap, our study presented a new performance-based robotic assistance training for rhythmic movements that should ideally complement similar discrete-specific therapies in order to recover the most complete motor repertoire.

The proposed assistance method relies on the repetitive nature of rhythmic movements to independently assist three movement features, i.e. smoothness, velocity, and amplitude, without constraining the participant to follow a predefined trajectory. Three assistance forces are combined in order to enhance these features. The forces are modulated as a function of corresponding real-time metrics and therefore assist the patient as needed to prevent slacking. Our approach ideally combines several blocks: an adaptive oscillator that extracts the real-time movement features while providing the movement main harmonic, three estimators that compute the real-time movement features, and three adaptive blocks that compute the feature-based assistance forces. Notably, these blocks consist of a few dynamic equations

and can thus be implemented in a discrete-time version with a limited amount of code and reasonable computational cost.

These different blocks were tested using both simulated and actual experimental data. The simulation data mainly served to validate the independent and decoupled computing of the different movement features using signals with controlled distortions. In particular, the proposed real-time smoothness metric proved to quantify movement smoothness while being independent of the mean movement amplitude and frequency. Patient data revealed the method efficiency in assisting patients to produce smoother movements while keeping them active in the task. In particular, we showed that the robot did not provide mechanical energy to the patient on average such that our strategy displayed passivity-like properties.

Rhythmic upper-limb movement training enhances motor skills of both rhythmic and discrete movements after stroke - A longitudinal study

4

in revision

**Patricia Leconte, Gaëtan Stoquart, Thierry Lejeune
& Renaud Ronsse**

Now that we have established an adequate assistance for rhythmic movements, we present in this chapter the effect of a rhythmic movement therapy in chronic stroke patient. The objective is to establish which movement features are being improved thanks to this type of therapy in stroke patients.

4.1 Introduction

A movement is said to be discrete if it is executed between two different postures with both zero velocity and acceleration. In contrast, rhythmic movements are periodic and display an acceleration peak at the zero-velocity movement reversal [18, 55, 67]. Current literature on motor control claims that these two movements form two different primitives in the motor repertoire [18, 31, 57, 66, 67, 71, 74, 144, 145, 149, 150, 155, 172]. For instance, imaging data in humans and animals showed that they recruit distinct neural circuitries - at least partially [66, 145]. Behavioral data with

healthy participants revealed that there is no learning transfer from rhythmic to discrete movements and few from discrete to rhythmic movements [71, 74]. However, these studies focused only on final movement errors, but report no result regarding a possible transfer of other kinematic metrics such as movement smoothness.

After a stroke, the execution of both movement types is potentially impaired [38, 50, 51, 56, 68, 88, 98, 132, 148, 186]. Although there is a consensus about the necessity to deliver intensive functional movement training during post-stroke therapy [181], very few studies have explored specific training of rhythmic movements [39, 64, 104, 178, 179], and this - to the best of our knowledge - is not frequently performed in daily practice. However, if they form two different primitives, both movement types should receive a specific training in order to recover the complete motor repertoire. This includes both purely discrete and rhythmic movements and - more importantly - daily life activities, which blend them together (wiping a table, playing music, etc [154]).

In chapter 2, we further established that discrete movements might be more impaired than rhythmic ones - for instance, regarding smoothness [98]. Training rhythmic movements might thus be beneficial not only for improving their own performance but also to use them to leverage the execution of discrete movements through combined exercises [154, 155].

Previous studies reported that post-stroke rhythmic movement training might lead to improvements (for instance, regarding general motor control, maximum voluntary force or movement amplitude) in upper-limb motor control [20, 39, 64, 104, 159, 178, 179]. However, these studies did not highlight the exact impact of rhythmicity on these improvements. Hesse et al. (2005) [64] and Bütefisch et al. (1995) [20] mainly established that training intensity is important to enhance motor control. The protocols described in several studies [39, 64, 104, 159, 178, 179] rely on bilateral training, so that this aspect might also play a significant role in the reported improvements. Whittall et al. [179] compared bilateral arm training with auditory cueing (BATRAC) to dose-matched therapeutic exercises and concluded that one was not superior to the other, although the adaptations in brain activation were greater after BATRAC. Auditory cueing can also play a role in the improvements made during BATRAC, since this is known to enhance movement kinematics after stroke [162, 163]. In summary, these studies suggested that rhythmicity might offer some therapeutic benefits after stroke, although the reported improvements might also be influenced by other aspects of the protocols.

Therefore, the goal of the present paper is to assess the impact of a pure unilateral rhythmic movement training on motor control after stroke. We investigated this question both regarding rhythmic and discrete movements. More precisely, the following two possibilities are tested:

- Rhythmic movement therapy enhance rhythmic movement features, as suggested by behavioral experiments of learning transfer with healthy subjects [71,74].
- Some transfer does exist from rhythmic training to discrete movement features.

In the latter case, this finding would support the claim that rhythmic movement training might be used to leverage the execution of the more impaired discrete movements, possibly because some neural overlap exists between rhythmic and discrete movement control after stroke.

To test these hypotheses, we built a longitudinal study where chronic stroke patients received a unilateral rhythmic movement therapy via a robotic device that delivered as-needed assistance. We report the evolution regarding several movement features (general motor control, smoothness, velocity and amplitude) as short- and long-term effects following the therapy in performing both rhythmic and discrete movements with and without the robot.

4.2 Methods

4.2.1 Participants

Fourteen chronic stroke patients were recruited for this study. Patients were eligible for the study if (i) they had suffered from a non-cerebellar stroke more than 6 months before the first assessment, (ii) they could understand the task instructions, (iii) they did not suffer from severe visual impairments or severe neuropsychological impairments like aphasia, attention deficit or neglect and (iv) they had an active shoulder range of motion above 20° of flexion and abduction. One patient faced health issues during the therapy and had to leave the study. Her data were withdrawn for the analyses. Another patient did not show up for the last assessment, so that the corresponding data is missing. Moreover, thirteen age-matched healthy subjects were further recruited in order to collect normative data for comparisons with the patient performances across the therapy. Patient and healthy subject characteristics are reported in Table 4.1. All subjects gave written informed consent prior to participate to the study, which was approved by the ethical committees of the Université catholique de Louvain (Comité d’Etique hospital-facultaire). This study has been registered on clinicaltrial.gov number NCT02139553.

4.2.2 Protocol

Chronic stroke patients were assessed twice (A1 and A2) before the first session of the therapy in order to measure whether their motor performances had reached a

Table 4.1: Individual features of the post-stroke patients (top) and averaged population data of the patients and control subjects (bottom). The clinical metrics being reported here are those measured during the first assessment session (A1). B&B stands for box and blockt [110], and FMA-UE stands for Fugl-Meyer assessment of the upper extremity [48]

Patient	Gender	Dominant hand	Paretic Side	Age	Months post stroke	B&B paretic	B&B non-paretic	FMA-UE	Ashworth (elbow flexors)
1	M	R	R	59	18	27	58	56	1+
2	M	R	L	64	23	12	38	46	2
3	M	R	L	60	49	2	52	24	3
4	M	L	L	53	11	0	38	18	2
5	M	R	R	49	14	0	54	20	1+
6	F	R	R	58	16	35	44	55	0
7	M	L	L	55	6	41	47	55	1
8	F	R	L	56	10	33	72	51	1
9	F	R	R	51	15	0	75	11	2
10	M	R	L	56	228	30	74	44	2
11	M	R	L	67	126	25	61	51	1
12	M	R	L	66	23	18	59	30	1
13	F	R	R	72	30	15	41	37	0

Participants (n = 26)		
	Control subjects	Stroke patients
Number of participants	13	13
Mean ages (SD)	56.15 (5.1)	58.9 (6.7)
Gender (male/female)	4/9	8/5
Dominant hand (right/left)	12/1	11/2

steady state, i.e. displayed no more natural or therapeutically-induced evolution. These two first assessments were conducted at least one month from each other. Next, patients practiced rhythmic movements with a rehabilitation robot during 12 sessions of 18 minutes spread over one month, i.e. approximately 3 sessions per week. After having completed these 12 training sessions, patients were evaluated a third time (A3) in order to assess the short-term evolutions in their motor performances

due to the intervention. Finally, patients were assessed a last time (A4), three months after the last session of the therapy, in order to assess the long-term retention of the intervention. Patients were asked to maintain the same intensity of conventional therapy over the 5 months of the study. However, none of the patients executed rhythmic upper-limb exercises during their conventional therapies. We exposed the thirteen age-matched control subjects to a single assessment session only in order to collect normative data with a healthy population.

4.2.3 Experimental setup

All the experiments were performed with the participant sitting on a chair in front of a planar robot. The robot used during this study was the REAplan (Figure 4.1A). This upper-limb end-effector robot can accurately measure the movement kinematics and deliver forces (i.e., haptic feedback) in the two dimensions of the movement plane using an actuated handle. Previous studies validated its use as a rehabilitation robot [50, 51, 98, 99]. The movement plane is adjustable in height, and the end-effector handle is equipped with force sensors in order to close the haptic loop. The exercises and the visual feedback given to the participants are projected on a vertical screen placed behind the horizontal movement plane. The therapist can tune the therapy parameters via a touch screen next to the patient.

4.2.4 Assessment

The assessment sessions were composed of two parts. The first part - performed with the patient group only - consisted of collecting clinical assessments through different scales, i.e. (i) Fugl-Meyer assessment of the upper extremity (FMA-UE) [48], (ii) the modified Ashworth scale [14] capturing elbow flexors muscle spasticity (the best note is 0 - no increase in tone - and the worst is 4 - rigidity in flexion or extension) and (iii) the box and block (B&B) test [110]. Note that Table 4.1 reports these clinical scales for each patient as collected during the first assessment session (A1).

The second part - performed with both groups - consisted of a robotic assessment with the REAplan in order to capture the ability to perform both rhythmic and discrete movements. In all the tasks being performed in these assessment blocks, the robot was controlled to be transparent in order to minimize the impact on the user's movement. Participants performed six different tasks with each arm to capture the fundamental rhythmic and discrete movements (see Figure 4.1B). Moreover, the rhythmic tasks were tested with and without visual targets, since we report in chapter 2 a potential difference in impairment in these two contexts [98]:

- R-T: rhythmic back-and-forth movements between two targets of $7 \times 7\text{cm}^2$ separated from each other by 14.5cm - 15 cycles

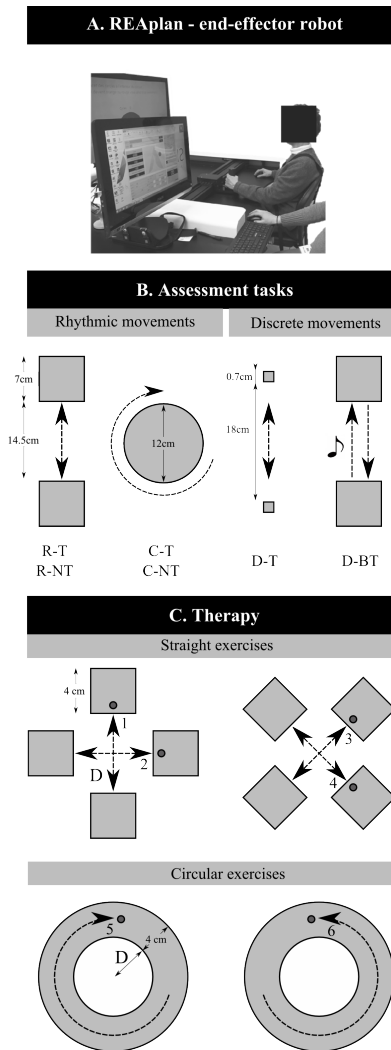


Fig. 4.1: panel A: The REAplan end-effector robot used during this study. Panel B: Robotic assessment tasks. The participants performed four rhythmic and two discrete tasks during the robotic assessment sessions. Panel C: tasks executed by the patients during the therapy while receiving robotic assistance. Distance D was determined as a function of the patient's performance during the initial short assessment phase at the beginning of each session. It could vary from 2cm to 15cm.

- R-NT: same task but with the targets disappearing after 5 seconds - 15 cycles after these 5 initial seconds
- C-T: rhythmic circular movements performed around a circular disc with a diameter of 12cm. With the right arm, participants had to turn clockwise,

with the left arm counter-clockwise - 10 circles

- C-NT: same task but the target disc disappeared after 5 seconds - 10 circles after these 5 initial seconds
- D-T: back-and-forth movements between two small targets ($0.7 \times 0.7\text{cm}$ separated from each other by 18cm) forcing kinematically discrete movements - 10 back-and-forth movements
- D-BT: back-and-forth movements between two targets similar as for the R-T task. In this condition, participants were specifically requested to stay inside the previous target and wait for an auditory cue before moving to the opposite target - 10 back-and-forth movements

The width W and amplitude A of the targets were determined according to the Fitt's law [45] in order to have an index of difficulty (ID) equal to 2.5 in the tasks with large targets and a ID equal to 5 in the D-T task ($ID = \log_2(2A/W)$). Previous studies established that executing back-and-forth movements between two targets without forcing the participant to stop inside the target with low ID induces kinematically rhythmic movements, i.e. movements with maximal acceleration at the movement reversal. In contrast, high ID induces kinematically discrete movements with zero acceleration at the movement reversal [18,57]. Note that this paper reports only the results of the paretic arm and the dominant arm of healthy subjects.

4.2.5 Therapy

Each rehabilitation session started with a short assessment in order to quantify the patient's daily level of performance. The patients were asked to draw ten circles while holding the robot handle at a comfortable speed and amplitude without stopping (such as steering in a pot). The robot was controlled to be transparent, while the algorithm computed the average amplitude, velocity and center of the circles as explained in a previous paper [99]. These features were then used as baseline values during the six exercises of the therapy session.

The exercises of the therapy session consisted of four rhythmic, straight, back-and-forth movements between two targets (Figure 4.1C - 1 to 4) and two rhythmic circular movements, which had to be executed inside of a 3cm wide track (Figure 4.1C - 5 and 6). The actual position of the patient was displayed as a circular dot. If the patient moved too slowly (below the desired velocity computed during the assessment phase), the targets or the track became orange then red; otherwise, it remained green.

During the 10 first seconds of the task, the robot was set in transparent mode. Next, the robot started to deliver performance-based assistance in amplitude, velo-

city and smoothness. In short, these three different types of assistance were triggered as follows:

- If the patient was moving too slowly, a velocity assistance was triggered;
- If the patient performed too small movements (i.e., did not manage to stay inside the targets or the track), an amplitude assistance was triggered;
- Finally, if the movement was detected to be too jerky, a smoothness assistance was delivered.

The smoothness assistance rendered the feeling of a damped-spring connected between the actual position of the patient (p_{pat} in Figure 4.2) and a smoother version of it (p_{osc} in Figure 4.2), which was computed in real time by an adaptive oscillator extracting the movement's main harmonic. The velocity assistance was a tangential force along the desired path. Finally, the amplitude assistance was a radial force that pushed the patient outwards (Figure 4.2). All mathematical foundations about the assistance forces and feedback given to the patients can be found in our previous paper [99] and in the appendix C.

The order of the exercises was randomized. Each exercise was executed during 60 seconds and was repeated 3 consecutive times. A feedback sentence was also displayed on the screen as a function of the average performance (see appendix C for more information).

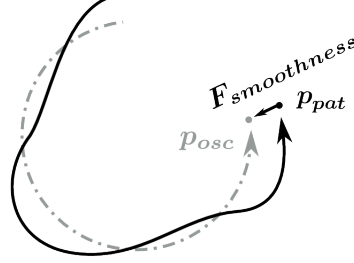
The patients could rest for two minutes if needed between each trial. Each patient was thus active for 18 minutes for each of the training sessions, but the whole therapy session could last up to one hour if all possible resting periods were taken.

4.2.6 Data processing and kinematic indices

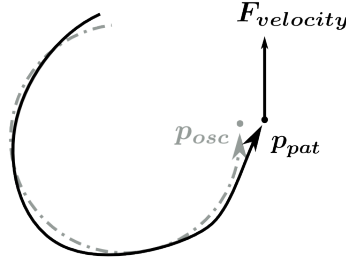
The raw position trajectories of the handle during the therapy and assessment sessions were recorded with a sampling frequency of 125 Hz. They were filtered backwards and forwards using a second-order Butterworth filter with a cutoff frequency of 6 Hz. Next, the velocity, acceleration and jerk were obtained by successive numerical differentiation of the filtered position signal. Thereafter, these signals were cut into individual movements. Only the last eight movements of each trial were kept for analyses in order to focus on steady-state behavior only. This further eliminated the first rhythmic cycles, which could be governed by discrete primitives [71, 74, 149].

For each movement, we computed the following metrics: the velocity peak (v_{max}), the dwell time (dwell) (not in D-BT task), the harmonicity index (H) (not in D-BT task), the number of peaks in the velocity profile (PEAK), the spectral arc length (SPARC) and the accuracy at the movement reversal (only in D-T and D-BT).

A. Smoothness assistance



B. Velocity assistance



C. Amplitude assistance

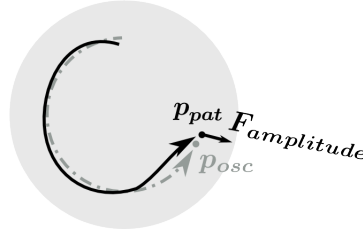


Fig. 4.2: Assistance forces, which can be provided to the patient, if needed. A. The smoothness assistance $F_{smoothness}$ is rendered by a virtual spring between the actual position of the patient p_{pat} and its smoothed version p_{osc} . B) The velocity assistance $F_{velocity}$ is a longitudinal force pulling the patient forward. C) The amplitude assistance $F_{amplitude}$ provides a radial force in order to help the patient to reach higher amplitudes.

The *dwell time* was computed to assess kinematic evolutions of rhythmic and discrete movements. It is a specific landmark of discrete movements [18, 67, 156]. The dwell time measures the duration around the movement reversal during which no movements occur as a percentage of the whole movement duration. Concretely, we measured the time interval between the first time both the movement speed went

below 5% of the velocity peak and the acceleration went below 5% of the acceleration peak of the preceding movement until the first time both the velocity went above 5% of the velocity peak and the acceleration above 5% of the acceleration peak of the following movement.

The *harmonicity index* H , which is bounded between 0 and 1, provides an overview of the movement type produced by the participant during each task [18,57,98]. The index requires measurement of the peak acceleration at movement reversal and normalizes it with the minimum acceleration between two consecutive acceleration peaks. If only one acceleration peak occurs at the movement reversal, H is set to 1. If the minimum acceleration is negative, it saturates to 0. Since a pure rhythmic movement displays a maximal acceleration at the movement reversal, its H index is close to 1. Discrete movements, on the other hand, have a zero acceleration at the movement reversal, so that the corresponding H index is equal to 0. This metric is not reported for the D-BT task, since the participants were forced to stop inside the targets, so that H will systematically be equal to 0.

The *PEAK* metric quantifies the number of velocity peaks in the velocity profile [24,80,98,132].

The *SPARC* metric is a recent smoothness metric developed by Buchanan and colleagues; it is intended to be less sensitive to noise than other metrics (for computational details, see their study [7]). It relies on a frequency analysis of the velocity profile by quantifying how close a signal is from a pure harmonic signal. Since the frequency spectrum of a jerky movement is richer than the one of a smooth movement - due to the large amount of submovements in its velocity profile - the corresponding SPARC will be lower (i.e., more negative). In sum, higher SPARC corresponds to smoother movement.

Finally, *accuracy* is obtained by measuring the distance between the center of the targets and the actual position of the movement reversal.

4.2.7 Data analysis and statistics

All statistics were performed with JMP pro 12 software (SAS Institute Inc.).

Clinical scales

FMA, B&B and Ashworth First, we performed statistics to evaluate the evolution of the clinical scales across the therapy. The results of the B&B test were first normalized [110] and afterwards an ANOVA was performed with the assessment number as factor. The FMA and Ashworth tests were analyzed through a non-parametric Friedman test.

Kinematic assessment Next, we performed statistics on the movement kinematics measured with the robot during the assessment sessions. For each task and for all abovementioned metrics, a mixed model was performed on the dataset. It contained the assessment number as a fixed effect and the participant number as a random effect. The models were solved using a "restricted maximum likelihood" method to estimate the variance parameters. The post hoc Tukey HSD test was used to compare the modalities of significant factors. Patient 9 was excluded from the analysis in the R-T, C-T, D-T and D-BT tasks since he was never able to reach the targets. The evolution of the performance across the therapy itself is reported in the supplementary materials. These findings support the preliminary results reported in a previous study [99].

Comparison with healthy control subjects In order to compare the performance level reached by the patients after the therapy with the performance of a healthy population, we compared the results of the patients' third assessments with the results of the thirteen age-matched control subjects. Again, for each task and metric, a similar mixed model was computed to measure the effect of each participant's type (control or patient). The participant number was again set as a random effect.

4.3 Results

Statistics are reported in Table 4.2, and the most relevant data of rhythmic (R-T, C-T) and discrete (D-T and D-BT) assessment tasks are graphically reported in Figures 4.3 and 4.4, respectively.

4.3.1 Validity of longitudinal study

Patients were stable across the two first assessment sessions, thus fulfilling a criterion for the validity of a longitudinal study: the post-hoc Tukey tests between A1 and A2 never reached significance ($p > 0.05$) for all tasks and metrics, except for the harmonicity index H of the C-NT task and for the accuracy during the D-T task. The latter is due to an outlier (patient 5), which was highly inaccurate during the first session and strongly improved this during the second session.

4.3.2 Clinical assessment did not highlight improvements

The three clinical tests that were performed at the beginning of each assessment session revealed no significant evolution, that is, all p-values were above the threshold: the box-and-block test obtained $p = 0.99$, the FMA $p = 0.08$, and the Ashworth $p = 0.58$. This confirms that patients were stable before the intervention (A1 vs A2), but this also shows that the intervention had no effect regarding the clinical assessment.

Table 4.2: Individual features of the post-stroke patients (top) and averaged population data of the patients and control subjects (bottom). The clinical metrics being reported here are those measured during the first assessment session (A1). B&B stands for box and blockt [110], and FMA-UE stands for Fugl-Meyer assessment of the upper extremity [48]

		mean [IQR, min, max]				Healthy n=10 (A3)	p	F	p	Stability			
		A1	A2	A3	A4					A1 vs A2	A1 vs A3	A2 vs A3	A1 vs A4
R-T	<i>v_{max}</i>	24.8 [21.3;28.3]	26.6 [23.1;30.14]	31.9 [28.4;35.41]	31 [27.5;34.54]	40.6 [48.5;57.8]	0.08	F(3;361.2)=28.37	<0.0001	0.17	<0.0001	<0.0001	<0.0001
	<i>H</i>	0.15 [0.01;0.3]	0.2 [0.03;0.35]	0.36 [0.21;0.52]	0.32 [0.17;0.48]	0.66 [0.74;0.9]	0.032	F(3;361.2)=18.5	<0.0001	0.45	<0.0001	<0.0001	<0.0001
	<i>DWELL</i>	0.08 [0.001;0.15]	0.08 [0;0.4]	0.01 [0.05;0.085]	0 [0.07;0.07]	0 [0.0]	0.15	F(3;362.1)=2.6	0.051				0.0014
	<i>PEAK</i>	1.97 [1.35;2.4]	1.94 [1.41;2.8]	1.36 [0.95;1.80]	1.4 [0.96;1.83]	1 [1.1]	0.02	F(3;361.3)=15.6	<0.0001	0.71	<0.0001	0.0003	<0.0001
C-T	<i>v_{max}</i>	-1.63 [-1.7;1.58]	-1.63 [-1.69;1.57]	-1.56 [-1.65;1.5]	-1.56 [-1.63;1.51]	-1.56 [-1.54;1.57]	0.59	F(3;361.3)=7.5	<0.0001	0.96	0.001	0.005	0.023
	<i>H</i>	17.2 [14.34;20.07]	18.2 [15.30;21.02]	23.8 [20.90;26.62]	24.4 [21.93;27.68]	34.9 [36.9;35]	0.002	F(3;361.2)=64.77	<0.0001	0.47	<0.0001	<0.0001	<0.0001
	<i>DWELL</i>	0.14 [0.06;0.23]	0.08 [0;0.18]	0.3 [0.21;0.38]	0.29 [0.21;0.38]	0.69 [0.68;0.7]	0.0015	F(3;361.4)=35.94	<0.0001	0.056	<0.0001	<0.0001	<0.0001
	<i>PEAK</i>	0.31 [0.14;0.47]	0.19 [0.0;0.35]	0.02 [0.15;0.18]	0.01 [0.16;0.17]	0 [0.0]	0.17	F(3;362.1)=6.5	0.0002	0.41	0.0015	0.14	0.0012
R-NT	<i>v_{max}</i>	2.85 [2.13;5.0]	2.49 [1.84;3.13]	1.36 [0.71;2.00]	1.25 [0.61;1.9]	1.02 [1.04;0.99]	0.0129	F(3;361.4)=33.6	<0.0001	0.23	<0.0001	<0.0001	<0.0001
	<i>H</i>	-1.79 [-1.93;1.65]	-1.81 [-1.96;1.68]	-1.57 [-1.71;1.43]	-1.56 [-1.7;1.41]	-1.54 [-1.53;1.55]	0.005	F(3;362.2)=7.8	<0.0001	0.98	0.0072	0.0022	0.0067
	<i>DWELL</i>	19.57 [16.67;22.47]	19.7 [16.81;22.59]	25.37 [21.47;27.28]	23.52 [20.62;26.42]	33.18 [35.53;30.9]	0.0244	F(3;355.4)=33.5	<0.0001	0.9988	<0.0001	<0.0001	<0.0001
	<i>PEAK</i>	0.3 [0.16;0.43]	0.19 [0.06;0.33]	0.41 [0.28;0.54]	0.27 [0.14;0.41]	0.48 [0.54;0.41]	0.59	F(3;355.4)=17.7	<0.0001	0.0074	0.001	<0.0001	0.52
C-NT	<i>v_{max}</i>	0.02 [0;0.04]	0.03 [0;0.05]	0.004 [-0.02;0.03]	0.008 [-0.02;0.03]	0 [0.0]	0.33	F(3;357.3)=1.25	0.29				0.848
	<i>H</i>	1.52 [1.27;1.78]	1.52 [1.26;1.78]	1.28 [1.03;1.54]	1.31 [1.04;1.57]	1.05 [1.09;1.01]	0.04	F(3;355.5)=11.2	0.0018	0.9959	0.02	0.019	0.048
	<i>DWELL</i>	-1.6 [-1.66;1.56]	-1.69 [-1.68;1.58]	-1.58 [-1.65;1.53]	-1.57 [-1.63;1.53]	-1.53 [-1.53;1.54]	0.0001	F(3;356.6)=1.6	0.18				0.046
	<i>PEAK</i>	27.7 [23.98;31.3]	25.4 [21.59;28.94]	32.3 [28.65;35.99]	32 [28.34;35.74]	36.5 [38.4;34.3]	0.27	F(3;361.3)=24.15	<0.0001	0.07	<0.0001	<0.0001	<0.0001
D-T	<i>v_{max}</i>	0.27 [0.13;0.42]	0.22 [0.07;0.37]	0.49 [0.29;0.58]	0.33 [0.19;0.48]	0.5 [0.57;0.49]	0.58	F(3;361.3)=11.1	<0.0001	0.53	0.0003	<0.0001	0.41
	<i>H</i>	0.001 [0.000;0.009]	0.01 [0.000;0.023]	0 [0.000;0.008]	0 [0.000;0.008]	0 [0.0]	*	F(3;364.5)=7.7	0.1				0.02
	<i>DWELL</i>	1.71 [1.45;1.97]	1.69 [1.37;1.88]	1.13 [0.88;1.39]	1.18 [0.91;1.45]	1.06 [1.1;1.01]	0.31	F(3;361.6)=17.88	<0.0001	0.33	<0.0001	<0.0001	<0.0001
	<i>PEAK</i>	-1.61 [-1.65;1.56]	-1.61 [-1.66;1.56]	-1.55 [-1.6;1.5]	-1.57 [-1.61;1.52]	-1.57 [-1.56;1.59]	0.39	F(3;361.4)=8.14	<0.0001	0.98	0.0015	0.0003	0.0299
D-BT	<i>v_{max}</i>	17.35 [15.65;19.07]	17.94 [16.22;19.67]	20.79 [19.07;22.5]	20.73 [19.00;22.47]	17.1 [18.2;16]	0.054	F(3;355.3)=15.8	<0.0001	0.33	<0.0001	0.0003	<0.0001
	<i>H</i>	0.001 [0;0.01]	0.005 [0.001;0.008]	0.003 [0;0.007]	0.001 [0.003;0.006]	0.03 [0.05;0.01]	0.16	F(3;358)=1.29	0.28				0.0065
	<i>DWELL</i>	0.77 [0.34;1.2]	0.86 [0.42;1.29]	0.55 [0.12;0.98]	0.49 [0.15;1.12]	0.14 [0.19;0.08]	0.0124	F(3;353.3)=1.3	0.21				0.079
	<i>PEAK</i>	4.8 [3.44;6.17]	5.2 [3.84;6.57]	3.88 [2.51;5.24]	4.24 [2.75;6.1]	2.73 [3.17;2.87]	0.1	F(3;355.3)=55	0.0038	0.73	0.079	0.0039	0.49
D-BT	<i>v_{max}</i>	-1.98 [-2.3;1.72]	-1.87 [-2.13;1.62]	-1.71 [-1.97;1.47]	-1.64 [-1.9;1.39]	-1.55 [-1.54;1.58]	0.0087	F(3;355.3)=6.4	0.0003	0.59	0.0088	0.233	0.0006
	<i>H</i>	1.22 [0.91;1.54]	0.77 [0.46;1.09]	0.71 [0.41;0.9]	0.64 [0.35;0.97]	0.41 [0.46;0.36]	0.0009	F(3;355.3)=59	<0.0001	0.005	0.0005	0.96	0.0002
	<i>DWELL</i>	20.12 [17.65;22.58]	21.61 [19.13;24.08]	23.9 [21.46;26.35]	25.08 [22.59;27.57]	27.8 [29;26]	0.21	F(3;356.1)=15.64	<0.0001	0.24	<0.0001	0.018	<0.0001
	<i>PEAK</i>	2.24 [1.69;2.79]	1.97 [1.42;2.52]	1.73 [1.18;2.27]	1.73 [1.18;2.18]	1.36 [1.51;1.21]	0.23	F(3;339)=6	0.0065	0.31	0.0048	0.42	0.0009
D-BT	<i>v_{max}</i>	-1.62 [-1.68;1.57]	-1.61 [-1.67;1.55]	-1.55 [-1.6;1.49]	-1.55 [-1.61;1.49]	-1.53 [-1.51;1.55]	0.56	F(3;357.7)=10.95	<0.0001	0.7	<0.0001	0.0003	<0.0001
	<i>H</i>	1.63 [1.31;1.95]	1.73 [1.41;2.05]	1.33 [1.04;1.67]	1.54 [1.21;1.86]	0.94 [1.05;0.84]	0.0001	F(3;337.4)=3.33	0.054				0.0014

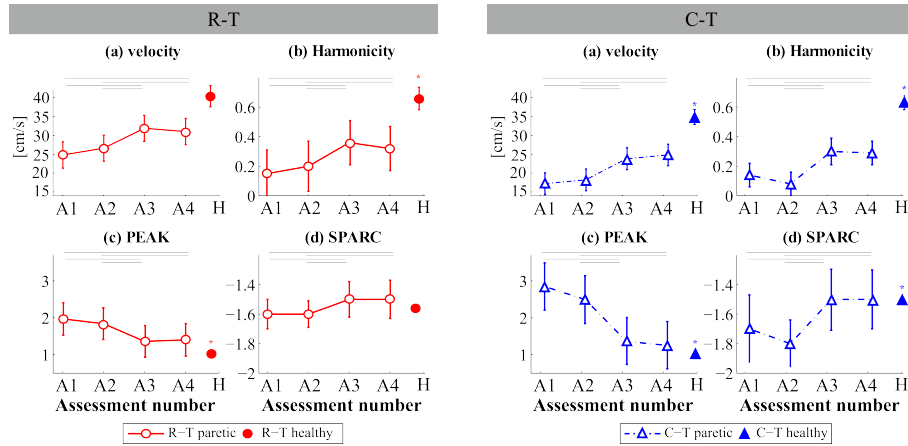


Fig. 4.3: Evolution over the 4 assessment days (A1, A2, A3 and A4) and the assessment of healthy subjects (H) during rhythmic tasks (R-T - left - and C-T - right) in, respectively, the (a) velocity, (b) harmonicity, (c) peak and (d) SPARC metrics. The error bars represent the confidence interval of 95%. The horizontal lines above the different panels capture the assessment numbers being significantly different from each other. When the healthy subjects were significantly different from the third assessment of the paretic arms, a (*) is displayed above the healthy results.

4.3.3 Rhythmic movements got improved due to the therapy

Right after the therapy (A3), the patients displayed significant improvements for almost all metrics during the rhythmic tasks. Patients moved faster and reached the same velocity as healthy subjects in the R-T and R-NT task. The harmonic nature of the movements was improved in the C-T, R-T and R-NT tasks (post-hoc Tukey tests of A1 vs A3 and A2 vs A3, all p 's < 0.05). It reached the same level as for healthy subjects in the C-NT and R-NT tasks. Finally, smoothness improved during the C-T, R-T and R-NT tasks for both smoothness metrics (PEAK and SPARC). The smoothness level reached the same level as for healthy subjects for the SPARC metric during the R-T and R-NT tasks and for the PEAK metric during the R-NT task. Most of these improvements were maintained at the three-month follow-up assessment (A4). Only the harmonicity during the R-NT task regressed back to the same level as during the pre-therapy assessment values. The dwell time did not significantly evolve after the therapy, but the level reached during A3 was not significantly different from that of healthy subjects.

4.3.4 Discrete movements also improved after the therapy, mainly regarding smoothness and speed

Interestingly, after this purely rhythmic therapy, patients also displayed a positive evolution in performing the discrete tasks, even if these movements were not specifically trained. Patients moved faster and movements were performed in a smoother way: SPARC improved during the D-BT task, and PEAK improved during the D-T task. These metrics reached the same level as for healthy subjects. The improvements were maintained after 3 months for the SPARC during the D-BT task, and A4 was significantly higher than A1 and A2 for the SPARC during the D-T task.

In contrast, the level of accuracy did not evolve. Significance was never reached for post-hoc Tuckey tests between A2, A3 and A4. Regarding A1, the difference with the other sessions reached significance only for the D-T task. A deeper analysis highlighted that this was due to patient 5, who behaved as an outlier during the first session of this task, displaying a poor accuracy for that task and that day only.

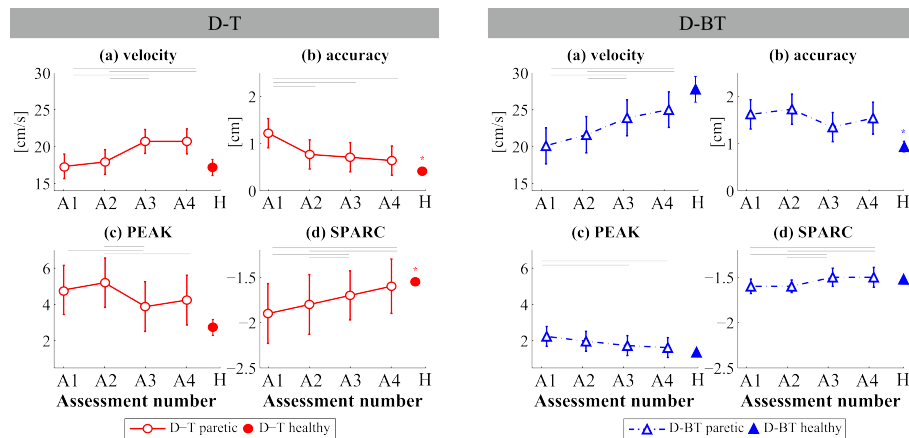


Fig. 4.4: Evolution over the 4 assessment days (A1, A2, A3 and A4) and the assessment of healthy subjects (H) during discrete tasks (D-T - left and D-BT - right) in, respectively, the (a) velocity, (b) accuracy, (c) peak and (d) SPARC metrics. The error bars represent the confidence interval of 95%. The horizontal lines above the different panels capture the assessment numbers being significantly different from each other. When the healthy subjects were significantly different from the third assessment of the paretic arms, a (*) is displayed above the healthy results.

4.4 Discussion

The aim of this study was to investigate whether a pure unilateral rhythmic movement training, after stroke, would (1) improve the performance of rhythmic movement execution and (2) trigger some transfers to the execution of discrete mo-

vements. This training relied on an assistive approach that we developed using adaptive oscillators. It provides an as-needed assistance force that continuously adapts to the pattern being performed and steered by the patient [99].

Since rhythmic movements were intensively trained during the proposed therapy, the enhancement of all metrics that quantify the performance of these movements was not surprising. Discrete movements, on the other hand, were not trained during the therapy, and behavioral experiments with healthy subjects revealed that no transfer occurs from rhythmic to discrete movements [71, 74]. Thus, a positive evolution of some metrics that capture the velocity and smoothness in discrete movements was not expected; although, on the other hand, stroke patients did not improve with regards to their accuracy metrics.

The need for accuracy is a hallmark of discrete movements, which typically aim for a specific target (e.g., reaching). Imaging data showed that even very simple discrete movements recruit cortical areas that are thought to play a role in such high level movement planning [137, 165], they are not recruited during rhythmic movements [145]. Therefore, this study found that our rhythmic movement therapy did not leverage the recruitment of these planning circuitries, so that movement accuracy was not exercised, which is in contrast to velocity and smoothness.

Several hypotheses could explain the transfer from rhythmic to discrete movements with regards to velocity and smoothness. First, patients tend to execute rhythmic movements with kinematic features being closer to discrete movements compared to healthy people [98]. Indeed, the harmonicity of the R-T and C-T tasks stayed below 1, i.e., the typical level of a healthy population. Therefore, executing such non-ideal rhythmic movements could facilitate the transition to discrete movements later on. Second, a partial overlap between the neural networks that govern rhythmic and discrete movements could exist, mainly, in the subcortical layers. Again, rhythmic training would then induce plastic neural adaptation that might be beneficial for discrete movements as well.

4.4.1 Limitations

The results of this study are promising, since no research has yet established the effect of a pure unilateral rhythmic training after stroke. However, this study is not randomized, the assessors were not blind and no control group was enrolled in the protocol. Therefore, future RCTs with a higher number of patients are needed.

Unfortunately, our observations reporting improvements in movement metrics did not correlate with evolutions in the tested clinical metrics. This was probably due to the nature of the exercises themselves. Our movements required limited shoulder amplitudes (maximum 10 to 85 degrees in flexion and extension and 0 to 45 degrees in ad-abduction) and limited elbow amplitudes (max 90 to 180 degrees). Both FMA

and the box-and-block test require performing movements with larger shoulder and elbowing amplitudes. Also, these movements require fine hand dexterity, i.e. a skill that was not practiced with our robot-assisted therapy.

4.4.2 Perspectives

Our results and others [20, 39, 64, 104, 159, 178, 179] lead us to claim that specific rhythmic movement training should be provided after stroke. Since rhythmic and discrete movements are different motor primitives, both should be trained in order to recover the complete motor repertoire. Moreover, since rhythmic movements are likely easier to be performed by stroke patients [98], they should be the first movements to train. Discrete movements could then be combined with rhythmic movements, leveraging the execution of movements with a higher degree of impairment to those that are performed more stably [98, 154, 155].

General discussion and perspectives

5

5.1 Objectives and contributions

Rhythmic and discrete motor primitives are two fundamental movement classes [18, 31, 53, 57, 67, 69–71, 74, 149, 150, 172] which are governed at least partially by distinct neural circuitries [100, 145]. Rhythmic movements involve less cortical activities - possibly because they rely more on oscillating spinal circuits - and no or little learning transfer occurs between both primitives. Until now, these primitives were mainly studied with healthy subjects. Since stroke patients are only affected in the brain, the first objective of this thesis was to establish whether rhythmic upper-limb movements were impaired to the same extent as discrete movements.

Next, this thesis studied whether rhythmic movement therapy would be interesting to offer to a post-stroke population. Indeed, nowadays, few to no recommendations are made to the physiotherapists to train these specific movements. However, since both primitives are not entirely governed by the same neural circuitries, we hypothesized that when both movement primitives are impaired, both movements should be trained in order to recover a complete motor repertoire.

Therefore, this thesis pursued three main objectives: (i) Better understanding how rhythmic and discrete upper-limb movements are impaired after a stroke, (ii) developing an assist-as-needed robotic therapy for training rhythmic upper-limb movements, (iii) assessing how a purely rhythmic upper-limb unimanual movement therapy can improve rhythmic motor features in a stroke population and establishing if a learning transfer occurs from rhythmic to discrete movements.

5.1.1 Rhythmic and discrete primitives in stroke patients

The first objective aimed at comparing rhythmic and discrete motor primitives in the upper-limb of stroke patients. In agreement with the literature, we established

that both primitives are potentially impaired after stroke. However, they were not impaired to the same extent. Patients were able to execute rhythmic movements in a smoother way than discrete ones. Rhythmic movements, though, were performed in a less "rhythmic" way as compared to a healthy control population. More precisely, most of the patients decelerated more at the movement reversal than healthy subjects.

The results of this experiment have therapeutic impacts. We reinforced the relevance to train discrete movements after stroke since they are the most affected ones. However, we postulated that both movements should be trained in order to recover the complete motor repertoire.

Moreover, patients who were impaired in rhythmic movements were always impaired in discrete ones and some patients were only impaired in discrete movements but not in rhythmic ones. This last result established a hierarchy of impairments of both movements. Therefore, we postulated that rhythmic movements could be used to leverage the execution in performing more complex discrete movements. In Section 5.4.2, we outline a follow-up experiment that could be performed for implementing this idea.

5.1.2 Rhythmic assistance-as-needed

The third objective of this thesis was to assess the interest of training rhythmic movements after stroke. Therefore, we developed a robotic rhythmic movement assistance framework. Rehabilitation robotics has the advantage to offer standardized, repeatable, and measurable therapies. Therefore, robots can be used to study the effectiveness of different training protocols. Moreover, rehabilitation robots can be programmed to give appropriate assistance, in order to optimize motor learning. Nowadays, it is established that the assistance that has to be provided to a patient during a task should be as low as possible. Too much assistance leads the patient to slack as he/she starts to rely more on the assistance than on his/her own abilities to execute the task [9,75,116,183]. On the other hand, in order to maintain the patient motivation and involvement, it is sometimes necessary to help him/her if he/she is not able to execute the task on his/her own. This type of assistance is called the "assist-as-needed" principle.

Having this in mind, a performance-based rhythmic assistance was designed. The assistance level was automatically tuned in real-time, based on the performances of the patient. More precisely, independent smoothness, velocity and amplitude assistance was offered to the patient, as a function of the corresponding performance. These performances were measured in real-time by relying on the repetitive nature of the task, by means of adaptive oscillators.

The performance-based assistance was first tested with two pilot stroke patients. Weaker patients executing their movements with lower performances received in-

deed higher assistance levels, while better patients executing the tasks with higher performances received no or little assistance. Moreover, we observed no slacking behavior, neither within the therapy sessions nor across them. Moreover, we observed that no active mechanical work, on average, was provided to the patient when he/she was receiving the smoothness assistance. In appendix B we showed that this type of assistance displays a passive-like behavior, which is a highly desirable feature for keeping the patient involved in the task and guaranteeing the stability of the patient-robot interaction. During the longitudinal study described below, the same assistance was implemented during the exercises. The assistance responded also as expected in this third study, which involved more patients.

5.1.3 Rhythmic movement therapy for stroke patients

The last objective of this thesis was to establish how purely unilateral rhythmic movement training could improve the upper-limb motor skills of stroke patients. We further questioned whether no transfer from rhythmic to discrete movements occurs, as suggested by the studies performed on healthy subjects, or if some learned features are being transferred from rhythmic to discrete movements.

A longitudinal study was performed to answer these questions. Thirteen patients were asked to participate to a one-month rhythmic therapy. It consisted of twelve therapy sessions with the end-effector REAplan robot. To assess the evolution of their upper-limb motricity, patients were evaluated four times: a first time, one month before the therapy, a second time shortly before the therapy, a third time shortly after the therapy and a last time 3 months after the rhythmic therapy. During these assessments, the kinematics of both rhythmic and discrete movements were measured through the robot, and the following clinical tests were conducted: (i) the Box-and-Block test, (ii) the Fugl-Meyer upper-extremity assessment and (iii) the Ashworth test of the elbow flexors.

The therapy sessions themselves were each composed of 18 exercises of 1 minute each. Patients were asked to perform rhythmic movements with the handle of the robot (rhythmic back-and-forth movements in four different directions and clock- or counter-clockwise circles). The provided assistance was the performance-based assistance described above. As expected, all features - velocity, smoothness, harmonicity - of the rhythmic movements improved thanks to the therapy. However, some discrete movement features, such as velocity and smoothness, also improved after the therapy. Accuracy on the other hand - which is a typical discrete movement feature - was not enhanced through rhythmic movement training.

The improvements on general motor features measured by clinical tests did not reach significance. These results are however surprising since both BATRAC (Repetitive bilateral arm training with rhythmic auditory cueing) [178] and RAE [187]

(resonating arm exerciser) improve the FMA outcome and since the intensity of our therapy was approximately the same. Several justification can be suggested why patients did not in our tests. (i) Our participants had a higher baseline FMA score (38.3; SD = 15.9) compared with other studies where FMA means ranged 25 and 34 [104, 178]. As suggested by [129], BATRAC might facilitate motor function for individuals with more severe motor impairments. (ii) The therapy mainly focused on the shoulder motricity and to a lesser extent on the elbow. The above cited clinical tests however, also rely on elbow, wrist and finger motricity. Moreover, unlike in BATRAC and RAE, movements were performed in front of the subject, and were not encouraged to train outside of their synergies. Working outside of the synergies however, may allow to increase joint coordination [42, 160]. (iii) We did not include daily life questionnaires in our assessment protocol such as the ABILHAND questionnaire [123] or Motor Activity Log [167]. The improvement measured by the robot might have an impact on the capacity to manage some daily activities. Some patients verbally reported to the experimenter their increased ability to perform some daily activities such as arm balancing during walking, smoother execution of their movements, or increased endurance.

5.2 Impact for the rehabilitation community

The results of this thesis helped to improve our knowledge about the organization of motor control, more particularly about the organization of rhythmic and discrete motor primitives of the upper-limb. Our first experiment showed that a hierarchy likely exists between them. Recovering rhythmic movements could be a necessary condition before properly recovering discrete movement primitives.

Moreover, since rhythmic movement training improves some movement features of discrete movements, rhythmic arm therapy could be an interesting complement to classic stroke rehabilitation protocols. Asking patients in a early stage of recovery to execute arm-cycling or other pure rhythmic movements would make sense and can be potentially interesting (see Section 5.4.4 for a possible protocol). They could do these alone, potentially, requiring less attention than for discrete movements, and even for example while watching television. As an anecdote, all patients involved in our studies, except those who were strongly impaired, were talking to the experimenter during the rhythmic therapy, without decreasing their performances.

In sum, this thesis supports recommendations that should be delivered to the rehabilitation community, regarding the inclusion of rhythmic exercises in the training program: (1) Rhythmic movement training per se is interesting, since rhythmic movements are likely impaired after stroke while being part of the intact motor repertoire, and could improve some features being shared by both primitives; (2) blending rhythmic and discrete movements in the same exercises is of potential interest

for having the latter being leveraged by the former (see Section 5.4.2 for a possible protocol).

5.3 Mitigation about the use of robots for assessment and rehabilitation

Throughout this thesis, an end-effector upper-limb robot was used to (i) assess patients and healthy subjects and to (ii) rehabilitate patients through a performance-based assistance. Using the same tool to do both assessment and rehabilitation is interesting since it decreases the amount of devices needed in post-stroke rehab.

5.3.1 Assessment

The advantage of robotics is their ability to accurately measure the movement kinematics of the robotic joints and the reaction forces applied to them. These measurements can be used to assess the movement quality, for instance to establish how healthy subjects and patients execute particular tasks. But they can also be used - when standardized - as clinical tests.

However, using the same robot for assessment and rehabilitation has some drawbacks. The non reversible robot used during this thesis has a relative high residual impedance (see Appendix A). Due to this impedance, movements are smoothed out by the robot. If our experiments would be repeated with a low impedance robot or even without contact (such as with a video motion analysis system) movement kinematics would likely be more jerky. The difference in impairments between rhythmic and discrete movements might be even more visible with such systems. Moreover the advantage of video motion analysis is the fact that movement compensation could be measured. With an end-effector robot, we have no idea about how patients move every single joint, since only the end-effector position can be measured.

5.3.2 Rehabilitation

A key advantage of rehab robots is their ability to allow for large numbers of practice repetitions. For example, over 600 movements were performed on average during each of our rehabilitation session. This compares favorably with the 400 to 600 repetitions per day used in animal studies to induce brain plasticity [84, 120], and significantly, this is an order of magnitude above the amount of repetitions performed in conventional, supervised therapy [95]. Rehab robot allow even severely impaired patient to benefit from a high intensity training program without the need to have a therapist next to him/her [126].

However, actual robotics are still relatively expensive and complex, making them impractical for widespread use. Therefore, rehabilitation robots should be further

improved so that they can be used under minimally supervised environments such as at home. One example of such device is described in [188, 189]. These researchers describe a simplistic mechanical device composed of a lever and a spring that can be mounted on a wheelchair. Even High-impaired patients can perform rhythmic back-and-forth movements with their upper limb relying on the resonance properties of the mechanism.

5.4 Perspectives beyond the present thesis

This thesis provided some critical results, but also further opens some perspectives for future research. In this section, some of them are described in more details.

5.4.1 Unravelling how rhythmic and discrete movements are managed by the CNS after stroke

Rhythmic self-paced back-and-forth movements performed by our patients were less harmonic than those of healthy subjects. Actually, their kinematics resembled more to those of healthy discrete movements. This could explain the learning transfer of some movement features such as smoothness and velocity to discrete movements.

Studying these movements in fMRI with stroke patients - similarly than what Schaal and colleagues did in 2004 for healthy subjects [145] - might give interesting results. Even if a large amount of patients would have to be included in such protocols since every brain damaged by stroke is unique, it would be interesting to see whether patients activate different cortical networks for both movements - like healthy subjects - or whether both networks overlap to a larger extent. The latter would suggest that they rely more on discrete pathways than on rhythmic pathways. The relationship between brain activation and kinematic impairments of both movements could also give interesting results.

Pendulum-like movement seem to rely more on peripheral circuits than rhythmic finger-tapping movements [174]. Three types of movements could therefore be compared. Self-paced rhythmic movements of the wrist or elbow, self-paced discrete movements and pendulum-like movements (with the joint being mechanically attached to a swinging pendulum).

5.4.2 Rhythmic movements to leverage the execution of discrete movements

In order to leverage the execution of discrete movements, it might be valuable to combine them with rhythmic movements, since the latter are typically less impaired. One could perform a similar experiment as de Rugy and colleagues (2003) [31] but with a stroke population. This experiment consisted in asking subjects to perform

sinusoidal rhythmic movements and to change a feature (offset and/or amplitude) of the rhythmic movement in a discrete way, at random time-intervals. The authors revealed that the EMG burst associated with the discrete and rhythmic sub-movement tended to occur in synchrony.

With a stroke population, a possible hypothesis is that discrete movements might be performed in a smoother and more precise way than when they are performed alone. This would also support the hypothesis that both movements are partly coupled to each other. Next, these types of exercises could be used to offer a progression in the difficulty of the rehab exercises with more and more discrete sub-movements within a rhythmic background. The final objective would be to compare this type of therapy to conventional therapy.

5.4.3 Other motor learning principles for rhythmic movement therapy

In this thesis, the motor learning paradigm that was chosen was reinforcement training (see Section 1.4.5). The patients were assisted in performing smooth movements above a minimum speed and above a minimum amplitude using a rehab robot. In order to smooth out the rhythmic movements, a virtual spring was attached between the ideal computed position and the actual position of the patient.

Other types of assistances could be offered to the patient. For example, the resonance property could be exploited in rhythmic movement therapy such as in [187]. A (virtual) spring could be attached to a fixed point at one end and on the other end to the hand of the participant. The patient would then have to perform rhythmic movements around that fixed point. Depending on the (virtual) mass and stiffness of the spring the resonance frequencies and amplitudes would differ, allowing practicing the desired rhythmic movement features. The advantage of this method is that the movements will be smoothed out by the spring-mass system and the amplitude of the movement could be higher than what a patient could perform without assistance. This assistance type has already been proven to increase amplitude in movements and increase distal FM scores in severe arm impairments after stroke [187, 188].

As already stated above, movements relying on resonance properties likely rely more on peripheral circuits, as shown e.g. by [174]. Training rhythmic movements with a resonance-based assistance might thus stimulate the patients to be more harmonic than when the movements are performed during self-paced rhythmic movements with our smoothness assistance. Therefore, it could be interesting to compare both assistance types in a rhythmic training with chronic post-stroke patients. More particularly, we question whether the same motor features will transfer for both performance-based and resonance assistance and whether the harmonicity of rhythmic movement would improve more with the resonance-based assistance.

5.4.4 Effect of a rhythmic movement therapy during the acute phase post-stroke

Brain plasticity increases during the acute phase post-stroke [21, 63]. During this phase, enhanced motor activity has been found to enhance functional recovery [77]. Since rhythmic movements seem to be lower in hierarchy, they might be the first movements to recover in order to use them to leverage the execution of more complex discrete movements (see above and Chapter 2).

An RCT with acute post-stroke patients could be performed to test this hypothesis. They could be randomised in a control group receiving rhythmic movement training and a control group trained with dose-matched discrete movement exercises, both on top of their conventional therapy. We could measure their abilities to perform both types of movements besides their motor function and daily life activities after 3 months and 6 months. We could establish which motor function is improved depending on the type of movements that are being trained. We suggest that patients trained with rhythmic movements might perform smoother movements than the control group.

5.4.5 Towards a patient-centered rehabilitation approach

Motor outcomes seem to be predictable early post-stroke [118, 157]. Knowing which patient would benefit the most from a therapy is important in order to optimize the rehabilitation process [157]. Therefore, establishing which patients would benefit the most from rhythmic therapy is interesting. In the longitudinal study presented in chapter 4, a learning transfer appeared from rhythmic to discrete movements. This transfer apparently appeared in both more and less impaired patients; however this cannot be statistically confirmed with our limited dataset.

If the experiment suggested in section 5.4.4 is performed with a large number of patients, we could study whether there is a correlation between the effectiveness of the therapy and one of the assessment scales (let it be a kinematic feature or a clinical scale). With these results and combined with the results of the other suggested experiments, the evolution of the therapy might be optimized in a patient-specific way.

5.4.6 Rhythmic movement therapy of wrist and fingers

About 65% of chronic stroke patients cannot use their affected hand in daily activities, reducing the perception of quality of life [25, 40, 90]. Rhythmic movements are significantly engaged in daily life activities of the hand (handwriting, dactylography, scratching, cuddling,...): recovering rhythmic movements might therefore be a necessary condition to recover these movements. Moreover Squeri et al. (2014) [153]

showed that assistance for small-amplitude oscillation of the wrist leads to improvements in all degrees of freedom of the upper extremity.

An experimental protocol that could be interesting to perform is to perform a similar experiment as in Chapter 4, i.e. train rhythmic flexion-extension movements of the fingers with the performance-based assistance.

5.4.7 Passivity and mutual adaptation of human-robot interactions

Presently, the passivity-like behavior of the performance-based assistance studied in this thesis was only experimentally illustrated (see Appendix B). However, due to the high non-linearity of the controller, the passivity should be further proven quantitatively through more in depth mathematical modelling.

Furthermore, since both human and robot learn, there is a mutual adaptation between both. It is established that adaptive assistance only works when the robot decreases its assistance faster than the rate at which the subject decreases force in the absence of error [43]. Therefore, it is essential to develop quantitative mathematical models of motor learning after post-stroke impairments in order to optimize the robot controller, as a function of the individual dynamics of motor adaptation during a rehabilitation process.

5.4.8 Other pathologies that could benefit from rhythmic therapy

Rhythmic movements are also impaired in other pathologies than stroke such as in the Parkinson disease [83] or after spinal cord injuries [10]. In Parkinson disease for example, training rhythmic movements showed some interests, for instance regarding locomotion [62]. Implementing a performance-based assistance relying on adaptive oscillators could be tested with such patients in order to compare its effectiveness with respect to unassisted gait training.

As a conclusion, this thesis opens many new research perspectives towards brain organization after stroke, and stroke rehabilitation, relying on rhythmic movement primitives.

Overview of the REAplan low-level controller



The low-level controller programmed in the REAplan and used in this thesis was implemented by Julien Sapin and reported in his PhD thesis. This appendix provides a general overview of it. More details can be found in [143].

A.1 General architecture

The REAplan robot is actuated by two DC motors provided with two optical encoders, moving a handle in the horizontal plane. The first motor actuates the handle from left to right through a rail (Rail 1 in Figure A.1 - left). The second actuator is

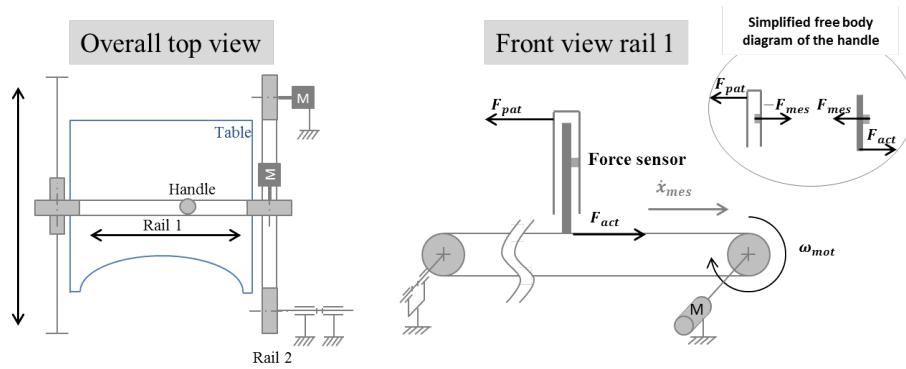


Fig. A.1: Left: Overall kinematic diagram top view of the REAplan. The handle is moved from left to right through rail 1 and back and forth through rail 2. Right: Front view of rail 1 moving the handle from left to right. F_{pat} is the force transmitted by the hand of the patient to the handle. This force is measured by the force sensor F_{mes} which is highlighted in the free body diagram of the handle. F_{act} is the actuation force transmitted by the robot to the handle.

perpendicular to the first one and actuates Rail 1 back and forth, through a second rail (Rail 2).

Figure A.1-right sketches a front view of the first rail with the handle. The handle is equipped with a force sensor in order to measure the forces applied to it, denoted F_{mes} . The hand is considered to be rigidly attached to the handle.

The controller of the REAplan robot is pictured in Figure A.2. The first block consists in a "Virtual system" block. It computes the desired haptic feedback force F_{ref} that the robot should render to the patient. In this thesis, we programmed the virtual system to render the following reference force:

$$F_{ref} = F_f + F_{ass} \quad (A.1)$$

$$= -c_r \dot{x}_{mes} + F_{ass} \quad (A.2)$$

with F_f being a virtual friction force, $\dot{x}_{mes}$ being the actual velocity of the handle, c_r a damping factor and F_{ass} is the assistance given to the patient, as computed by the performance-based assistance presented in details in Chapter 3.

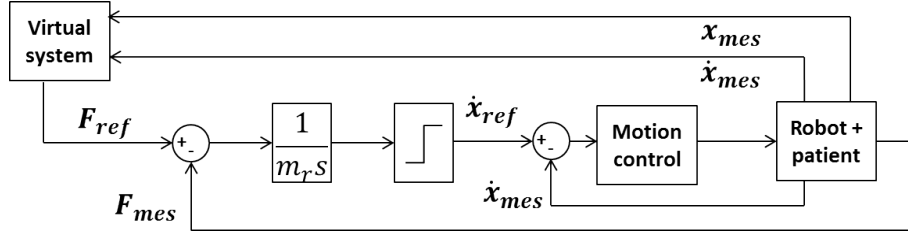


Fig. A.2: REAplan admittance controller, see [143] for more details

The robot is programmed to behave like an admittance operator, governed by the Newton's First law, i.e. the reference acceleration is computed as a function of the force error:

$$F_{ref} - F_{mes} = m_r \ddot{x}_{ref} \quad (A.3)$$

The reference acceleration is next integrated in order to provide a reference velocity $\dot{x}_{ref}$. Finally, m_r is the virtual mass of the robot.

This reference velocity signal $\dot{x}_{ref}$ is controlled by an industrial velocity controller (MAXON EPOS2 50/5)¹, embedded in the robot.

The virtual mass m_r was set as low as possible, as a compromise between actual transparency (the lower the virtual mass, the more transparent the robot), and closed-loop stability (the lower the virtual mass, the higher the reference accelerations). The

¹The sample rate of the PI velocity controller is 1kHz [1]

damping factor c_r was also introduced in order to enhance the robot stability, and also to emulate the behavior of a hand sliding on a table with friction [143].

In our experiments, m_r was set to 0.526kg and $c_r = 2.5\text{kg/s}$. Masses below this value rendered unstable behaviors.

A.2 Experimental validation of the robot impedance in transparent mode

If the low-level velocity controller is considered to be perfect (i.e. $\dot{\mathbf{x}}_{mes} = \dot{\mathbf{x}}_{ref}$) and if the virtual system gives no assistance (i.e. the robot is controlled to be transparent, with $\mathbf{F}_{ass} = 0$), the theoretical impedance of the robot is equal to $Z(s) = \mathbf{F}_{mes}(s)/\dot{\mathbf{x}}_{mes}(s) = c_r - m_r s$ (Figure A.3).

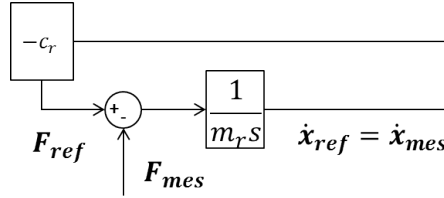


Fig. A.3: Simplified REAplan controller in the transparent mode

Interestingly, the actual equivalent mass m_{equ} and damping factor c_{equ} can further be experimentally computed by fitting an equation similar to (A.2) and (A.3) to actual data, i.e.: $F(t) = m_{equ}\ddot{\mathbf{x}}(t) - c_{equ}\dot{\mathbf{x}}(t)$ in the least squares sense:

$$\min_{[m_{equ}, c_{equ}]} \sum_i (F([m_{equ}, c_{equ}], [\ddot{\mathbf{x}}_{mes}, \dot{\mathbf{x}}_{mes}]_i) - F_{mes,i})^2 \quad (\text{A.4})$$

We performed a short supplementary experiment to identify these parameters, where a subject was asked to perform back and forth movements in the saggital plane (i.e. along rail 2 in Figure A.1). Movements were requested to cover the widest range of frequencies that can be executed with the robot. The subject managed to execute back and forth movements at frequencies from 0.5Hz to 4.5Hz (Figure A.4). The least-square fit provided the following results: equivalent mass $m_{equ} = 0.527\text{kg}$ and equivalent damping factor $c_{equ} = 2.58\text{kg/s}$, using the MATLAB function `lsqcurvefit`. These are thus very close to the values that were actually injected in the robot controller.

The experimental and theoretical Bode diagrams of the transfer function between from $\mathbf{F}_{mes}$ to $\dot{\mathbf{x}}_{mes}$ are pictured in Figure A.5. The theoretical Bode diagram was

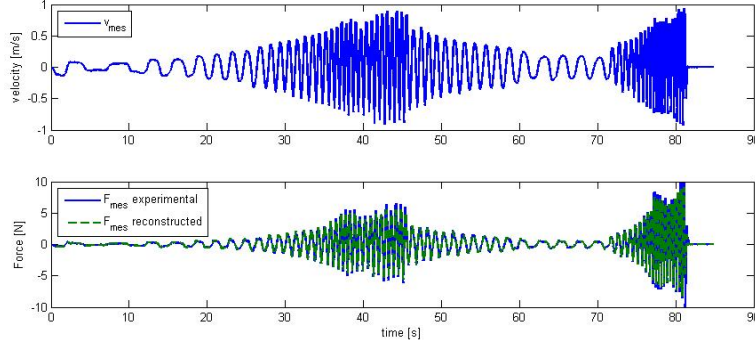


Fig. A.4: Experimental data used to compute the equivalent mass and damping factor m_{equ} and c_{equ} respectively. On the top $\dot{x}_{mes}$ and on the bottom F_{mes} and the reconstructed force vector computed with the equivalent mass and damping factor.

obtained from the following transfer function

$$\frac{1}{m_{equ}s + c_{equ}} = 1/c_{equ} \frac{1}{1 + c_{equ}/m_{equ}s}. \quad (\text{A.5})$$

The experimental curve is obtained by estimating the empirical transfer functions. This was performed using the MATLAB functions `iddata` and `etfe`.

Both experimental and theoretical Bode diagrams match on average, validating the hypothesis that the time constant of the low-level velocity controller is much smaller than the time constant of this admittance controller, and thus that $\dot{x}_{mes} = \dot{x}_{ref}$ is a valid hypothesis.

Moreover, Figure A.3 and Equation (A.5) straightforwardly reveal the transfer function from F_{mes} to F_{ref} is equal to $\frac{-c_r}{c_r - m_r s}$. The cut-off frequency of this first-order operator is thus equal to $\omega_c = c_r/m_r = 4.75\text{Hz}$. This means that the measured forces are significantly low-pass filtered with respect to the reference one. Said differently, this puts a limit to the controller bandwidth since any higher harmonics of the reference force will be filtered out in the measured one.

A.3 Virtual walls

In all experiments reported in this work, the robot workspace was limited by virtual walls. Moreover, in Chapter 2, the handle was constrained to move on a vertical line, so that the vertical virtual walls were moved very close to each other. This section briefly explains how the robot was controlled to render these virtual walls.

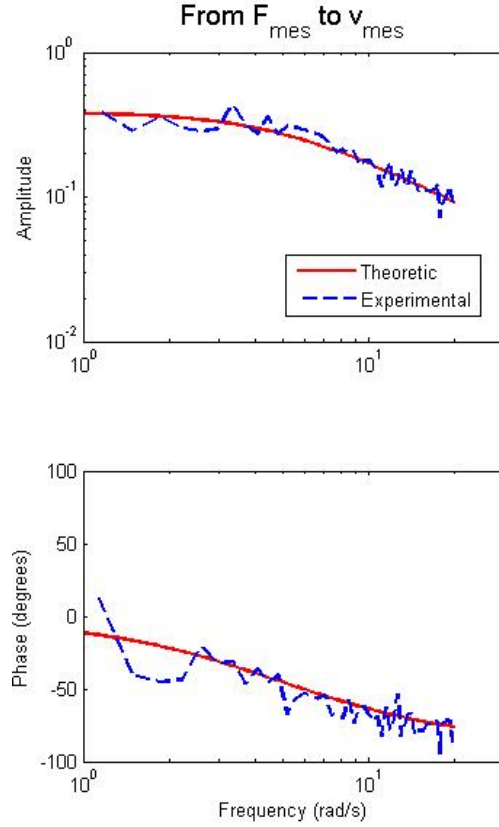


Fig. A.5: REAplan experimental (blue) and theoretical (red) Bode diagram from F_{mes} to $\dot{x}_{mes}$.

The virtual walls of the REAplan are implemented this way: If the actual position of the handle goes beyond one of the virtual walls of the workspace and if the desired velocity is pointing outwards of the workspace, the desired velocity commanded to the actuator, i.e. $\dot{x}_{ref}$, is set to zero.

The stiffness of these walls depend thus on the bandwidth of the low-level velocity controller. In chapter 2, the participants could not move out of the straight line. The reference velocity in this direction $\dot{x}_{ref,x}$ was thus always set to 0.

A.4 Conclusion

The REAplan robot behaves thus as a damped mass, with a virtual mass of 0.528kg and a damping factor of about 2.58kg/s. This gives a cut-off frequency being equal to

4.75Hz for the force measurement loop. Therefore, all frequencies above this value will be smoothed out. This is not negligible since human motion can go far beyond this threshold.

Mechanical work from the robot to the patient

B

The mechanical work done by a force $\mathbf{F}$ acting at a point on a component that moves from one point s_1 to another s_2 is

$$W = \int_{s_1}^{s_2} \mathbf{F} \cdot d\mathbf{s} \quad (\text{B.1})$$

From equations (A.2) and (A.3) in Appendix A, we know that the low-level robot dynamics is rendered by:

$$\mathbf{F}_{ass} - \mathbf{F}_{mes} = m_r \ddot{\mathbf{x}}_{mes} + c_r \dot{\mathbf{x}}_{mes} \quad (\text{B.2})$$

with $\mathbf{F}_{mes}$ being the interaction force between the patient and the robot, measured by the force sensors of the handle. $\mathbf{F}_{ass}$ is the assistance force, $c_r \dot{\mathbf{x}}_{mes}$ is a virtual friction force and $m_r \ddot{\mathbf{x}}_{mes}$ is an inertial force due to the robot's virtual mass m_r .

The mechanical work transferred from the robot to the patient during one movement cycle is therefore equal to:

$$W = \int^{cycle} \mathbf{F}_{mes} \cdot d\mathbf{s} \quad (\text{B.3})$$

$$= \int^{cycle} (\mathbf{F}_{ass} - c_r \dot{\mathbf{x}}_{mes} - m_r \ddot{\mathbf{x}}_{mes}) \cdot d\mathbf{s} \quad (\text{B.4})$$

$$= \int^{cycle} (\mathbf{F}_{ass} + \mathbf{F}_{imp}) \cdot d\mathbf{s} \quad (\text{B.5})$$

$$= \int^{cycle} (\mathbf{P}_{ass} + \mathbf{P}_{imp}) dt \quad (\text{B.6})$$

where $\mathbf{F}_{imp} = -c_r \dot{\mathbf{x}}_{mes} - m_r \ddot{\mathbf{x}}_{mes}$ was defined to be the force rendered by the virtual impedance of the robot, and $\mathbf{P}_{imp} = \mathbf{F}_{imp} \cdot \dot{\mathbf{x}}_{mes}$ and $\mathbf{P}_{ass} = \mathbf{F}_{ass} \cdot \dot{\mathbf{x}}_{mes}$ are the respective powers produced to the impedance and assistance forces. Moreover, in this appendix, we will only focus on the smoothness assistance force, i.e. the one that was by far the most recruited during the experiments reported in chapters 3 and 4. Remember that this force was defined as

$$\mathbf{F}_{ass} = k_{sm}(\mathbf{x}_{osc} - \mathbf{x}_{pat}) + c(\dot{\mathbf{x}}_{osc} - \dot{\mathbf{x}}_{pat}) \quad (\text{B.7})$$

where $\mathbf{x}_{osc}$ and $\dot{\mathbf{x}}_{osc}$ are estimates of the patient's position and velocity provided by an adaptive oscillator (see Chapter 3). Here, we can consider that $\mathbf{x}_{pat} = \mathbf{x}_{mes}$ and $\dot{\mathbf{x}}_{pat} = \dot{\mathbf{x}}_{mes}$.

B.1 Passivity-based control

Previous research established passivity-based control as an valuable tool to design controllers for human-robot interaction [121]. The basic idea behind passivity-based control is that it is safer to let a human interact with a passive robot, since the closed-loop human-robot behavior can then never become unstable as long as the human is stable. This claim makes even more sense if the human is a patient with disabled motor control capacities.

Proving passivity requires to prove that the mechanical work (or energy) produced by the robot is always smaller than a positive value, representing the initial energy stored in the system at initial time [152]. In passive systems, the amount of energy that can be extracted is thus bounded.

It is not trivial to prove that the smoothness assistance induced a passive behavior, since the dynamics governing the adaptive oscillator and the modulation of the assistance gains are highly non-linear. Instead, we completed a series of experiments illustrating that the amount of energy injected into the system is bounded, even in very extreme scenarios.

The mechanical work provided by the robot to the patient can be decomposed into three contributions, following (B.4): the work provided by the virtual friction force, the rendered inertial force and the actual assistive force. The work provided by the friction force is always negative. The work provided by the rendered mass over one cycle by should be equal to zero¹, assuming the movement to be circular with a constant speed on average. Therefore, the work done by the sum of these two terms (i.e. by the robot virtual impedance force $\mathbf{F}_{imp}$) should always be negative.

¹Since the the displacement vector $d\mathbf{s}$ and $m\ddot{\mathbf{x}}$ are perpendicular when moving in a circle and the scalar product of two perpendicular vectors is equal to zero.

If the patient performs a perfectly circular trajectory, the adaptive oscillator will eventually get perfectly synchronized to the patient movement, so that, the work done by the smoothness assistive force F_{ass} is equal to zero, since this force will also be equal to zero.

During very jerky movements, the assistance should dissipate mechanical energy from the patient due to its damping factor. When a participant deviates from the steady state, for example if he/she accelerates or decelerates, the smoothness assistance will attract him/her to the previously learned kinematics. If he/she maintains a new steady-state behavior, the adaptive oscillator will synchronize to his/her new movement features and the assistance will decrease accordingly. The amount of energy injected into the system should therefore stay bounded.

In Chapter 3, we already pointed out that our two patients did not receive mechanical energy from the robot controlled by the performance-based assistance, on average. This result was obtained by measuring the overall mechanical work (equation B.3) provided to these patients over each cycle during each trial.

In the following sections, we report some complementary experiments that were conducted in order to further illustrate the passivity-like behavior of this performance-based assistance.

B.2 Methods

One female subject was requested to perform different behaviors during circular rhythmic exercises with the REAplan. The subject was 30 years old and was familiar with the REAplan and the smoothness assistance.

First, the subject was requested to draw 10 rhythmic circles at a comfortable speed and amplitude. This corresponded to the initialization phase as described in details in Chapter 3. During this phase, the robot was configured to be transparent (see Appendix A) and learned the movement features such as the amplitude, offset and frequency of the rhythmic circular movements by means of an adaptive oscillator.

Next, the subject was asked to perform rhythmic circular movements inside a circular path with inner radius set at the learned amplitude (computed during the initialization phase). The performance-based smoothness assistance was activated after 10 seconds (the amplitude and velocity assistance were set to zero). Each trial lasted 60 seconds.

The first trial was requested to be performed as smoothly as possible while adopting constant amplitude, offset and frequency. During the second trial, the subject was asked to perform jerky submovements (lateral and longitudinal errors) on top of her steady-state circular trajectory. In the third trial, the subject was asked to move

with a lower frequency during the first 20 seconds following the 10 first seconds without assistance. Next the participant had to adopt again the initial frequency. During the last trial, the subject was requested to smoothly accelerate during 20 seconds and next to smoothly decelerate to reach the initial frequency after 20 seconds.

During these trials, measurements from the force sensors $\mathbf{F}_{mes}$ and the absolute position of the handle $\mathbf{x}_{mes}$ were recorded at a sample frequency of 125Hz, while the position filtered by the adaptive oscillator $\mathbf{x}_{osc}$ and the amount of assistance $k\%$ were also recorded with the same sampling rate.

The work done by the robot to the patient was reconstructed by decomposing this work into the one due to the robot impedance (by using the equivalent mass and viscous factor computed in Appendix A) and the one due to the assistance force (Equation B.7) with $k_{sm} = k\%k_{max}$ and $k_{max} = 157.4\text{kg/s}^2$. In trial 1 and 2, $k\%$ is the gain of the assistance proportional to a smoothness metric (see Chapter 3 for computational details). In trial 3 and 4, the gain was set to 30%¹. The estimated total work W_{tot} is the sum of these two works, and it should be equal to the work actually provided by the robot, which can be retrieved with the recorded interface force $\mathbf{F}_{mes}$.

B.3 Results

B.3.1 Trial 1: smooth movements require no assistance

During the first trial the subject performed the task without receiving the performance based assistance since the smoothness of her movements stayed below the threshold for triggering this assistance (Figure B.1). Indeed, the gain of the performance-based assistance stayed almost always equal to zero (except between 10 and 15 seconds where it reached about 3%). In this trial, the work done by the rendered impedance $\mathbf{F}_{imp}$ is, as expected, always negative (second graph of Figure B.1) and consequently, the integral of this power over each cycle (W_{imp}) is also always negative (fourth graph of Figure B.1). In sum, the robot dissipated energy from the human participant.

B.3.2 Trial 2: negative work during jerky movements

During this jerky trial, the amount of assistance provided to the participant saturated to 100% from the 15th second until the end of the trial. During the first 10 seconds, when the assistance was not activated, only the robot impedance generated negative work transfer between the robot and the participant (Figure B.2). Next, the work

¹Otherwise, the gain would be almost always equal to zero since smooth acceleration and steady-state behavior makes the assistance gain saturate to zero (see Chapter 3 for more details).

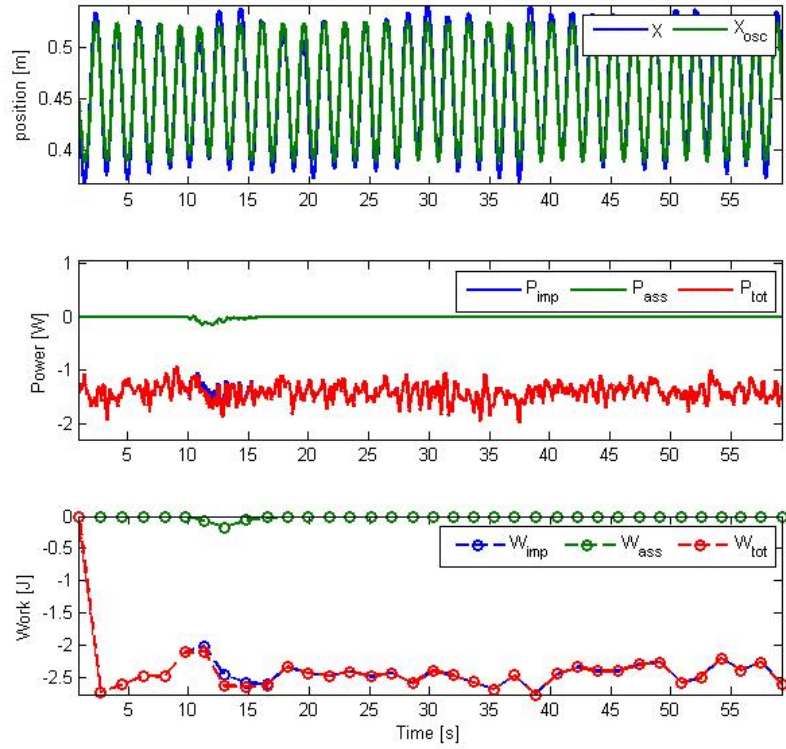


Fig. B.1: The top graph presents the position signal on the X-axis (from left to right), in blue the actual position of the handle, in green, the computed signal by the adaptive oscillator. The second graph presents the power done by the residual impedance of the robot and by the smoothness assistance force. The third graph presents the amount of work done by these forces during each cycle. During the first 10 seconds no assistance is delivered. Next, the gain of the assistance is proportional to the performance. Since smooth movements are performed the gain reaches maximum 1% during the next 5 seconds and stays at 0% afterwards.

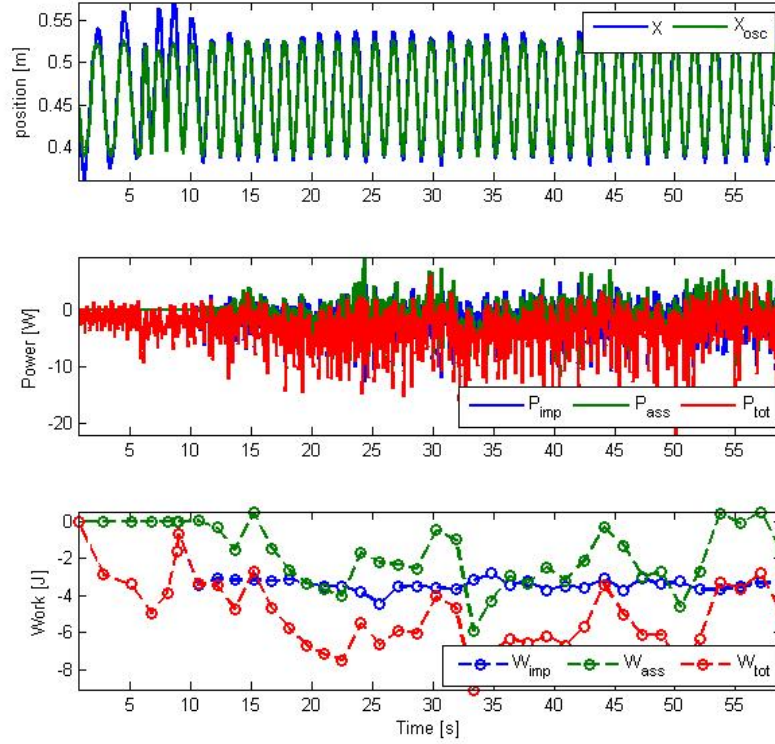


Fig. B.2: The top graph presents the position signal on the X-axis (from left to right), in blue the actual position of the handle, in green, the computed signal by the adaptive oscillator. The second graph presents the power done by the residual impedance of the robot and by the smoothness assistance force. The third graph presents the amount of work done by these forces during each cycle. During the first 10 seconds no assistance is delivered. Next, the gain saturates at 100%.

done by the smoothness assistance was negative over each cycle. This is likely due to the virtual friction component of the assistance force (Equation B.7).

B.3.3 Trial 3: bounded work during step velocity

In this trial, the subject performed movements with a lower pace once the assistance was switched on. Therefore, the assistance tried to accelerate the participant since the adaptive oscillator is in front of the actual position of the subject. The assistance therefore produced positive work transferred to the subject. Interestingly, it remained bounded since the adaptive oscillator progressively synchronised to this new frequency. This is visible in Figure B.3 (between $t = 12s$ and $t = 22s$). The power

provided by the assistance force decreased because the error between the adaptive oscillator and the actual position of the subject and the adaptive oscillator gradually decreased. Moreover, during this trial, the work dissipated by the robot impedance was lower since the viscous component of this force was proportional to the velocity of the subject.

When the subject reached again her initial frequency, the assistance force was negative while the adaptive oscillator was no longer synchronized with the movement frequency. Once the steady-state behavior is reached (after 45 seconds in Figure B.3), the work produced by the assistance force over each cycle reached almost zero, since the oscillator was again synchronized to the actual movement.

B.3.4 Trial 4: bounded work during smooth acceleration

Similar observations can be reported for the last trial (Figure B.4). Indeed, the work dissipated by the robot impedance decreased or increased with the movement frequency. The work produced by the assistance force was negative when the subject accelerated and positive when she decelerated. During the acceleration phase (between $t = 15\text{s}$ and $t = 30\text{s}$), the subject accelerated faster than the learning rate of the adaptive oscillator, inducing increasing velocity and position errors between the adaptive oscillator and the actual position. Therefore, the work decrease after each cycle.

During the deceleration phase (between $t = 30\text{s}$ and $t = 55\text{s}$), the frequency decreased more slowly, giving enough time to the adaptive oscillator to progressively synchronise to the actual frequency (after 55 seconds). The work done over each cycle was thus more or less stable over this interval. Moreover, this work was positive since the subject was always in front of the adaptive oscillator. After 55 seconds, the subject reached again a steady-state behavior. The work done by the assistance force reached zero again, since neither velocity nor position errors were detected.

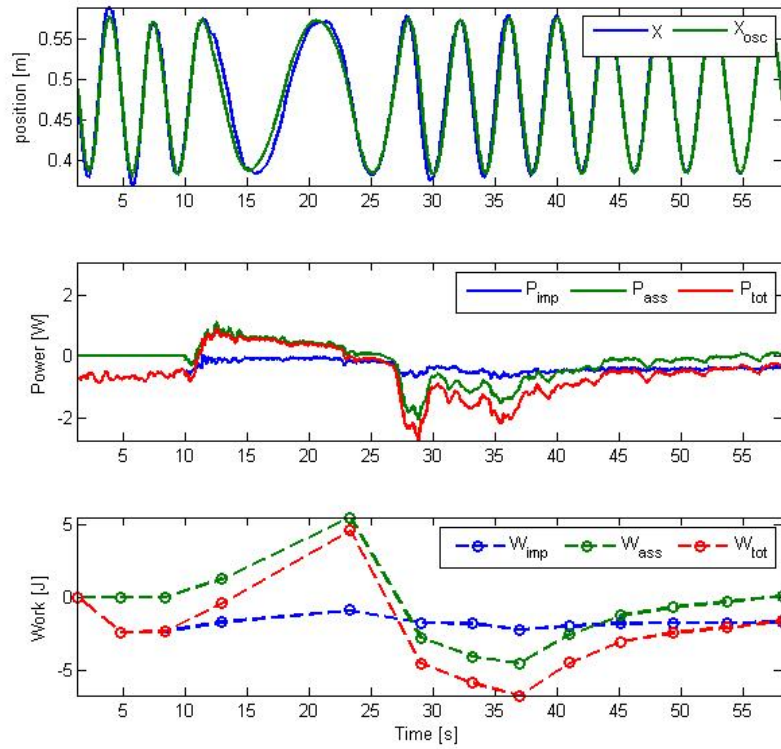


Fig. B.3: The top graph presents the position signal on the X-axis (from left to right), in blue the actual position of the handle, in green, the computed signal by the adaptive oscillator. The second graph presents the power done by the residual impedance of the robot and by the smoothness assistance force. The third graph presents the amount of work done by these forces during each cycle. During the first 10 seconds no assistance is delivered. Next, the gain of the assistance is set to 30%.

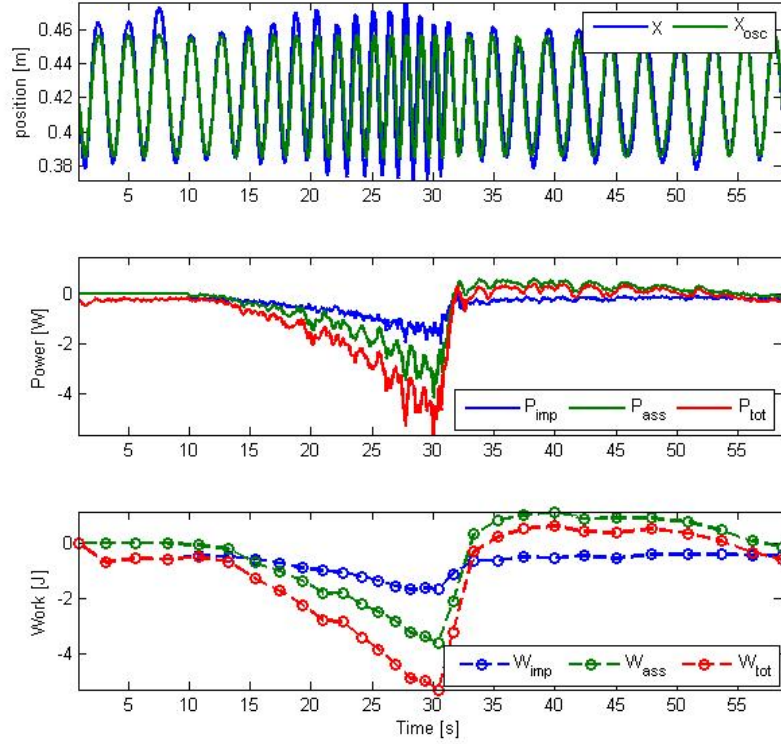


Fig. B.4: The top graph presents the position signal on the X-axis (from left to right), in blue the actual position of the handle, in green, the computed signal by the adaptive oscillator. The second graph presents the power done by the residual impedance of the robot and by the smoothness assistance force. The third graph presents the amount of work done by these forces during each cycle. During the first 10 seconds no assistance is delivered. Next, the gain of the assistance is set to 30%.

B.4 Conclusion

Even when the participant was performing very unlikely movements, such as very jerky movements, or when she abruptly changed her pattern during the exercise, the amount of energy injected by the robot over each cycle stayed bounded.

This short complementary experiment thus showed that the smoothness assistance (i.e. the one that was mainly recruited by our stroke participants) rendered a passive-like behavior, even if jerky movements were produced, or if the movement frequency was abruptly changed. Similar results can be observed if changing the other state variables, like amplitude and offset.

Some safety rules were further implemented in the smoothness assistance in order to saturate the force being delivered. If the position error exceeded 0.03m or the velocity error exceeded 0.05m/s, the errors saturated at these threshold values.

Details about the mixed model equation



The mixed model equation that was used in our analyses in section 2.2.5 is the following:

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\boldsymbol{\gamma} + \boldsymbol{\epsilon}$$

where $\mathbf{Y}$ is the $n \times 1$ vector of responses (n being the number of observations), $\mathbf{X}$ is the $n \times p$ design matrix for the fixed effects (p being the number of variables, i.e. the factors and their interactions); $\boldsymbol{\beta}$ is a $p \times 1$ vector of unknown fixed effects with the design matrix $\mathbf{X}$; $\mathbf{Z}$ is the $n \times s$ design matrix for the random effects (with s being the number of subjects); $\boldsymbol{\gamma}$ is a $s \times 1$ vector of unknown random effects with the design matrix $\mathbf{Z}$; and $\boldsymbol{\epsilon}$ is a $n \times 1$ vector of unknown random errors. Note that both $\boldsymbol{\gamma}$ and $\boldsymbol{\epsilon}$ follow a Gaussian distribution, i.e. $\boldsymbol{\epsilon} \sim N(0, \mathbf{G})$ with $\mathbf{G}$ being a $s \times s$ diagonal matrix with identical entries for each effect, and $\boldsymbol{\epsilon} \sim N(0, \sigma^2 \mathbf{I}_n)$ with $\mathbf{I}_n$ being the $n \times n$ identity matrix. The covariance structure for this model is also called a "variance component structure". A distinct variance component is assigned for each of the random effects (here, one single random effect, i.e. the subject effect), and the covariances are null.

Reference: SAS/STAT 9.2 User's Guide, 2008, p.3955

Performance-based assistance and feedback delivered to the patient during the longitudinal study

D

During the first 10 seconds of the task, the robot was set in transparent mode. Next, the robot started to deliver a performance-based assistance in amplitude, velocity and smoothness. These three types of assistance proportionally increased with a corresponding on-line performance index ($\epsilon_{sm}, \epsilon_{vel}, \epsilon_{amp}$). These performance indexes offered to tune the gains of the assistance ($k_{\%,sm}, k_{\%,vel}, k_{\%,amp} \in [0, 1]$) in order to deliver appropriate assistive forces in smoothness, velocity and amplitude, i.e. $F_{smoothness}, F_{velocity}, F_{amplitude}$. For more information about these assistances, refer to chapter 3 or [98].

Each exercise was executed in a random order during 60 sec and was repeated 3 consecutive times. At the end of each trial, the patient received a feedback about his/her average performance in amplitude, velocity and smoothness and an overall score computed as 100 minus the maximum between the three average levels of the corresponding assistive gains. A feedback sentence was also displayed on the screen as a function of their average performance.

- If score > 98% : Well done!
- If score > 90% : A few more efforts before reaching perfection
- If score < 90% : To improve your score, try to
- If $avg(k_{\%,sm}) < 90\%$: make smoother movements,

- If $avg(k_{(\%,vel)}) < 90\%$: go fast enough in order to keep a green track/target,
- If $avg(k_{(\%,amp)}) < 90\%$: stay inside the displayed track/target.

Evolution of the assessment during the therapy of the longitudinal study

E

In chapter 3 (and corresponding [98]), we reported preliminary results of the evolution of the performance based assistance with two patient, during one therapy session only. These results highlighted that no slacking occurred neither during one trial, nor across 5 consecutive trials. The "slacking hypothesis" suggests that too much assistance will cause a progressive decrease in patient effort to accomplish a desired task and reduce motor recovery. If patients display slacking behavior, the amount of assistance should increase over time. These results are confirmed with our larger stroke population, as illustrated in this appendix.

E.1 No slacking over sessions

The amount of assistance provided to the patients did not increase from one session to the other. This demonstrates that the patients did not rely more and more on the assistance to fulfil the exercises. Practically speaking, we computed the regression slope of the average amount of assistance provided over the twelve therapy session, for each exercise independently. The slope was statistically not different from zero ($p > 0.05$) for every exercise and for the three assistive forces.

E.2 No slacking within one trial

The amount of assistance provided during one trial did not increase either, for all exercises. Here, we computed the average level of assistance during every movement

of each patient and trial. Next, these levels were plotted as a function of the time when the corresponding movement started, time 0 being the beginning of the trial. Next a linear regression slope was computed, capturing thus the evolution of the assistive gain as a function of time. This slope was significantly higher than zero for none of the 234 tests we performed (13 patients x 3 trials x 6 tasks).

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