Adaptation, Consolidation, and Generalization Mechanisms in Human Motor Control and Learning

Development of a methodological framework and conduction of psychophysical studies

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Summary

Movements are important aspects of human life because they are our only possibility to interact with the world. For instance, talking, gestures, writing, object manipulation, et cetera require well-coordinated muscle contractions. In order to enable skilled movements, the human sensorimotor system has to solve the highly complex problem of controlling a redundant system comprising a multitude of degrees of freedom. Against this background, arm movements are of particular interest. Arm movements have a high practical value in terms of manipulating objects, but they also demonstrate many aspects which make motor control and learning hard to decode. Besides the problem of redundancy, the sensorimotor system is constantly exposed to changes in the internal and external conditions. This requires permanent adaptation in order to maintain the control and enable skilled movements. Yet, it remains puzzling how the sensorimotor system manages these control and learning processes. A more profound understanding of the mechanisms underlying motor control and learning is a prerequisite for designing safer workplaces, better tools, prostheses, and robots, as well as more effective training schedules in sports and neurorehabilitation. For these reasons, this thesis investigates motor control and learning of arm movements with special consideration of motor memory adaptation as well as its consolidation and generalization.

The thesis encompasses five main chapters. Chapter 1 gives a general introduction. Therein, the outline of the thesis is depicted and the theoretical and methodological fundamentals of motor control and learning are introduced. In particular, the current state of research on adaptation of motor memory as well as its consolidation and generalization is considered. Furthermore, the theory of internal models is introduced. Internal models are assumed to be neural representations of the mechanical properties of the body and the environment which enable the sensorimotor system to perform skilled movements. Moreover, the experimental paradigm of robot-assisted force field adaptation is introduced. Therein, subjects interact with a robotic manipulandum and adjust reaching movements to robot-induced dynamic perturbations by adapting their internal models of the task. The introductory chapter ends with the specification of the aims and scope of the thesis.

In Chapter 2, a methodological basis for the investigation of motor control and learning using robot-assisted force field experiments is established. Despite the wide-spread usage of this experimental paradigm, no methodological standards exist. Rather, diverse methods are used which respectively emphasize different aspects of motor control and learning. This chapter reviews the existing analytic approaches, integrates them in a methodological framework, and introduces a tailor-made software application, named ManipAnalysis, for the analysis of force field experiments. The developed methodological framework serves as basis for the subsequently reported psychophysical studies.

Chapter 3 presents a study on the adaptation and consolidation of motor memory. It is well accepted that motor memory consolidation is a time-dependent process. Yet, the detailed influence of the practice schedule during motor adaptation on the subsequent consolidation process remains a contentious issue. Therefore, we investigated the consolidation of motor adaptation under diverse practice conditions. Therein, different subject groups adapted their reaching movements to dynamic perturbations of different stability. On the one hand, we found that unstable compared to stable practice conditions impair the adaptation of an internal model of the task. On the other hand, the results indicate that unstable practice conditions can foster the consolidation of motor memory by increasing its resistance to interfering factors. Thus, consolidation of motor adaptation is not only a time-dependent but also a practice-dependent process. This study is the first considering these issues across a wide range of different practice conditions. It reveals that not instability per se is crucial to foster motor memory consolidation, but rather there seems to exist an optimal amount of instability.

The study reported in Chapter 4 considers motor adaptation and its generalization. Generalization of motor learning denotes the ability to transfer previously learned motor actions to different tasks or contexts. Accordingly, knowledge gained through practice in one situation changes motor performance in a different situation. In particular, we investigated intermanual transfer (i.e., generalization of motor learning across hands) with special consideration of its direction and coordinate frame as well as the influence of consolidation processes on this transfer. Therein, subjects adapted their reaching movements to dynamic perturbations and were tested for transfer to the contralateral hand either immediately after practice or after a 24 h consolidation period. The study is the first detecting transfer of dynamic adaptation both from dominant to non-dominant hand and vice versa. This transfer occurred in an extrinsic (Cartesian-based) coordinate frame. However, after the consolidation period, transfer effects were weakened. Moreover, the study is the first to account for two different features of intermanual transfer. First, practice-dependent bias, i.e., the change in the prediction of the task conditions due to previous contralateral practice. Second, interlimb savings, i.e., the ability of faster relearning of the task due to previous contralateral practice.

The final Chapter 5 comprises a general discussion of the considered research issues, deduces implications for future research, and states general conclusions. We regarded several analytic approaches for the assessment of motor performance and outlined that they emphasize different aspects of motor control and learning (e.g., different control mechanisms), which may lead to different concluding outcomes. Our psychophysical experiments reveal that unstable practice conditions impair internal model formation during adaptation but can foster subsequent consolidation processes. Furthermore, for the first time, we found that intermanual transfer of dynamic adaptation is a bidirectional phenomenon which occurs in extrinsic coordinates and weakens with time. These findings offer valuable information for our understanding of human motor control and learning and, thus contribute to an interdisciplinary field of research involving human movement science, neuroscience, and robotics.

Zusammenfassung

Bewegungen sind eine wichtige Facette des menschlichen Lebens, da sie unsere einzige Möglichkeit sind mit der Umwelt zu interagieren. So basieren beispielsweise Sprache, Gestik, Schrift, Objektmanipulation etc. auf koordinierten Muskelkontraktionen. Zur Ausführung präziser Bewegungen, muss das sensomotorische System ein hochkomplexes Problem lösen, das die Kontrolle eines redundanten Systems mit einer Vielzahl an Freiheitsgraden verlangt. Vor diesem Hintergrund sind insbesondere Armbewegungen von Interesse. Zum einen haben diese eine hohe praktische Relevanz, da sie die Manipulation von Objekten ermöglichen. Zum anderen können anhand von Armbewegungen viele jener Aspekte betrachtet werden, welche die Komplexität motorischer Kontrolle und motorischen Lernens begründen. Neben dem Problem der Redundanz, ist das sensomotorische System zudem ständig veränderten internalen und externalen Bedingungen ausgesetzt. Dies verlangt eine fortwährende Anpassung motorischer Gedächtnisinhalte, um die Kontrolle über das System sicherzustellen und präzise Bewegungsausführungen zu ermöglichen. Allerdings bleibt bis dato unklar wie das sensomotorische System diese Kontroll- und Lernprozesse steuert. Ein fundamentales Verständnis motorischer Kontroll- und Lernprozesse und deren zugrundeliegender Mechanismen ist eine wichtige Voraussetzung für die Entwicklung sicherer Arbeitsplätze, besserer Werkzeuge, Instrumente, Prothesen sowie Roboter, aber auch effektiver Trainingsprogramme im Bereich des Sports und der Neurorehabilitation. Aus genannten Gründen wird im Rahmen der voliegenden Dissertation die motorische Kontrolle sowie motorisches Lernen bei Armbewegungen untersucht. Dabei wird im Speziellen die Adaptation motorischer Gedächtnisinhalte sowie deren Konsolidierung und Generalisierung betrachtet.

Diese Dissertation umfasst fünf Kapitel. Kapitel 1 liefert eine allgemeine Einführung in die Thematik. Dabei werden die Gliederung der Arbeit vorgestellt sowie die theoretischen und methodischen Grundlagen zu motorischen Kontroll- und Lernprozessen aufbereitet. Insbesondere wird der aktuelle Forschungsstand zur Adaptation motorischer Gedächtnisinhalte sowie deren Konsolidierung und Generalisierung betrachtet. Weiterhin wird die Theorie der Internen Modelle vorgestellt. Interne Modelle stellen neuronale Repräsentationen der mechanischen Eigenschaften des Körpers und der Umwelt dar, welche dem sensomotorischen System die präzise Ausführung von Bewegungen ermöglichen. Zudem wird das experimentelle Paradigma der robotergestützen Kraftfeldexperimente eingeführt, bei dem Probanden mit einem Robotermanipulandum interagieren und ihre Armbewegungen an dynamische Störungen anpassen. Diese Anpassung wird mit der Adaptation des zugrundeliegenden Internen Modells der Aufgabe erklärt. Das einleitende Kapitel schließt mit der Bestimmung von Zielsetzung und Aufgabenstellung der Arbeit.

In Kapitel 2 wird die methodische Grundlage für die nachfolgenden Untersuchungen motorischer Kontroll- und Lernprozesse entwickelt. Dabei stehen robotergestützte Lernexperimente im Mittelpunkt. Trotz der weiten Verbreitung dieses experimentellen Paradigmas existieren keine methodischen Standards, sondern es findet vielmehr eine Vielzahl an Methoden Anwendung. Hierbei werden jeweils unterschiedliche Aspekte motorischer Kontrolle bzw. motorischen Lernens akzentuiert, was vermeintlich Ergebnisse und die darauf basierenden Schlussfolgerungen beeinflusst. Daher werden die bestehenden analytischen Ansätze aufgearbeitet und in einen gemeinsamen methodischen Rahmen integriert. In diesem Zusammenhang wird die Softwareapplikation ManipAnalysis vorgestellt, welche zur Analyse von Kraftfeldexperimenten entwickelt wurde. Der hierbei geformte methodische Rahmen bildet die Basis für die nachfolgend durchgeführten Experimente.

In Kapitel 3 wird eine erste Studie zur Adaptation und Konsolidierung motorischer Gedächtnisinhalte beschrieben. Zwar ist weitestgehend anerkannt, dass die Konsolidierung motorischer Gedächtnisinhalte ein zeitabhängiger Prozess ist, der detaillierte Einfluss der Übungsbedingungen während der motorischen Adaptation auf den nachfolgenden Konsolidierungsprozess ist jedoch unklar. Aus diesem Grund wurde die Konsolidierung nach motorischer Adaptation unter verschiedenen Übungsbedingungen untersucht. Dabei haben Probanden verschiedener Gruppen ihre Armbewegungen an dynamische Störungen unterschiedlicher Stabilität adaptiert. Zum einen zeigen die Ergebnisse, dass instabile Übungsbedingungen die Adaptation eines Internen Modells der Aufgabe beeinträchtigen. Zum anderen zeigte sich, dass instabile Übungsbedingungen den Konsolidierungsprozess begünstigen, da die dabei ausgebildeten motorischen Gedächtnisinhalte eine erhöhte Resistenz gegenüber Interferenz besitzen. In der Studie wurde erstmals die Adaptation und Konsolidierung über eine große Bandbreite verschiedener Übungsbedingungen hinweg untersucht. Dabei ergab sich, dass nicht Instabilität per se eine Begünstigung des Konsolidierungsprozesses bewirkt, sondern vielmehr ein optimales Maß an Instablität zu existieren scheint. Somit belegt die Studie, dass instabile Übungsbedingungen zwar die Adaptation Interner Modelle beeinträchtigen, jedoch deren Konsolidierungsprozess begünstigen. Damit deuten die Befunde darauf hin, dass Konsolidierung motorischer Adaptation nicht nur ein zeitabhängiger sondern auch ein übungsabhänginger Prozess ist.

Die in Kapitel 4 beschriebene Studie untersucht motorische Adaptation und deren Generalisierung. Dabei bezeichnet die Generalisierung motorischer Gedächtnisinhalte die Fähigkeit zuvor gelerntes motorisches Handeln auf eine andere Aufgabe oder in einen anderen Kontext zu transferieren. Demzufolge können durch Übung erlangte Erkenntnisse in einer Situation die motorische Leistungsfähigkeit in einer anderen Situation beeinflussen. Im Speziellen wird in der Studie der intermanuelle Transfer (d.h. die Generalisierung motorischen Lernens zwischen Händen) betrachtet. Hierbei werden Richtung und Koordinatensystem (interne Repräsentation) des intermanuellen Transfers analysiert sowie der Einfluss von Konsolidierung auf diesen Transfer. Dazu adaptierten Probanden ihre Armbewegungen an ein Kraftfeld und wurden daraufhin entweder unmittelbar oder nach einer 24-stündigen Konsolidierungsphase auf der kontralateralen Hand auf Transfereffekte getestet. In dieser Studie konnte erstmals Transfer einer dynamischen Adaptationsaufgabe sowohl von der dominanten auf die nicht-dominante Hand, als auch von der nicht-dominanten auf die dominante Hand gezeigt werden. Der Transfer erfolgte in einem extrinsischen (kartesischen) Koordinatensystem. Nach der Konsolidierungsphase waren die Transfereffekte jedoch abgeschwächt. Zudem werden in der Studie erstmals zwei unterschiedliche Merkmale intermanuellen Transfers berücksichtigt: Zum einen *practice-dependent bias*, welcher die veränderte Prädiktion der Aufgabenstruktur aufgrund vorangehenden kontralateralen Übens beschreibt, zum anderen *interlimb savings*, d.h. die Fähigkeit zum schnelleren Erlernen der Aufgabe aufgrund vorangehenden kontralateralen Übens.

Im abschließenden Kapitel 5 findet eine Diskussion der zuvor betrachteten Forschungsinhalte sowie deren Bedeutung für die zukünftige Forschung statt. Diese Dissertation zeigt auf, dass eine Vielzahl analytischer Methoden zur Beurteilung motorischer Leistung existiert und dass die verschiedenen methodischen Ansätze jeweils unterschiedliche Aspekte motorischer Kontrolle und motorischen Lernens akzentuieren. Entsprechend können verschiedene analytische Ansätze zu unterschiedlichen Schlussfolgerungen führen. Unsere Experimente zur motorischen Adaptation zeigen auf, dass instabile Übungsbedingungen zwar die Ausbildung Interner Modelle während der Adaptationsphase beeinträchtigen, jedoch Konsolidierungsprozesse begünstigen können. Zudem konnte erstmals intermanueller Transfer von dynamischer Adaptation in beide Richtungen nachgewiesen werden. Dieser Transfer erfolgte in extrinsischen Koordinaten und ließ im Zeitverlauf nach. Die Resultate liefern wertvolle Einsichten in motorische Kontroll- und Lernprozesse und tragen damit zum Erkenntnisgewinn in einem interdisziplinären Forschungsfeld bei, welches die Bewegungswissenschaft, Neurowissenschaft und Robotik umfasst.

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1 General Introduction

1.1 Preface

Movements are important aspects of human everyday life since they are our only possibility to interact with the world. Talking, gestures, writing, object manipulation, et cetera require well-coordinated muscle contractions. For this purpose, the human senosorimotor system comprises billions of neurons which coordinate hundreds of highly interdependent muscles in order to control a plethora of mechanical degrees of freedom (Bernstein, 1967; Rosenbaum, 2010). Accordingly, movements in general and arm movements in particular have been fascinating researchers for generations. At first glance, arm movements seem to be an oversimplified selection of the diversity of human movements to be investigated. However, arm movements have a high practical value in terms of manipulating objects, but they also demonstrate many aspects which make motor control and learning hard to decode (Shadmehr & Wise, 2005). For instance, when writing, the sensorimotor system has to stabilize the torso, control the arm, hand, and fingers but also needs to manipulate a foreign object attached to the own body, which may have varying mechanical properties. Thus, the sensorimotor system faces a complex control problem.

An aggravating aspect is that humans are not proficient in performing all possible motor tasks and its variations by birth. Rather, the sensorimotor system must be able to learn new motor skills during lifetime, to adapt existing skills to changes in the body or environment as well as to generalize previously learned motor actions to new tasks and objects (Schmidt & Lee, 2011; Shadmehr & Wise, 2005). Therefore, the sensorimotor system must constantly learn and adapt in order to maintain the control and enable skilled movements. Yet, it remains puzzling how the sensorimotor system manages these motor control and learning processes.

Understanding the mechanisms of motor control and learning is one of the major topics in human movement science (Rosenbaum, 2010), robotics (Schaal & Schweighofer, 2005), as well as neuroscience (Wolpert et al., 2011) and neurorehabilitation (Huang & Krakauer, 2009). However, many features of motor control and learning remain unresolved and are, thus in the scope of current research, e.g., acquisition of new motor skills as well as adaptation of existing motor skills to changing conditions and their generalization to other contexts, or consolidation of motor memory. A more profound understanding of these features and the underlying processes is an important prerequisite for designing safer workplaces, better tools, prostheses, and robots as well as more effective training schedules in sports and neurorehabilitation. For this purpose, this thesis investigates motor control and learning of arm movements. More precisely, adaptation, consolidation, and generalization of human motor memory with respect to reaching movements is considered.

1.2 Outline of this thesis

The current thesis comprises five main chapters. In this first chapter (Chapter 1), theoretical and methodological fundamentals of human motor control and learning are introduced. Therein, the current state of research on motor adaptation as well as consolidation and generalization of motor memory is briefly reviewed (Section 1.3). Furthermore, the general methodology is introduced (Section 1.4). Finally, unresolved research issues are deduced in order to determine the aims and scope of this thesis (Section 1.5).

Each of the three subsequent chapters (Chapter 2, Chapter 3, and Chapter 4) respectively considers one of those deduced unresolved research issues. These chapters encompass research articles that were published in international peer-reviewed journals:

- Chapter 2: ManipAnalysis – A Software Application for the Analysis of Force Field Experiments

  Stockinger, C., Pöschl, M., Focke, A., & Stein, T. (2012). ManipAnalysis - a software application for the analysis of force field experiments. *International Journal of Computer Science in Sport*, 11:52–57.

- Chapter 3: Adaptation and Consolidation of Motor Memory

  Stockinger, C., Focke, A., & Stein, T. (2014). Catch trials in force field learning influence adaptation and consolidation of human motor memory. *Frontiers in Human Neuroscience*, 8:231.

- Chapter 4: Adaptation and Generalization of Motor Memory

  Stockinger, C., Thürer, B., Focke, A., & Stein, T. (2015). Intermanual transfer characteristics of dynamic learning: direction, coordinate frame, and consolidation of interlimb generalization. *Journal of Neurophysiology*, 114(6):3166–3176.

Finally, Chapter 5 gives an overall discussion and conclusion of the presented work and deduces implications for future research.

1.3 Theoretical background and terminology

This section aims to introduce and define the terms of motor control and learning as well as features of motor learning that are of particular interest for this thesis: motor skill acquisition, motor adaptation, as well as consolidation and generalization of motor memory. Furthermore, different motor learning processes and the theory of internal models are introduced. This serves as the theoretical basis of the thesis. To allow a readily accessible approach to these terminologies, this introductory section is based on behaviorally observable phenomena. The underlying computational mechanisms and neural substrates are only considered as far as relevant for the purpose of the subsequently presented research.

1.3.1 Motor control and motor learning

Diverse scientific disciplines contribute to research on motor control and learning, e.g., human movement science and sports science, neuroscience, psychology, physiology, medicine, but also engineering and physics. This makes motor control a highly interdisciplinary field of research (Rosenbaum, 2010; Shadmehr & Wise, 2005). Accordingly, it is hard to give an overall definition of motor control. However, for the purpose of this thesis, it is sufficient to give a quite generous description: *motor control* describes the field of studies investigating how humans and animals control their movements. This comprises questions about how the central nervous system is organized in order to coordinate the multitude of muscles and joints, how sensory information is utilized to control movements, and how the system maintains stability (Schmidt & Lee, 2011; Rosenbaum, 2010). Motor control is a highly complex challenge for the central nervous system, in particular for the sensorimotor system. This becomes clear when considering the redundancy (degrees of freedom of the involved joints, muscle co-contractions), the noisy and delayed sensory information, or the nonstationarity (fatigue, growth) the sensorimotor system is exposed to (Franklin & Wolpert, 2011).

Facing these problems, the sensorimotor system needs to be able to acquire or adjust motor control strategies both on short time scales of fatigue or interactions with objects and over the long timescale of development and aging (Franklin & Wolpert, 2011). This capability to acquire new or to adjust existing motor control strategies refers to motor learning.

In the literature, there exist diverse definitions of *motor learning*. Shadmehr and Wise offer a quite broad description of motor learning. They think of motor learning as "the acquisition of information about movements (and other motor outputs), including what output to produce as well as how and when to produce it. Motor learning results in the formation of motor memory" (Shadmehr & Wise, 2005, p. 39). According to Schmidt and Lee, "motor learning is a set of processes associated with practice or experience leading to relatively permanent changes in the capability for skilled movement" (Schmidt & Lee, 2011, p. 327). Yet, it is important to add that off-line processes after practice also play an important role in motor memory formation and, thus in motor learning (Robertson et al., 2004b).

The focus of this thesis lies on particular features of motor learning rather than on its overall structure. Therefore, it might be more appropriate to consider motor learning as an aggregate of diverse phenomena associated with motor performance. For instance, Magill and Anderson give a more handy definition: "motor learning is the acquisition of motor skills, the performance enhancement of learned or highly experienced motor skills, or the reacquisition of skills" (Magill & Anderson, 2014, p. 3). Thereby, a *motor skill* refers to an activity or task that requires voluntary control over movements of the joints and body segments in order to achieve a goal (Magill & Anderson, 2014).

Given these different definitions of different breadth and particularity, one can condense the following characteristics of motor control and learning:

- Motor learning can be seen as the acquisition of new or the adjustment of existing motor control strategies.
- Motor learning comprises several features and behaviorally observable phenomena which are associated with motor performance.
- This motor performance depends on the sensorimotor system's competence to control movements.
- The motor learning features encompass internal processes comprising formation of motor memory.
- Motor memory formation is associated with movement-related information and develops with practice but also during post-practice off-line processing.

Below, some of the features and internal processes of motor learning as well as motor memory formations will be introduced. In particular, motor skill acquisition, motor adaptation, motor memory consolidation, and generalization of motor learning will be considered.

1.3.2 Motor skill acquisition and motor adaptation

Considering the example of handwriting illustrates several basic features of motor control and learning. First, the sensorimotor system has to control a redundant system involving diverse limb segments, joints, and muscles. Furthermore, control of a foreign object is required. Second, the handwriting example clearly illustrates the motor learning capability of the sensorimotor system because humans are not proficient in writing by birth but have to learn this motor skill by practicing. Learning of new movements is usually referred to as *motor skill acquisition* and is the basis for the diversity of motor skills humans are able to learn during their lifetime. More precisely, motor skill acquisition involves acquiring new patterns of muscle activation and attaining a higher level of performance by reducing errors without a reduction in movement speed (Kitago & Krakauer, 2013; Shadmehr & Wise, 2005). Accordingly, motor skill acquisition implies a systematic change in the learner's speed-accuracy trade-off function. This process may last for several days, weeks, or even years (Kitago & Krakauer, 2013).

Human motor actions are constantly exposed to changes in external and internal conditions. For instance, when adding a big eraser to the top of a pencil, its mechanical properties change and the handwriting will be affected. However, after some lines of practice, the handwriting will regain its initial shape despite the changed conditions. But also the internal conditions may change because, for instance, muscles fatigue. Accordingly, the sensorimotor system has to account for such conditional changes in order to ensure movement goal achievement. This illustrates that the sensorimotor system also needs to be adjustable on shorter timescales. Such ability to adjust previously learned motor skills to changes in the external or internal conditions is referred to as *motor adaptation*. This type of learning is characterized by regaining (or retaining) a given level of performance by gradual improvements in response to altered conditions, i.e., incremental reduction of motor error. However, performance can not get better than baseline performance but at best can return to it (Shadmehr & Wise, 2005; Krakauer & Mazzoni, 2011).

Research suggests that in contrast to motor skill acquisition, motor adaptation is learned rather implicitly without subjects' awareness (Kitago & Krakauer, 2013) and that after motor adaptation, no new capability emerges but the system's state is regained to a prior state of performance (Shadmehr & Wise, 2005). Compared to motor skill acquisition, motor adaptation takes place on shorter time scales and can occur within a single practice session (Kitago & Krakauer, 2013). In this thesis, motor adaptation is the learning feature of particular interest. If a dissociation is negligible, the umbrella term *motor learning* will be used. Unless otherwise indicated, all subsequent remarks refer to motor adaptation.

1.3.3 Theory of internal models

Motor adaptation in response to altered environmental conditions has been demonstrated by several research groups, mostly considering adaptation of arm reaching movements (e.g., Shadmehr & Mussa-Ivaldi, 1994; Krakauer et al., 1999; Flanagan et al., 1999). The most common explanation of motor adaptation bases upon the theory of *internal models*. Internal models are neural representations of the own body and the environment. They can be seen as neural circuits that compute sensorimotor transformations and allow the estimation of limb positions if joint angles, segment lengths, and environmental conditions are known. Two types of internal models are distinguished: inverse internal models and forward internal models (Wolpert et al., 1995; Kawato, 1999).

Forward models represent the causal relationship between motor commands and their consequences by estimating future states of the own body and the environment. Motor commands are neural outputs that act on the muscles causing them to contract and generate movements. Thereby, an efference copy of the motor command is passed into a forward model which acts as a neural simulator (Franklin & Wolpert, 2011; Wolpert et al., 2013). Thus, a forward model estimates the change of the sensorimotor system's state as a result of an outgoing motor command and predicts consequences of an upcoming action before they actually happen (Wolpert et al., 2011; Karniel, 2011). This property is important because estimates about the state of the body and the environment are impaired by time delays and noise. To deal with this problem, forward models predict motor behavior and sensory consequences to enable predictive control (Franklin & Wolpert, 2011). In particular, this property is important to control rapid movements that are too fast to wait for sensory feedback.

An internal model that computes motor commands from sensory inputs is called an *inverse model*. Inverse models allow the determination of motor commands which are necessary to produce a particular action in order to achieve a desired sensory consequence. Hence, inverse models are suitable to act as controllers (Wolpert et al., 2013; Wolpert & Kawato, 1998). In engineering, this is comparable to an inverse dynamic calculation, i.e., the inverse of the controlled system (Karniel, 2011). This necessitates knowledge of the mechanical properties of the own body.

In the case of correct structure and parameter values of forward and inverse model, the output of the forward model (predicted behavior) will be the same as the input to the inverse model (desired behavior) (Wolpert et al., 2013). Within this thesis, mostly the main term *internal model* will be used when the detailed distinction of inverse and forward model is negligible.

Facing a change in the conditions of movement execution, the input-output relationship of the sensorimotor system is altered and the internal model will fail to generate an appropriate motor command. This results in a prediction error. Consequently, the generated motor commands need to be adapted in order to ensure task goal achievement. During motor adaptation, the internal models are assumed to be adapted in order to account for the conditional changes (Shadmehr & Mussa-Ivaldi, 1994; Wolpert & Kawato, 1998; Krakauer et al., 1999).

Evidence for the existence and adaptability of internal models comes from the observation of *after-effects* of motor adaptation. Thereby, after motor adaptation to an external perturbation, subjects show distinctive motor errors when the perturbation is suddenly removed. These after-effects show a mirrored pattern compared with the initially observed errors when the perturbation was introduced. This indicates that the sensorimotor system specifically changes its predictions about the task conditions due to motor adaptation (Shadmehr & Mussa-Ivaldi, 1994). In particular, this demonstrates that motor actions are partially planned in advance and that motor commands are sent out in a feedforward manner.

Contrary to the theory of internal models, one might assume that subjects simply memorize past experience and learn to play out some kind of motor command “tape” as a function of time. This tape may be built as an average record of previous movements and refers to a mapping of direction and time onto forces. However, such an approach could not explain the previously mentioned generalization phenomena. For instance, it was shown that subjects who adapted their reaching movements to a perturbing force field in short, straight point-to-point reaching movements also demonstrated enhanced performance in longer, circular movements (Conditt et al., 1997). Such generalization to other task types rules out the possibility of a merely time- and direction-dependent tape of motor commands (Conditt et al., 1997; Shadmehr, 2004). Rather, this suggests that the sensorimotor system develops internal representations of the own body and the environment that can be generalized to other movements.

Altogether, there is strong evidence that the sensorimotor system is capable of adapting motor commands by relating sensory states of the hand to forces using internal models (Shadmehr, 2004).

1.3.4 Processes of motor learning

As mentioned above, sensory information is critical for motor learning. Depending on the type and quality of this information, different processes of motor learning can be distinguished (Wolpert et al., 2011).

First, in *error-based learning* processes the prediction error of a motor action is reduced on a trial-by-trial basis (Thoroughman & Shadmehr, 2000). The prediction error is the discrepancy between the predicted (or desired) and the actually sensed outcome of a motor action. The basis of error-based learning is a directional (signed) motor error vector that offers a gradient to move the system towards the direction of steepest error reduction (Wolpert et al., 2011). As such, error based learning is a form of supervised learning (Franklin & Wolpert, 2011) originating from machine learning.

A second learning process is *reinforcement learning* which is driven by information about the relative success and failure of the movement. In contrast to error-based learning, the provided signal is a scalar reward obtaining less information and no specific direction of error reduction (Franklin & Wolpert, 2011; Huang et al., 2011). Therefore, the sensorimotor system needs to explore different possibilities to improve its motor performance so that reinforcement learning tends to be slow compared with error-based learning (Wolpert et al., 2011).

Third, *use-dependent learning* describes the phenomenon that neural or behavioral changes occur through the pure repetition of movements, even in the absence of systematic errors (Diedrichsen et al., 2010; Wolpert et al., 2011). Such repetition results in a bias toward the repeated motor action (a form of habituation), thereby reducing variability of the movement (Wolpert et al., 2011; Huang et al., 2011).

Potentially, the different learning processes simultaneously contribute to the learning of a motor task. Reliance on each process seems to depend on the type of task to be learned or on specific aspects of a task, as well as on the type of information provided and its reliability (Diedrichsen et al., 2010). Yet, most motor adaptation paradigms are designed to investigate error-based learning mechanisms (Wolpert et al., 2011) as it is the case in this thesis.

1.3.5 Consolidation of motor memory

Clearly, practice – i.e., performing a motor task – plays a fundamental role in motor learning. However, it is known that practice alone is not sufficient to gain long-lasting expertise because newly formed motor memories are highly fragile and, thus susceptible to disruption. For this reason, newly formed motor memories need to be stabilized and protected against forgetting and interfering factors. After a session of practice, the brain continues processing motor-related information. During such off-line processing between practice sessions, newly formed motor memory undergoes structural modifications yielding stabilization of motor memory (i.e., reduction in fragility of a motor memory trace after encoding). These processes are denoted as *consolidation* of motor memory (Robertson et al., 2004b; Krakauer & Shadmehr, 2006).

To investigate motor memory consolidation in the context of motor adaptation research, so-called ABA-paradigms have evolved. Thereby, it is tested whether successive learning of two tasks A and B interferes with each other. More precisely, after learning of task A, the second task B is learned before testing the retention performance of task A (Robertson et al., 2004b). For motor adaptation tasks, it was shown that motor memory consolidation of task A can be impaired by learning the second task B (e.g., Brashers-

Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Krakauer et al., 2005). Several studies demonstrated that the interference effect diminishes as the time between learning A and B is increased (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Walker et al., 2003; Krakauer et al., 2005). This indicates that consolidation is a time-dependent process and was shown to be a robust feature in motor adaptation (Robertson et al., 2004b).

Motor memory consolidation is likely to be supported not only by a replay of past events but also by a reorganization of the movement-related information (Walker et al., 2005). Potentially, this yields a shift of the internal representation of the learned movement which has previously only been associated with practice, therefore fostering consolidation of motor memory (Robertson et al., 2004b). For instance, Shadmehr & Holcomb (1997) reported such processes of reorganization during consolidation. They found that the brain engages new regions shifting from prefrontal regions of the cortex to structures of the premotor, posterior parietal, and cerebellar cortex. This suggests that consolidation processes change the neural representation, thus potentially increasing the functional stability of the underlying task (Shadmehr & Holcomb, 1997). Altogether, the importance of consolidation processes in motor learning is well-accepted.

1.3.6 Generalization of motor memory

Humans are able to perform previously learned motor skills in different contexts than in that of initial acquisition. For instance, a subject who learned handwriting with a pen will also be able to write with chalk on a blackboard or even write with the other hand. This feature refers to a *generalization* of motor learning from one task or context to another, i.e., knowledge gained through practice in one situation changes performance in a different situation (Criscimagna-Hemminger et al., 2003; Seidler, 2010; Kitago & Krakauer, 2013).

Generalization is not only of interest in neuroscience (Shadmehr, 2004) but also in sports science (Magill & Anderson, 2014). In the latter case, generalization is more often denoted as *transfer* of learning with respect to motor skills. Thereby, one might further distinguish in positive and negative transfer, which describe that previous experience facilitates or hinders learning of new skills or the generalization of a skill to new contexts, respectively (Magill & Anderson, 2014). However, the amount of transfer is typically small (Schmidt & Lee, 2011).

In more fundamental research, generalization is mostly considered with respect to motor adaptation of arm movements. Therein, generalization was shown to occur across different types of movements (Conditt et al., 1997), movement directions (Thoroughman & Shadmehr, 2000), workspaces (Shadmehr & Moussavi, 2000), and limb configurations (Malfait et al., 2002). In the special case of motor memory generalization across arms (Criscimagna-Hemminger et al., 2003), this feature is denoted by the terms *intermanual generalization* or *intermanual transfer*. The present thesis concentrates on intermanual transfer of motor adaptation.

In order to explain such intermanual transfer effects, two prominent models have been proposed (for review, see Ruddy & Carson, 2013). First, the cross-activation model suggests that unilateral practice causes bilateral adaptation both in the contralateral and the ipsilateral hemisphere. Second, the bilateral access model suggests that motor memory which is formed during unilateral practice is not effector-specific but is encoded in an abstract form that can be utilized for motor control for both the trained and the untrained hand (Ruddy & Carson, 2013; Anguera et al., 2007). Yet, the detailed mechanisms underlying intermanual transfer remain elusive.

This chapter introduced the terms of motor control and learning as well as related features. This thesis concentrates on motor adaptation (rather than motor skill acquisition) in the form of error-based learning processes (rather than reinforcement learning or use-dependent learning) as well as the consolidation and generalization (in terms of intermanual transfer) of motor learning.

1.4 General methodology

1.4.1 Experimental paradigms for the investigation of motor adaptation

To investigate motor adaptation, different experimental paradigms have evolved. One example are saccade adaptation experiments in which the adaptation of eye movements is studied. Therein, a target is presented and as soon as the eyes start moving toward it, the target is extinguished and presented somewhere else (McLaughlin, 1967). This results in a motor error because the predicted proprioceptive feedback by the eye muscles do not match the actual visual feedback. With practice, primates are able to adapt to this distortion by changing their motor outputs (Shadmehr et al., 2010).

Another wide-spread experimental paradigm considers the adaptation of arm movements to external perturbations. Therein, two main adaptation paradigms exist: kinematic and dynamic adaptation paradigms. In kinematic adaptation paradigms, subjects are exposed to a visual perturbation like prism-induced displacements (Held & Freedman, 1963). In other approaches, subjects manipulate a handle or a stylus to perform movement tasks that are displayed on a screen. Thereby, the relationship between hand position and displayed cursor position is altered by visuomotor rotations or shifts (Krakauer et al., 2005). Dynamic adaptation paradigms most often use robotic manipulanda. Thereby, subjects grasp the handle of a robotic device and perform reaching movement tasks. The robotic devices can induce forces to alter the dynamic conditions resulting in perturbed arm movements (Shadmehr & Mussa-Ivaldi, 1994; Figure 1.1). In other approaches, the task dynamics are altered by attaching inertial loads to the subject's arm (Krakauer et al., 1999) or inducing Coriolis forces by seating subjects in a rotating environment (Lackner & DiZio, 2005). In all these cases, subjects need to adapt their motor commands by producing additional forces in order to compensate the induced dynamic disturbance.

Altogether, in motor adaptation paradigms the task conditions are altered by inducing perturbations. This results in motor errors – or more precisely, in prediction errors – because the predicted and the actual conditions differ. With practice, subjects are capable to account for the perturbations by adapting their motor outputs (Shadmehr et al., 2010).

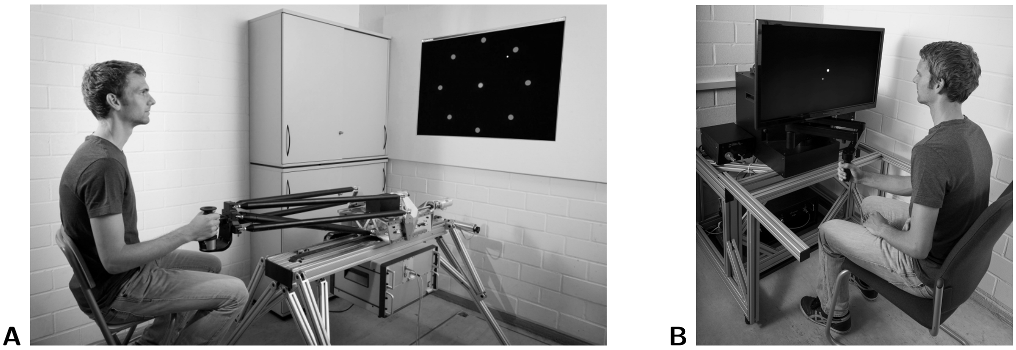


Figure 1.1: Robotic manipulanda for the investigation of motor adaptation. **A**, Self-developed robotic device "BioMotionBot" (Bartenbach et al., 2013). **B**, Robotic manipulandum "Kinarm End-Point Lab". The subject grasps the handle of the manipulandum. On a vertical screen, the movement task as well as the cursor, representing the handle, are presented. The robotic device can induce forces to alter the dynamic conditions.

1.4.2 Force field adaptation experiments

This thesis concentrates on motor adaptation to robot-induced dynamic perturbations – so-called *force field adaptation experiments.* For this reason, the classical experimental setup as first introduced by Shadmehr & Mussa-Ivaldi (1994) and the common adaptation progression shall be depicted in detail.

In robot-assisted force field experiments, the subjects interact with a robotic manipulandum by grasping its handle and perform goal-directed reaching movements (Figure 1.1). The task to be performed is visualized on a screen. The robotic device has computer-controlled motors that can apply forces to the subjects' hand via the handle and, therewith, alter the dynamic conditions of task execution. Hence, the subjects' movements can be perturbed under consideration of the current state of movement (e.g., velocity-dependent forces). The movement tasks as well as its visualization can be programmed in tailor-made fashion, thus meeting research-specific requirements. The movements of the handle can be recorded in high resolution by measuring the position of the handle and the forces acting at the handle. Those quantities serve as basis for on-line task specifications as well as for the analysis of motor performance.

A typical adaptation progression of a subject handling a robotic manipulandum is illustrated in Figure 1.2 (Shadmehr & Brasher-Krug, 1997). When the robot's motors do not produce perturbing forces (null field condition), movement paths are straight-lined (Figure 1.2A). When a velocity-dependent force field (Figure 1.2B) affects the subject's hand, hand paths are distinctively deviated from desired movement path (Figure 1.2C). With practice, the subject's hand paths converge to those observed under null field conditions (Figure 1.2D). Hence, the subject adapted its motor commands by predicting the altered force environment.

One might argue that subjects simply increase arm stiffness by muscular co-contraction, therewith freezing the degrees of freedom, to control their movements when the perturbing forces are applied. However, when turning off the force field after adaptation, after-effects

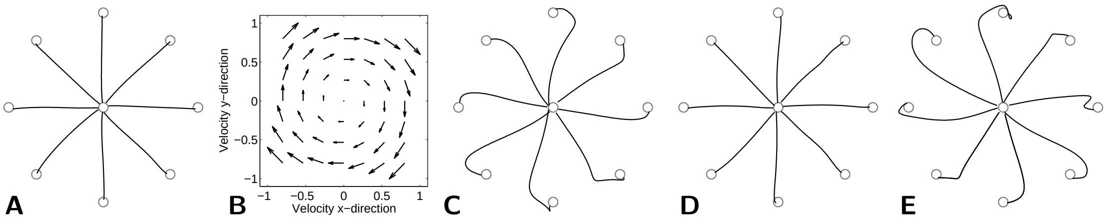


Figure 1.2: Robot-assisted force field adaptation paradigm. **A**, Hand paths of a representative subject performing unperturbed two-dimensional point-to-point reaching movements (null field condition). The hand paths are nearly straight-lined. **B**, Visualization of an velocity-dependent curl force field produced by a robotic manipulandum. **C**, Deviated hand paths of a subject when first exposed to the force field. **D**, Hand paths of a subject after approximately 300 movement trials under force field conditions showing nearly straight-lined trajectories similar to those observed under null field conditions (**A**). **E**, After-effects of force field learning when turning off the force field after adaptation. Hand paths are deviated in the counter-direction of initial deviation under force field conditions (**C**) indicating predictive force field compensation (acc. to Shadmehr & Brasher-Krug, 1997).

of force field adaptation can be observed (Figure 1.2E). These after-effects indicate predictive force compensation and are approximately a mirror image of the hand paths observed in early force field trials (Figure 1.2A). This is taken as evidence that subjects adapt an internal model of the task dynamics and, thus change their motor commands to specifically counter the disturbing forces – i.e., the sensorimotor system learns something specific about the motor task (Shadmehr, 2004).

1.5 Aims and scope of this thesis

This thesis aims to investigate motor control and learning mechanisms with special consideration of motor memory adaptation as well as its consolidation and generalization. For this purpose, the above-introduced experimental paradigm of robot-assisted force field experiments is used.

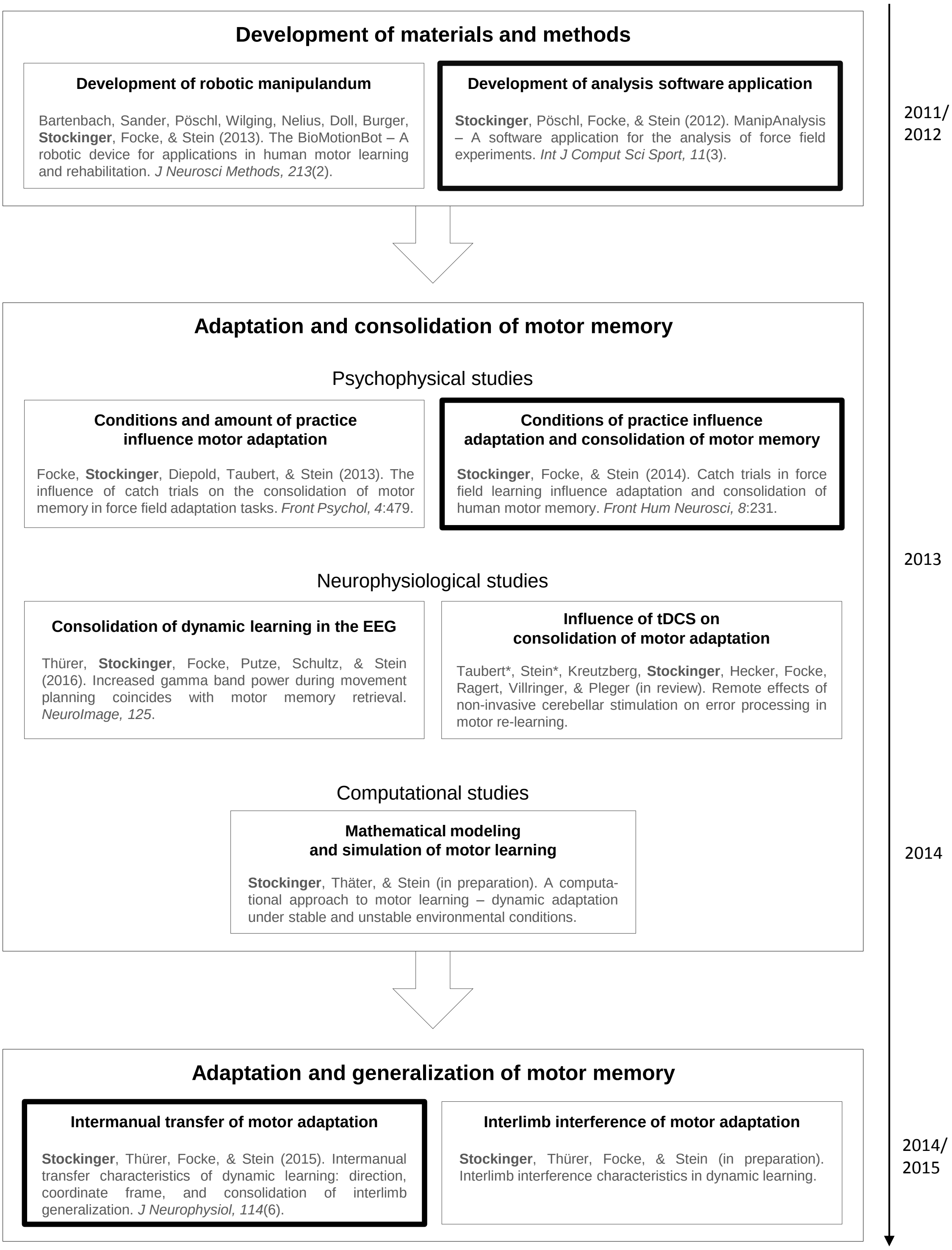
The work depicted in this thesis was embedded in the research program of the Young Investigator Group (YIG) “Computational Motor Control and Learning” which was supported by the “Concept for the Future” of Karlsruhe Institute of Technology within the framework of the German Excellence Initiative. The subsequent Chapters 2, 3, and 4 comprise research articles which represent three different research projects of the YIG. These three projects, in turn, are related to other work performed within the framework of the YIG. Figure 1.3 illustrates the integration of these projects to the overall context of the YIG. This work encompasses three main parts:

(1) development of materials and methods,

(2) investigation of adaptation and consolidation of motor memory,

(3) investigation of adaptation and generalization of motor memory.

The Chapters 2, 3, and 4 each consider one of the three main parts, respectively.



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Stockinger, Thäter, & Stein (in preparation). A computational approach to motor learning – dynamic adaptation under stable and unstable environmental conditions.

Stockinger, Thürer, Focke, & Stein (2015). Intermanual transfer characteristics of dynamic learning: direction, coordinate frame, and consolidation of interlimb generalization. *J Neurophysiol, 114*(6).

Stockinger, Thürer, Focke, & Stein (in preparation). Interlimb interference characteristics in dynamic learning.

Figure 1.3: Schematic of scientific work performed within the Young Investigator Group (YIG) “Computational Motor Control and Learning”. Bold-framed boxes indicate the work presented in the Chapters 2, 3, and 4 of this thesis.

1.5.1 Development of materials and methods

The first step was to develop a methodological basis for the investigation of motor control and learning mechanisms using robot-assisted experiments. Despite the well-known experimental paradigm of robot-assisted learning experiments, no standards for the use of materials and methods existed. For instance, most robotic manipulanda which are used in research contexts are tailor-made devices (e.g., MIT-Manus, Krebs et al., 1998; Johns Hopkins Manipulandum, Charnnarong, 1991; Braccio di Ferro, Casadio et al., 2006; vBOT, Howard et al., 2009). Accordingly, sales and distribution of commercial robotic devices for research purposes are rare. Rather, the vast majority of robotic devices was designed for neurorehabilitation and clinical settings (e.g., Kinarm EndPoint Lab, BKIN Technologies, Kingston, Canada, Scott, 1999; Phantom Haptic Device, Sensable, Wilmington, MA, USA; InMotion, Interactive Motion Technologies, Watertown, MA, USA) or for the investigation of one specific aspect of motor control research, respectively (for review, see Howard et al., 2009).

Similarly, neither software applications nor standards for data processing and analysis of robot-assisted motor control and learning experiments existed. However, the usage of automatized analytic software tools is required because robot-assisted experiments accumulate a great amount of digital data. In the literature, a diversity of algorithms and strategies to process such data is used. Likewise, multiple concepts exist to define and assess motor performance (cf. Shadmehr & Brasher-Krug, 1997; Caithness et al., 2004; Scheidt et al., 2000). This underpins the necessity to deal with motor performance assessment as well as analytic processing procedures and to build a common framework for the analysis of robot-assisted experiments.

Consequently, our initial work concentrated on the development of materials and methods (Figure 1.3). First, this encompassed the development of a novel 3D robotic manipulandum for the research in human motor learning, rehabilitation, and sports (Bartenbach et al., 2011, 2013). Secondly, a tailor-made software application for the automatized analysis of robot-assisted experiments was designed (Stockinger et al., 2012). This latter work is presented in Chapter 2 and introduces the software application ManipAnalysis.

1.5.2 Adaptation and consolidation of motor memory

On the basis of the initially developed materials and methods, the second part of the YIG work (Figure 1.3) comprised experiments on adaptation and consolidation of motor memory both on the psychophysical level (Focke et al., 2013; Stockinger et al., 2014) and using neurophysiological methods like electroencephalography (EEG, Thürer et al., 2016) and transcranial direct current stimulation (tDCS, Taubert et al., in review). Moreover, we used a computational approach by mathematically modeling and simulating motor control and learning processes to reproduce the previously gained findings. Chapter 3 presents one of the psychophysical experiments (Stockinger et al., 2014).

This work preliminary concentrated on adaptation and consolidation of motor memory with respect to the applied practice schedule. As outlined in Subsection 1.3.5, it is well-accepted that motor memory consolidation is a time-dependent process (Robertson et al., 2004b; Krakauer & Shadmehr, 2006). From a practical perspective, it is also interesting to ask whether motor memory consolidation is also practice-dependent, i.e., whether it relates to the applied practice schedule. Research in skill learning exhibited that the type of practice affects motor memory consolidation (Schmidt & Lee, 2011). However, in the context of motor adaptation, there is no coherent theory on such relations. Indeed, there are indications that the encoding and consolidation of motor memory can be influenced by the practice structure during motor learning. Research suggests that variable or unstable practice conditions facilitate consolidation processes compared with blocked practice (Tanaka et al., 2009; Kantak et al., 2010). Such variable or unstable conditions of practice provoke unexpected motor errors during learning which are fed back to the sensorimotor system. As motor adaptation is assumed to be a predominantly error-based learning process (see Subsection 1.3.4, Thoroughman & Shadmehr, 2000), such interferences may distinctively influence formation of motor memory and engage deeper cognitive processing of task-related information yielding more robust motor memories (e.g., Shea & Kohl, 1991; Overduin et al., 2006; Tanaka et al., 2009; Kantak & Winstein, 2012). Yet, the detailed influence of unstable conditions of practice on motor adaptation and subsequent consolidation processes remains elusive.

Therefore, the aim of the study presented in Chapter 3 was to investigate the influence of unstable practice conditions on motor adaptation and consolidation in a dynamic learning task. For this purpose, subjects were tested in an ABA-paradigm and different subject groups adapted their movements to force field perturbations of different stability.

1.5.3 Adaptation and generalization of motor memory

The third main part of the YIG work (Figure 1.3) considered motor adaptation and its generalization. Within the framework of the YIG, two experiments were conducted regarding this issue, one of which is presented in Chapter 4 (Stockinger et al., 2015).

Generalization of motor memory is a well-accepted feature of motor learning that is of high theoretical and practical value (Magill & Anderson, 2014). From a fundamental neuroscientific point of view, knowledge about generalization mechanisms helps gaining insights into the interaction of different brain areas or into the internal representation of movement. From a practical point of view, knowledge about generalization characteristics provides valuable information for enhancing training schedules in sports or neurorehabilitation in terms of bilateral practice. Hence, research on generalization of motor learning is promising, yet, “still not well understood at all” (Schmidt & Lee, 2011, p. 483). In particular, this holds for intermanual transfer of dynamic adaptation, i.e., generalization of motor adaptation across hands – as there are several open questions regarding its characteristics.

For instance, there are open questions on the symmetry or asymmetry of this transfer. Previous studies that investigated intermanual transfer of dynamic adaptation reported a unidirectional – in particular asymmetric – transfer only from the dominant to the non-dominant arm (Criscimagna-Hemminger et al., 2003; Wang & Sainburg, 2004; Galea et al., 2007). However, it remains unresolved why transfer should be exclusively unidirectional.

Moreover, there are diverging results considering the coordinate frame of intermanual transfer. Such transfer could occur in an extrinsic (Cartesian-based) coordinate frame – i.e., for a certain movement the forces on the left and the right hand should be similar. Transfer might also occur in intrinsic (joint-based) coordinates – i.e., if the workspace is near the midline transfer would lead to the same joint torques and mirror symmetric force profiles on the contralateral arm (for details, see Criscimagna-Hemminger et al., 2003). Knowledge about the coordinate frame of transfer offers valuable information about the internal representation of motor actions.

It is generally accepted that consolidation and sleep play a major role in the formation of motor memory. By downscaling synaptic strength and eliminating noise, sleep might enhance the signal to noise ratio as well as facilitate the interactions with higher-order brain areas (Diekelmann & Born, 2010). Thus, sleep-related consolidation seems to support generalization processes by structural reorganization and formation of more general motor memory representations (Rasch & Born, 2013; Censor, 2013). Likely, these processes facilitate the context-independent applicability of the related motor task (Censor, 2013). Yet, an increased intermanual transfer after a period of consolidation including nocturnal sleep was only demonstrated for a finger sequencing task (Witt et al., 2010) but not for motor tasks involving more implicit learning mechanisms. So far, it remains unresolved whether consolidation processes also facilitate intermanual transfer effects in dynamic adaptation.

The study depicted in Chapter 4 (Stockinger et al., 2015) specifically addresses these issues. Therein, intermanual transfer of dynamic adaptation is investigated with respect to the direction (asymmetry/symmetry) and the coordinate frame of transfer as well as the influence of a 24 h consolidation period (incl. nocturnal sleep) on the transfer.

2 ManipAnalysis – A Software Application for the Analysis of Force Field Experiments

Extended version of the published paper

Stockinger, C., Pöschl, M., Focke, A., & Stein, T. (2012). ManipAnalysis - a software application for the analysis of force field experiments. *International Journal of Computer Science in Sport*, 11:52–57.

Acknowledgments

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Abstract

In human movement science, the plasticity of the sensorimotor system is one of the most important issues as it enables humans to adapt their movements to changing environmental conditions. It is generally accepted that human motor memory contains so-called internal models which are neural representations of the mechanical properties of the limbs and objects in the environment. Robot-assisted force field experiments are an established tool to investigate the characteristics of such internal models. However, these force field experiments produce a great amount of data which needs to be organized, stored, and analyzed. Moreover, despite the wide-spread use of robot-assisted experiments, no standards for data processing and analysis exist. Rather, a multitude of methods is used which might have an impact to the gained results and conclusions. Thus, we considered existing analytic approaches, integrated them in a methodological framework, and developed a tailor-made software application, called ManipAnalysis, for the analysis of force field experiments. Therefore, we first extracted general and research-specific software requirements. On this basis, we designed an application in C# which has a flexible modular structure and only depends on .NET framework, MongoDB database server, and MATLAB. Altogether, ManipAnalysis offers a hand-in-hand solution for the analysis of force field experiments ranging from data import and storage, up to visualization and export of calculated performance parameter values. Thus, ManipAnalysis fills the gap between data acquisition with the help of a robotic device and statistical analysis with specific software applications.

2.1 Introduction

The human's ability to adapt movements to changing environmental conditions is a main issue in human movement science. Thereby, understanding the involved mechanisms of motor learning is one of the core problems (Rosenbaum, 2010). The last couple of years, especially computational approaches have led to rapid advances in our understanding of these mechanisms (Wolpert et al., 2011). One of the key concepts in this context is the theory of so-called internal models. Internal models are neural representations of the mechanical properties of the limbs and objects in the environment (Kawato, 1999). On the one hand, internal models allow the determination of required motor commands that are necessary to achieve a certain motor action (internal inverse model). On the other hand, internal models can be used as neural simulators to estimate the consequences of a motor command (internal forward model) (Kawato, 1999; Wolpert et al., 2011). It is assumed that subjects are able to adjust their internal models when facing systematic changes in the environmental conditions. In such cases, internal model adaptation is necessary to ensure movement goal achievement.

Our group developed a novel 3D robotic manipulandum with end-point force control, called BioMotionBot (Bartenbach et al., 2011; Figure 2.1). The BioMotionBot can be used in the context of internal model learning and additionally enables the development of tailor-made robot-assisted training programs for rehabilitation purposes. In this context, force field experiments are commonly used. Thereby, subjects interact with the robotic device which can alter the dynamic conditions of movement execution by perturbing, constraining, or supporting the movements. However, in such force field experiments, a great amount of data is accumulated. This recorded data has to be organized and stored in a way that enables fast and easy access to the data, even for multiple users simultaneously. Moreover, the data needs to be properly analyzed.

In the corresponding research literature, a multitude of methods is used (diverse robotic manipulanda and analytic approaches). Potentially, these heterogeneous methods have an impact to the gained results and conclusions. Thus, the precise consideration of existing analytic approaches and the integration in a methodological framework would be advantageous. To our best knowledge, there exists no software application for this purpose. Therefore, we developed a tailor-made software application that manages all analytic steps for the analysis of robot-assisted force field experiments within a single framework. This software application, called *ManipAnalysis*, is presented in this paper.

2.2 Methodological basis

2.2.1 Experimental setup

In 1994, Shadmehr & Mussa-Ivaldi introduced an experimental setup to investigate properties of internal model formation under changing environmental conditions. This setup was constantly enhanced and is commonly used today (Criscimagna-Hemminger & Shadmehr, 2008; Arce et al., 2010; Howard et al., 2011). In this setup, subjects grasp the

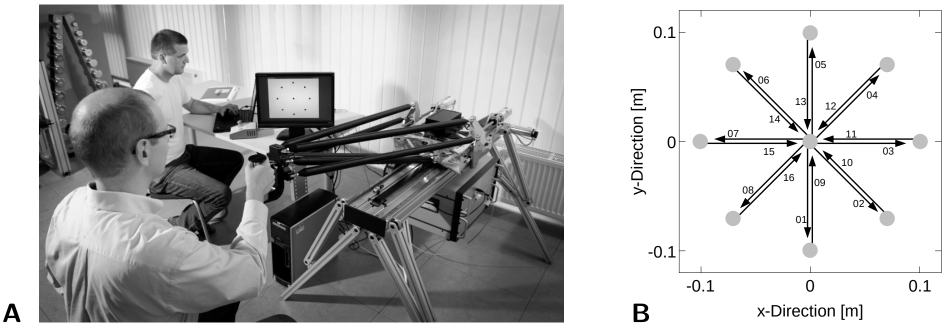


Figure 2.1: Classical two-dimensional center-out movement task. **A**, Subject performing center-out movements handling the robotic manipulandum BioMotionBot. The cursor representing the position of the handle and the target points are visualized on a screen. **B**, The center-out movement task typically comprises movements from a center point to circumjacent target points and back.

handle of a robotic manipulandum and perform horizontal point-to-point reaching movements in a center-out task. Usually, this center-out movement task comprises movements from a center point to circumjacent target points and back which are arranged on a circle with a diameter of about 0.1–0.4 m (Figure 2.1). After a habituation period under null field conditions, the robotic manipulandum produces forces which affect the subjects' hand via the robot handle. In the majority of the cases, a velocity-dependent curl force field is generated that pushes the handle perpendicular to the current movement direction (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Figure 2.2A):

$$\begin{aligned}\begin{pmatrix} F_x \\ F_y \end{pmatrix} &= k \cdot \begin{pmatrix} \cos\big((-1)^n \cdot \Phi\big) & -\sin\big((-1)^n \cdot \Phi\big) \\ \sin\big((-1)^n \cdot \Phi\big) & \cos\big((-1)^n \cdot \Phi\big) \end{pmatrix} \\ &\overset{\Phi=90^\circ}{=} (-1)^n \cdot \begin{pmatrix} 0 & -k \\ k & 0 \end{pmatrix} \cdot \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix}.\end{aligned} \tag{2.1}$$

Thereby, the robot-generated force $(F_x, F_y)^\top$ in clockwise ($n = 1$) or counterclockwise ($n = 2$) direction is determined by the force field viscosity k and the hand velocity $(\dot{x}, \dot{y})^\top$. Occasionally, other types of velocity-dependent force fields are used, e.g., skew fields (Shadmehr & Mussa-Ivaldi, 1994; Howard et al., 2011; Franklin et al., 2008):

$$\begin{pmatrix} F_x \\ F_y \end{pmatrix} = \begin{pmatrix} -k & -k \\ -k & k \end{pmatrix} \cdot \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix}, \tag{2.2}$$

$$\begin{pmatrix} F_x \\ F_y \end{pmatrix} = \begin{pmatrix} 0 & k \\ k & 0 \end{pmatrix} \cdot \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix}, \qquad \text{or} \tag{2.3}$$

$$\begin{pmatrix} F_x \\ F_y \end{pmatrix} = \begin{pmatrix} k_1 & -k_2 \\ k_2 & k_1 \end{pmatrix} \cdot \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix}, \tag{2.4}$$

where, $k, k_1, k_2 \in \mathbb{R}$ (Figure 2.2B–D).

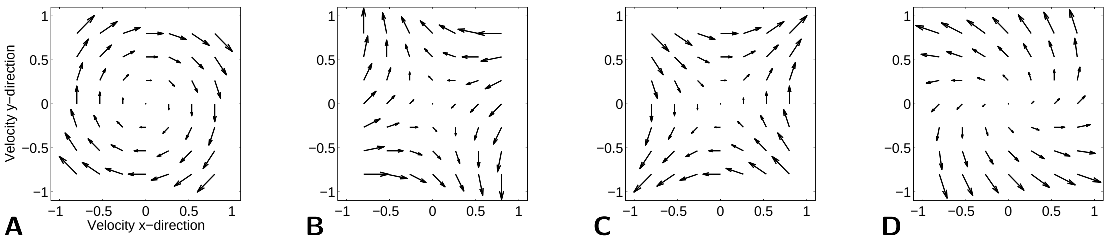


Figure 2.2: Visualization of different viscous force fields: **A**, curl force field (Equation 2.1); **B**–**D**, skew force fields (Equations 2.2–2.4).

Due to the velocity-dependency of the applied forces, subjects are normally requested to perform their reaching movements within a requested time (usually 500±50 ms; Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997).

If the reaching movements are unperturbed, only little deviations and therefore almost straight-lined hand trajectories are observed. When exposed to a force field, the hand trajectories of the subjects initially reveal large deviations compared with the null field condition indicating that the subjects' internal model is not suitable anymore. With ongoing practice in the force field, these deviations decrease leading to straightened trajectories similar to those under the null field condition. In order to perform such accurate reaching movements, the sensorimotor system has to account for the altered dynamic conditions and produce additional forces to counteract the perturbation. This is assumed to be done by adapting the internal model of the task dynamics (Shadmehr & Mussa-Ivaldi, 1994).

2.2.2 Assessment of motor performance

Force field trials

Most commonly in dynamic adaptation experiments, the motor performance is assessed in force field trials using kinematic data by quantifying the deviation of the performed hand path from an ideal hand path (e.g., Shadmehr & Brasher-Krug, 1997) or by quantifying the correlation of the performed hand trajectory to a baseline trajectory (e.g., Brashers-Krug et al., 1996). Thereby, motor performance is determined both by the ability to predict the dynamic conditions and the ability to react to sensed motor errors. Accordingly, both feedforward and feedback motor control mechanisms influence motor performance assessed on force field trials, thus evaluating net motor performance facing the dynamic perturbation.

Null field catch trials

When the force field is removed after adaptation and the subjects perform the task under unperturbed conditions, the hand trajectories show distinct deviations once again – now in the opposite direction as compared to the beginning of force field exposure. These so-called *after-effects* indicate that the sensorimotor system did not just increase stiffness to resist the perturbation but learned to deal with the new environmental conditions. This is taken as evidence that an internal model of the task was adapted in order to account for the conditional changes. In particular, after-effects indicate a feedforward motor control strategy because the motor action is executed prior to receiving sensory feedback.

In order to assess after-effects, researchers commonly induce so-called (null field) *catch trials* to the learning schedule. On these trials, the dynamic perturbation is randomly and without prior announcement removed such that subjects unexpectedly perform their movements under null field conditions (e.g., Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Overduin et al., 2006). This allows the assessment of after-effects throughout the course of the learning schedule. Herein, a kinematic error measure can be used to evaluate the magnitude of the after-effects and therewith infer feedforward motor control mechanisms. However, catch trials produce large motor errors that are fed back to the subjects. For this reason, motor performance on catch trials is also influenced by the subjects' ability to react to motor errors (feedback mechanisms).

Error clamp trials

As mentioned above, in force field adaptation tasks, subjects have to learn to compensate the perturbing forces applied by the robot. When adapting to the force field, subjects change their force production in order to predictively cancel out the perturbation. For instance, when a curl force field (Equation 2.1) has to be learned, the subjects need to produce additional compensatory forces perpendicular to the current movement direction. Note, that these forces are not produced to move the hand towards that direction but only to maintain on the desired trajectory. Therefore, the subjects' forces measured at the handle of the robotic manipulandum offer information about the degree of adaptation.

Recently, so-called *error clamp trials* (or *force channel trials*) are used to assess motor adaptation of reaching movements under dynamic perturbations (Figure 2.3). On these trials, the robot produces a virtual force channel that constrains the movement to a straight line toward the target point counteracting all movements perpendicular to the target direction. This allows assessment of the forces that subjects produce in perpendicular direction against the virtual channel wall (Figure 2.3B,D) and serves as indicator for predictive force field compensation (Scheidt et al., 2000; Smith et al., 2006). Note, that on error clamp trials the perturbing force field is turned off and, thus there is no need to produce perpendicular forces against the channel wall to maintain on the desired hand path. Altogether, as on these trials motor errors are clamped to zero and the learning stimulus (force field) is not present, these trials allow measurement of motor adaptation with respect to feedforward adaptation mechanisms without overlapping reflex, error feedback, or learning mechanisms. This serves as indicator for the adaptation of the internal model of the task dynamics (Scheidt et al., 2000; Joiner et al., 2013). Similar to catch trials, error clamp trials can be randomly interspersed during the learning schedule to evaluate progression of motor learning.

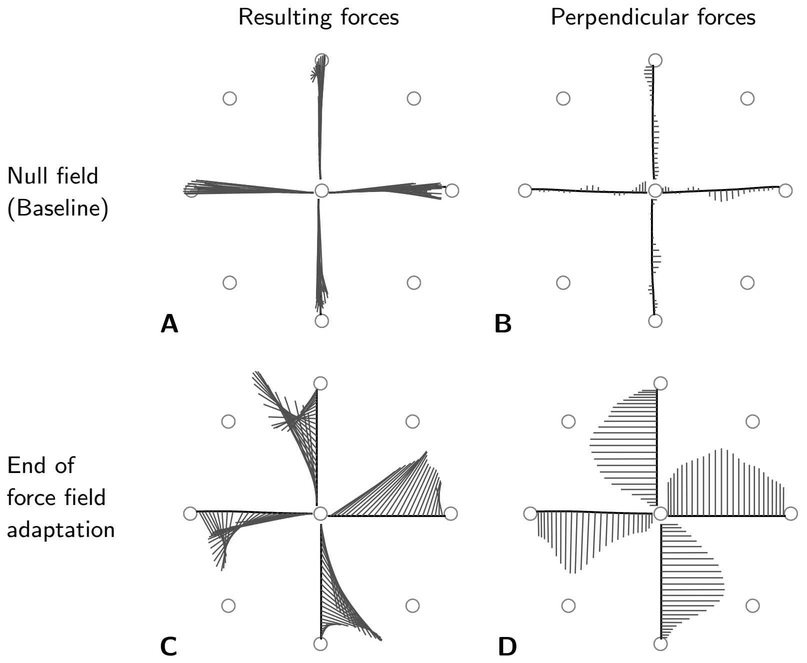


Figure 2.3: Resulting and perpendicular forces on error clamp trials measured at the handle during a dynamic adaptation experiment for a representative subject and selected movement directions. Gray arrows attached to the straight-lined hand paths indicate subject-applied forces with respect to the hand position. Under null field conditions, forces are almost exclusively produced parallel to the movement direction (**A**) resulting in almost no perpendicular forces (**B**). When adapted to the force field, the force output is changed (**C**) by applying additional perpendicular forces (**D**) to cancel the predicted force field.

2.3 ManipAnalysis

2.3.1 Software requirements

In human movement science generally as well as in force field experiments particularly, the used measurement instruments produce a great amount of data. Thus, the problem of organization, processing, analysis, and storage of this data needs to be solved. In case of the BioMotionBot, movements are recorded in the form of Cartesian coordinates alongside with dynamic data measured at the robotic handle. Most often, measuring instruments store these data in human-readable txt-files or some proprietary format as c3d. These files are the basis for all upcoming analytic steps. Hence, an analytic software application needs to be able to read these different file formats and manage all upcoming processing steps.

In software development, several requirements need to be considered. First of all, general software quality requirements form a basic framework as stated for example by the International Organization for Standardization (ISO). Thereby, the ISO distinguishes in basic software quality characteristics (functionality, reliability, usability, efficiency, maintainability, portability) and corresponding subcharacteristics (ISO/IEC 9126, 2001; Figure 2.4). We followed these general requirements as far as relevant for the considered specific scientific purpose.

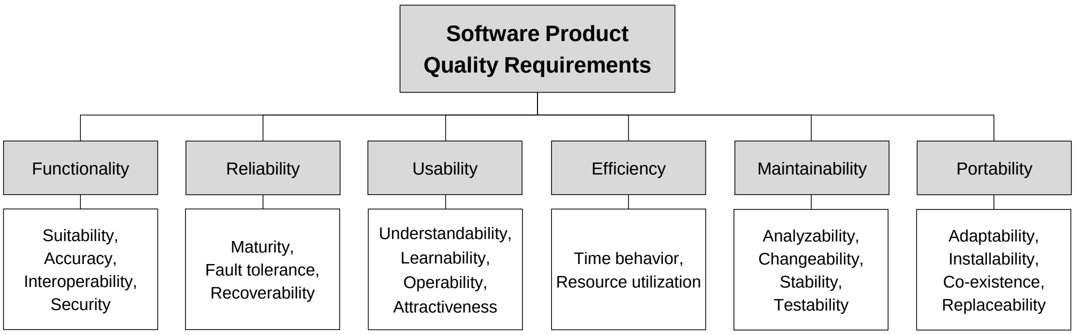


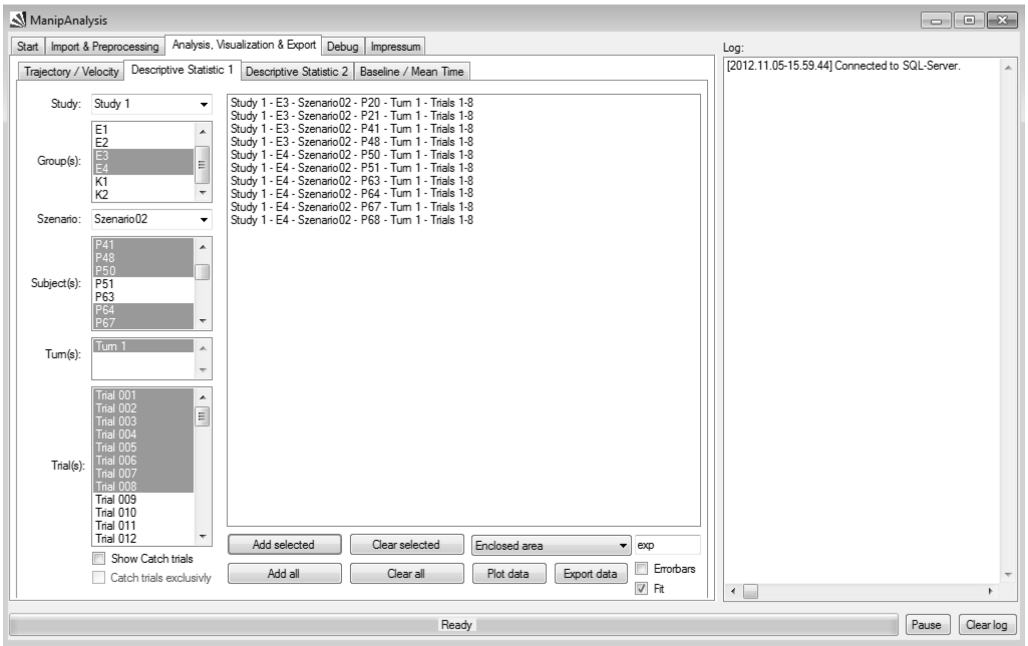
Figure 2.4: ISO software product quality requirements (acc. to ISO/IEC 9126, 2001).

Besides these general quality requirements, several research-specific requirements were formulated for the special case of the analysis of force field experiments:

- Import and convenient storage of collected data in order to have effective and fast access to the required data in further analytic steps.
- Preprocessing of imported raw data by filtering, calculation of movement velocities, segmentation, and time normalization.
- Calculation of baseline trajectories which are recorded while no forces affect subjects' hand. In further steps, these baseline trajectories shall be used as reference for the degree of adaptation to induced perturbations.
- In research on internal models, the adaptation to induced perturbations is of general interest. To assess a subject's motor performance and the degree of adaptation, the software needs to support flexible selection and calculation of commonly used performance parameters.
- Ability to select and analyze movement data of individual or groups of subjects.
- Visualization of collected and calculated data in appropriate form.
- Flexible export options of all calculated intermediate and end results for further data analysis using specific software applications (e.g., SPSS, R, MATLAB).

2.3.2 Software architecture

ManipAnalysis is programmed in C# using .NET framework (v4.5 or later). All recorded data alongside all preprocessed data and all analytic results are imported into a document-oriented database, MongoDB, which can be located on an arbitrary network connected server running a MongoDB-supported operating system (e.g., Microsoft Windows (Server), Linux/Unix, MacOS). All calculations are executed using MathWorks MATLAB accessing a provided COM interface. MATLAB instances are used to maximize processing speed because there are (virtual) CPU-cores available on the system and distributes the workload



Study: Study 1

Group(s): E1, E2, E3, E4, K1, K2

Szenario: Szenario02

Subject(s): P41, P48, P50, P51, P63, P64, P67

Turn(s): Turn 1

Trial(s): Trial 001, Trial 002, Trial 003, Trial 004, Trial 005, Trial 006, Trial 007, Trial 008, Trial 009, Trial 010, Trial 011, Trial 012

☐ Show Catch trials

☐ Catch trials exclusivly

```
Study 1 - E3 - Szenario02 - P20 - Turn 1 - Trials 1-8
Study 1 - E3 - Szenario02 - P21 - Turn 1 - Trials 1-8
Study 1 - E3 - Szenario02 - P41 - Turn 1 - Trials 1-8
Study 1 - E3 - Szenario02 - P48 - Turn 1 - Trials 1-8
Study 1 - E4 - Szenario02 - P50 - Turn 1 - Trials 1-8
Study 1 - E4 - Szenario02 - P51 - Turn 1 - Trials 1-8
Study 1 - E4 - Szenario02 - P63 - Turn 1 - Trials 1-8
Study 1 - E4 - Szenario02 - P64 - Turn 1 - Trials 1-8
Study 1 - E4 - Szenario02 - P67 - Turn 1 - Trials 1-8
Study 1 - E4 - Szenario02 - P68 - Turn 1 - Trials 1-8
```

Enclosed area

exp

☐ Errorbars

☑ Fit

```
[2012.11.05-15.59.44] Connected to SQL-Server.
```

Ready

Figure 2.5: ManipAnalysis user interface showing plot and export opportunities for selected performance parameters for a defined group of subjects and specific movement trials..

among them. ManipAnalysis runs stable with MATLAB v7.12 (R2011a) or later. All MATLAB calculations are performed in the background meaning that the MATLAB workspace is not shown, but only the ManipAnalysis user interface itself (Figure 2.5). However, switching to the software's debug mode provides the possibility to access the MATLAB workspace and shell for debug purposes.

Modules

ManipAnalysis is composed of different modules performing specific tasks. There are five basic modules (Import, Preprocessing, Analysis, Visualization, Export) each containing several submodules (Figure 2.6). This separation of tasks ensures a maximum degree of flexibility. Due to this modular structure, only corresponding modules need to be adjusted if requirements change. The software structure itself remains unaffected, allowing for easy refactoring. This property is of general interest for research-specific use because the concrete experimental paradigm will change from case to case.

Import

In robot-assisted experiments, raw data obtained by robotic manipulanda usually contain time stamps, Cartesian coordinates, as well as forces and torques acting at the handle of the manipulandum. Furthermore, raw data includes information about the experimental setup such as type of force field, type of task, movement number, and subject-related information. The import module is able to parse this information, reorganize it, and store it in the database. Thereby, different data formats can be handled (e.g., txt, c3d). Altogether, selected raw data is automatically imported, classified, and stored.

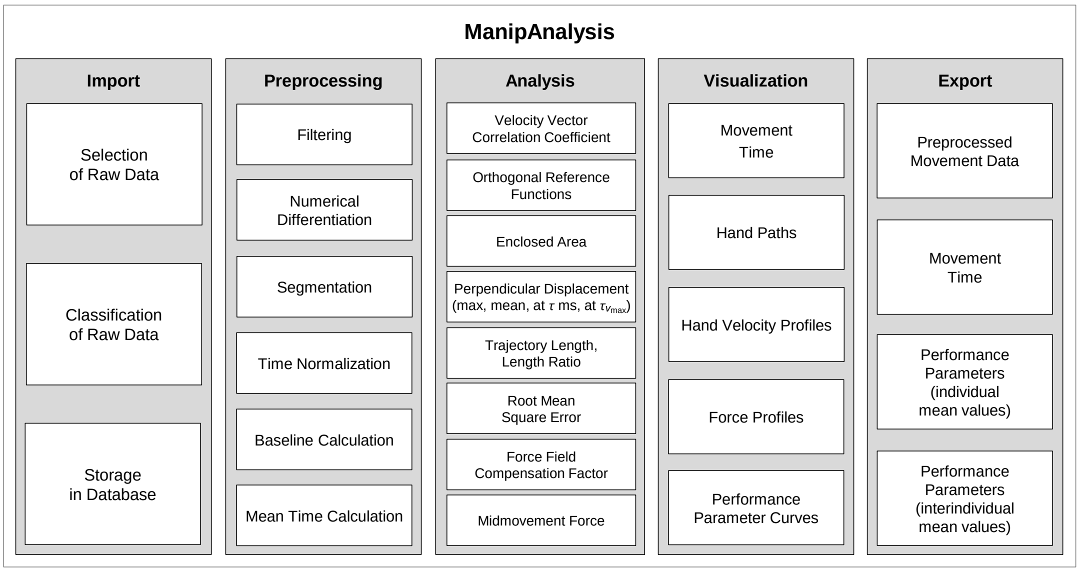


Figure 2.6: Modular structure of ManipAnalysis containing five basic modules and corresponding submodules, each performing specific tasks.

Preprocessing

The preprocessing module is composed of raw data filtering, calculation of movement velocities, data segmentation, and time normalization. Furthermore, baseline trajectories (hand paths, velocity profiles) and baseline force profiles as well as movement mean times are calculated.

In human movement science, recorded data is often affected by high-frequent noise. In order to attenuate this noise, raw data is processed using digital filtering. Thereby, using Fourier transform, the frequency spectrum is determined and certain frequencies are selectively rejected or attenuated (Winter, 2005). ManipAnalysis performs digital filtering using a Butterworth low-pass filter. Hereby, filter order and cut-off frequency can be adjusted on the user interface. In particular, these filter parameters can be adjusted independently for kinematic and dynamic data.

Based on the filtered data, movement velocities are numerically calculated using central difference method (Robertson et al., 2004a):

$$\begin{aligned} v(t) = \dot{x}(t) &= \frac{dx(t)}{dt} \\ &\approx D_{\Delta t}[x](t) = \frac{x(t+\Delta t) - x(t-\Delta t)}{2\Delta t}. \end{aligned}$$

Hereby, $x(t)$ denotes the Cartesian positional data at time t and Δt denotes the incremental time step. Considering this equation for time discretized data yields to the following formulation

$$v_j = \frac{x_{j+1} - x_{j-1}}{2\Delta t} \qquad (j = 1, \ldots, n-1)$$

where, $v_j = v(\Delta t \cdot j)$ and $x_j = x(\Delta t \cdot j)$ denote the measured velocity and position at the discretized time point j, respectively, and n is the total amount of recorded data points.

Afterwards, data sets are segmented in order to dissociate different movement trials. The implemented segmentation algorithm provides two options:

- Segmentation based on position data:
  All data points after the cursor leaves the start point up to the arrival at the target point are selected.

- Segmentation based on velocity data:
  Data points are selected based on a velocity threshold. Thereby, in a first step, the maximal movement speed is calculated for each movement trial. Based on a (freely selectable) percentage value, a velocity threshold as percentage of maximum speed is determined. Movement onset (and offset) is then selected as the time point at which hand speed exceeds (or falls under) this velocity threshold (e.g., 5%: Yang et al., 2007; 10%: Scott et al., 2001; 15%: Donchin et al., 2002).

Afterwards, for the purpose of comparability, movement data is time normalized (Robertson et al., 2004a). In ManipAnalsis, this is performed by using cubic spline interpolation with not-a-knot end conditions and subsequent rescaling of movement data as percentage of duration.

For the cubic spline interpolation, a piecewise polynomial is determined (consisting of polynomials of degree three, i.e., $p_i \in \mathcal{P}_3$, $i = 1, \dots, n$) such that

$$\begin{aligned} p : [t_0, t_{\text{end}}] \to \mathbb{R}, &\qquad p \in C^2([t_0, t_{\text{end}}]), \\ p_i = p|_{[t_{i-1}, t_i]}, &\qquad (i = 1, \dots, n) \end{aligned}$$

for (equidistant) nodes $t_0 < t_1 < \dots < t_{\text{end}}$. Thereby, p has to fulfill the interpolation condition,

$$p(t_i) = x_i, \qquad (i = 1, \dots, n).$$

Moreover, p has to be continuous and two times continuously differentiable at interior nodes:

$$\begin{aligned} p_i(t_i) = p_{i+1}(t_i), &\qquad (i = 1, \dots, n-1), \\ p_i'(t_i) = p_{i+1}'(t_i), &\qquad (i = 1, \dots, n-1), \\ p_i''(t_i) = p_{i+1}''(t_i), &\qquad (i = 1, \dots, n-1). \end{aligned}$$

Finally, not-a-knot boundary conditions are required to uniquely define the spline:

$$p_1^{(3)}(t_1) = p_2^{(3)}(t_1) \qquad \text{and} \qquad p_{n-1}^{(3)}(t_{n-1}) = p_n^{(3)}(t_{n-1}).$$

In order to rescale the movement data, the above-defined cubic spline p is evaluated at the discrete time points

$$\tau_i = \frac{i}{N}(t_{\text{end}} - t_0), \qquad (i = 0, \dots, N)$$

which yields

$$\mathbf{x}_{\text{norm}} = \big(p(\tau_1), \dots, p(\tau_N)\big)^\top \in \mathbb{R}^N.$$

For rescaling the movement data as percentage of duration, one sets $N = 100$.

In the final step of the preprocessing, baseline trajectories are calculated. This is conducted by averaging (pointwise arithmetic mean) selected movement paths, velocity profiles, and force profiles which were recorded under null field conditions. Such baseline trajectories are determined for each movement direction and subject, respectively. In subsequent processing steps, these baseline trajectories are used as reference functions.

All of the above-described preprocessing submodules can be executed automatically or manually. Furthermore, ManipAnalysis allows individual adjustments of the preprocessing procedures. Results of each processing step are stored in the database.

Analysis

Centerpiece of ManipAnalysis is the calculation of performance parameters to quantify the magnitude of adaptation to dynamic perturbations. As mentioned above, force field experiments are a common tool in human movement science. Nevertheless, researchers use diverse methods to quantify a subject's ability to perform movements under force field conditions. In literature, diverse performance parameters are considered, which in turn are calculated with different algorithms. ManipAnalysis supports the calculation of all commonly used performance parameters enabling the user their individual selection.

In principle, ManipAnalysis supports calculation of kinematic (based on hand path and velocity profiles) and dynamic (based on forces at the handle) measures. The measures can further be distinguished in correlation measures, error measures, and measures offering absolute quantities (Table 2.1):

Kinematic measures

- *Velocity vector correlation coefficient*
  The velocity vector correlation coefficient (Pearson correlation) quantifies the similarity between a trial trajectory and a corresponding baseline trajectory depending on the velocity profiles (Brashers-Krug et al., 1996; Caithness et al., 2004; Overduin et al., 2006):

$$\begin{aligned}\text{VCorr}(\mathbf{v}, \mathbf{v}^*) &= \frac{\text{Cov}(\mathbf{v}, \mathbf{v}^*)}{\sqrt{\text{Var}(\mathbf{v}) \cdot \text{Var}(\mathbf{v}^*)}} \\ &= \frac{\text{E}(\mathbf{v} \cdot \mathbf{v}^*) - \text{E}(\mathbf{v}) \cdot \text{E}(\mathbf{v}^*)}{\sqrt{[\text{E}(\mathbf{v}^2) - \text{E}(\mathbf{v})^2] \cdot [\text{E}(\mathbf{v}^{*2}) - \text{E}(\mathbf{v}^*)^2]}}.\end{aligned}$$

Table 2.1: Classification of performance measures supported by ManipAnalysis.

Type of measure	Kinematic	Dynamic
Correlation/ Similarity	• Velocity vector correlation coefficient • Orthogonal reference function correlation	• Force field compensation factor
Error/ Difference	• Enclosed area • Perpendicular displacement (maximum, mean, at $v_{\max}$, at arbitrary t) • Root mean square error	
Absolute values	• Trajectory length • Length ratio	• Midmovement force

Here, $\mathbf{v} = (\dot{\mathbf{x}}, \dot{\mathbf{y}}) \in \mathbb{R}^{N\times 2}$ denotes the velocity profile of the measured movement trial to be evaluated and $\mathbf{v}^* = (\dot{\mathbf{x}}^*, \dot{\mathbf{y}}^*) \in \mathbb{R}^{N\times 2}$ denotes the corresponding baseline velocity profile.[1]
The multiplications of two matrices are meant as scalar product in the dimension 2 and $\mathrm{E}(\cdot)$ denotes the expected value (mean value) of a vector's entries and accordingly the mean value for each column of a matrix.

- *Orthogonal reference function correlation*
  This correlation measure estimates the similarity between trial and baseline trajectories (Stein et al., 2010). Thereby, in a first step, the correlation coefficients (Pearson correlation) of all movement velocity profiles and a given set of orthogonal reference functions (orthonormal system of Taylor polynomials of degree 1 to m) are calculated. This leads to a m-dimensional vector of correlation coefficients for each movement trial. In a second step, the actual correlation is computed by calculating the cosine of the ankle between the correlation vectors of trial movement, $\mathbf{k}$, and corresponding baseline movements, $\mathbf{k}^*$:[2]

$$\mathrm{ORF} = \cos(\mathbf{k}, \mathbf{k}^*) = \frac{\mathbf{k}^\top \mathbf{k}^*}{\|\mathbf{k}\|_2 \cdot \|\mathbf{k}^*\|_2}.$$

Whenever performance is assessed using correlation coefficients, ManipAnalysis performs Fisher z-transforms in order to enable the calculation of mean values across dif-

---

[1] In accordance to standard notation, *scalar* quantities are denoted by italic symbols (e.g., x, v, F); *vectorial* quantities are denoted by bold symbols (e.g., $\mathbf{x}$, $\mathbf{v}$, $\mathbf{F}$); *desired* or *baseline* states, functions, or values are indicated by the "asterisk" notation (e.g., $\mathbf{x}^*$, $\mathbf{v}^*$, $\mathbf{F}^*$); N denotes the number of data points of a movement as given by the time normalization.

[2] Here, $\|\cdot\|_2$ denotes the Euclidean norm; in two-dimensional space this refers to the length of a vector.

ferent subjects or trials:

$$\begin{cases} [-1,1] & \to \mathbb{R}, \\ r & \mapsto z := \operatorname{arctanh}(r) = \frac{1}{2}\ln\left(\frac{1+r}{1-r}\right). \end{cases}$$

For visualization purposes as well as export of data (see paragraphs *Visualizaion* and *Export*), the z-values can be transformed back to correlation coefficients.

- *Enclosed area*
  The area enclosed by trial trajectory and straight line joining start and target point (Caithness et al., 2004; Burdet et al., 2001) is determined using Gauss' area formula for polygons:

$$\mathrm{A} = \frac{1}{2}\sum_{i=1}^{N-1}\Big(x^{(i)} - x^{(i+1)})(y^{(i)} + y^{(i+1)}\Big) + \frac{1}{2}\Big(x^{(N)} - x^{(1)})(y^{(N)} + y^{(1)}\Big).$$

  Here, $(x^{(i)}, y^{(i)}) = \mathbf{x}^{(i)}$, $(i = 0, \ldots, N+1)$ are the vertices of a two-dimensional polygon which in case of movement trajectories are given by start point $(i = 0)$, trial trajectory $(i = 1, \ldots, N)$, and target point $(i = N+1)$.

- *Perpendicular displacement*
  Maximal perpendicular displacement ($\mathrm{PD}_{\mathrm{max}}$, Schabowsky et al., 2007; Howard et al., 2010) and mean perpendicular displacement ($\mathrm{PD}_{\mathrm{mean}}$, Davidson & Wolpert, 2004; Arce et al., 2010) of trial trajectory from straight line joining start and target point is determined by

$$\mathrm{PD}_{\mathrm{max}} = \max\Big\{ \min_{i=1}^{N} \|\mathbf{x}^{(i)} - \mathbf{x}^{*}_{\mathrm{straight}}\|_2 \Big\} \qquad \text{and}$$
$$\mathrm{PD}_{\mathrm{mean}} = \frac{1}{N}\Big(\sum_{i=1}^{N} \min \|\mathbf{x}^{(i)} - \mathbf{x}^{*}_{\mathrm{straight}}\|_2 \Big)$$

  where, $\mathbf{x}^{(i)} = (x^{(i)}, y^{(i)})$ indicates the two-dimensional coordinates of the trial trajectory and $\mathbf{x}^{*}_{\mathrm{straight}}$ represents the straight line joining start and target point.

  Furthermore, the perpendicular displacement of trial trajectory to straight line joining start and target points can be calculated at arbitrary time points τ after movement start based on non-normalized data:

$$\mathrm{PD}_{\tau} = \min \|\mathbf{x}(\tau) - \mathbf{x}^{*}_{\mathrm{straight}}\|_2.$$

  Due to its simplicity, the perpendicular displacement measure is frequently used in literature. Depending on the chosen time point of evaluation, different motor control mechanisms can be considered. For small time windows, preliminary feedforward control mechanisms affect this measure (e.g., $\mathrm{PD}_{100\mathrm{ms}}$, de Xivry et al., 2011). When evaluating at later time points, reflex and feedback mechanisms become relevant (e.g.,

$PD_{200\mathrm{ms}}$: Shadmehr & Holcoumb, 1999; $PD_{250\mathrm{ms}}$: Thoroughman & Shadmehr, 1999, 2000; $PD_{300\mathrm{ms}}$: Shadmehr & Brasher-Krug, 1997; Donchin et al., 2002; Criscimagna-Hemminger et al., 2003) such that this measure accounts for different control mechanisms.

Similarly, the perpendicular displacement can be calculated at the time point of maximal velocity $\tau_{v_{\max}}$ (Thoroughman & Taylor, 2005; Donchin et al., 2003; Pekny et al., 2011):

$$\mathrm{PD}_{\tau_{v_{\max}}} = \min \|\mathbf{x}(\tau_{v_{\max}}) - \mathbf{x}^*_{\mathrm{straight}}\|_2.$$

This measure has the advantage to be independent of the segmentation algorithm.

The perpendicular displacement values can be calculated both as absolute and signed values indicating the direction of displacement (clockwise or counterclockwise) from the straight line.

- *Trajectory length*
  Length of trial trajectory as well as length ratio of trial trajectory and baseline (Novakovic & Sanguineti, 2011):

$$d = \sum_{i=1}^{N-1} \|\mathbf{x}^{(i+1)} - \mathbf{x}^{(i)}\|_2$$

and

$$\mathrm{LengthRatio} = \frac{d}{d^*} = \frac{\sum_{i=1}^{N-1} \|\mathbf{x}^{(i+1)} - \mathbf{x}^{(i)}\|_2}{\sum_{i=1}^{N-1} \|\mathbf{x}^{*(i+1)} - \mathbf{x}^{*(i)}\|_2}.$$

- *Root mean square error*
  of trial trajectory and baseline trajectory (Boutin et al., 2012):

$$\mathrm{RMSE} = \sqrt{\frac{1}{N} \sum_{i=1}^{N} \|\mathbf{x}^{(i)}) - \mathbf{x}^{*(i)})\|_2^2}.$$

Dynamic measures

Based on the recorded forces on error clamp trials (see Section 2.2.2), ManipAnalysis supports the calculation of two dynamic measures of performance: force field compensation factor and midmovement force.

- *Force field compensation factor*
  The force field compensation factor is found by linear regression (in a least-squares sense) of the actually measured perpendicular forces F_{actual} on error clamp trials and the ideal perpendicular forces F_{ideal}. The ideal perpendicular force profile $F_{\mathrm{ideal}}(t)$ refers to the forces necessary to cancel the force field if it had occurred and can be determined by the definition of the perturbing force field. Thus, the linear regression problem is

given by

$$F_{\text{actual}}(t) = a_0 + a_1 \cdot F_{\text{ideal}}(t) + \epsilon(t)$$

where, ϵ is an additive error term, a_0 is the intercept, and the parameter a_1 serves as the force field compensation factor (Joiner & Smith, 2008; Joiner et al., 2013).

- *Midmovement force*
  ManipAnalysis offers the calculation of the Midmovement force as the average perpendicular force produced against the channel wall during error clamp trials within an arbitrary time window $[\tau_a, \tau_b]$ (e.g., from 70 ms before to 70 ms after maximum speed of that movement; Joiner et al., 2013):

  $$\overline{F}_{\text{mid}} = \frac{1}{\tau_b - \tau_a} \int_{\tau_a}^{\tau_b} F_{\text{actual}}(t)dt.$$

  This integral is numerically integrated using trapezoidal rule.

Visualization

To illustrate calculated results, ManipAnalysis offers four kinds of result visualization:

- Plot of mean movement times of a subject or group of subjects itemized by movement type (Figure 2.7). This is supported to control whether subjects stick to a predefined movement time because in most experiments the induced force field is a function of hand velocity. Thereby, the required movement time depends on the specific movement task, in particular on the range of movement. In conventional center-out movement tasks, center point and peripheral points are 0.1 m apart (Figure 2.1A) and subjects are requested to perform the task within 500±50 ms (Shadmehr & Mussa-Ivaldi, 1994; Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997).
- Visualization of baseline and trial trajectories supporting individual selection of specific subjects or movement trials (Figure 2.8B). Moreover, calculation and visualization of mean trajectories is possible. Thereby, computation of mean trajectories of one subject averaged over several trials as well as mean trajectories of several subjects is possible.
- As mentioned above, unperturbed point-to-point reaching movements are approximately straight. Moreover, such movements show bell-shaped velocity profiles (Flash & Hogan, 1985). This characteristic changes when forces affect subjects' hands yielding a curve with multiple peaks (Shadmehr & Mussa-Ivaldi, 1994). To visualize such changes, ManipAnalysis generates movement velocity profiles of individually selected subjects or movement trials. Furthermore, averaged velocity profiles can be calculated and visualized (Figure 2.8C).
- Furthermore, force profiles of forces measured at the handle can be plotted. In particular, ManipAnalysis supports separate illustration of the force components perpendicular and parallel to movement direction (Figure 2.8D). This allows description of changes in the subjects' force output when adapting to the force field.

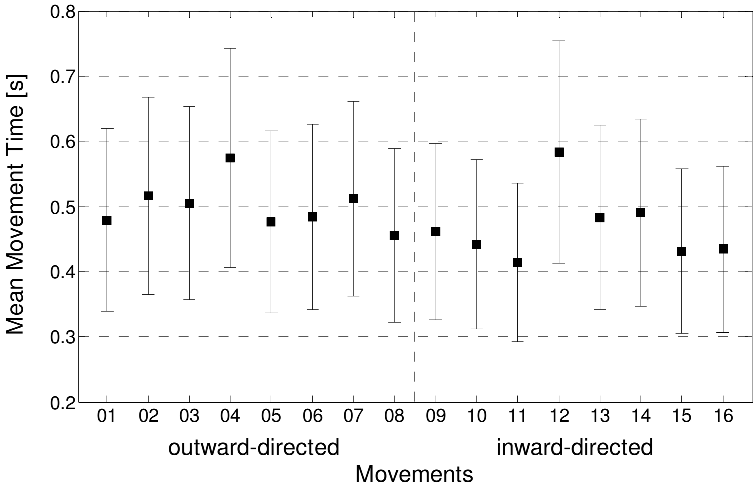


Figure 2.7: Mean movement time and standard deviation of a subject for each of the 16 types of movements averaged over 16 sets: eight outward directed (01-08) and eight inward-directed (09-16), respectively.

- Most importantly, ManipAnalysis generates performance parameter curves illustrating performance changes in the course of a practice session. Thereby, the above-mentioned performance parameters can be selected. These can be shown for single subjects as well as mean values of selected groups of subjects. Optionally, user-defined fitting curves can be inserted to approximate the time curve (Figures 2.8A, 2.9).

Export

For further data analysis with specific statistical software applications or additional data analysis using different applications, ManipAnalysis offers following export options:

- Export of preprocessed movement data (baseline trajectories, movement hand paths, velocities, forces) for single subjects and as mean values of selected groups of subjects. This enables manual database unrelated movement analysis using analysis applications of interest.
- Export of movement time mean values and corresponding standard deviations.
- Export of performance parameters averaged over selected movement intervals for individual subjects enabling further statistical comparisons of several subjects at selected points of time (intraindividual mean values).
- Export of performance parameters for each single movement of selected groups of subjects enabling both the analysis of homogeneity within groups and the comparison of different groups (interindividual mean values).

ManipAnalysis saves the export data as txt-files which are structured in a way enabling straightforward processing with common statistical software applications. For all exports the requested data can be selected individually.

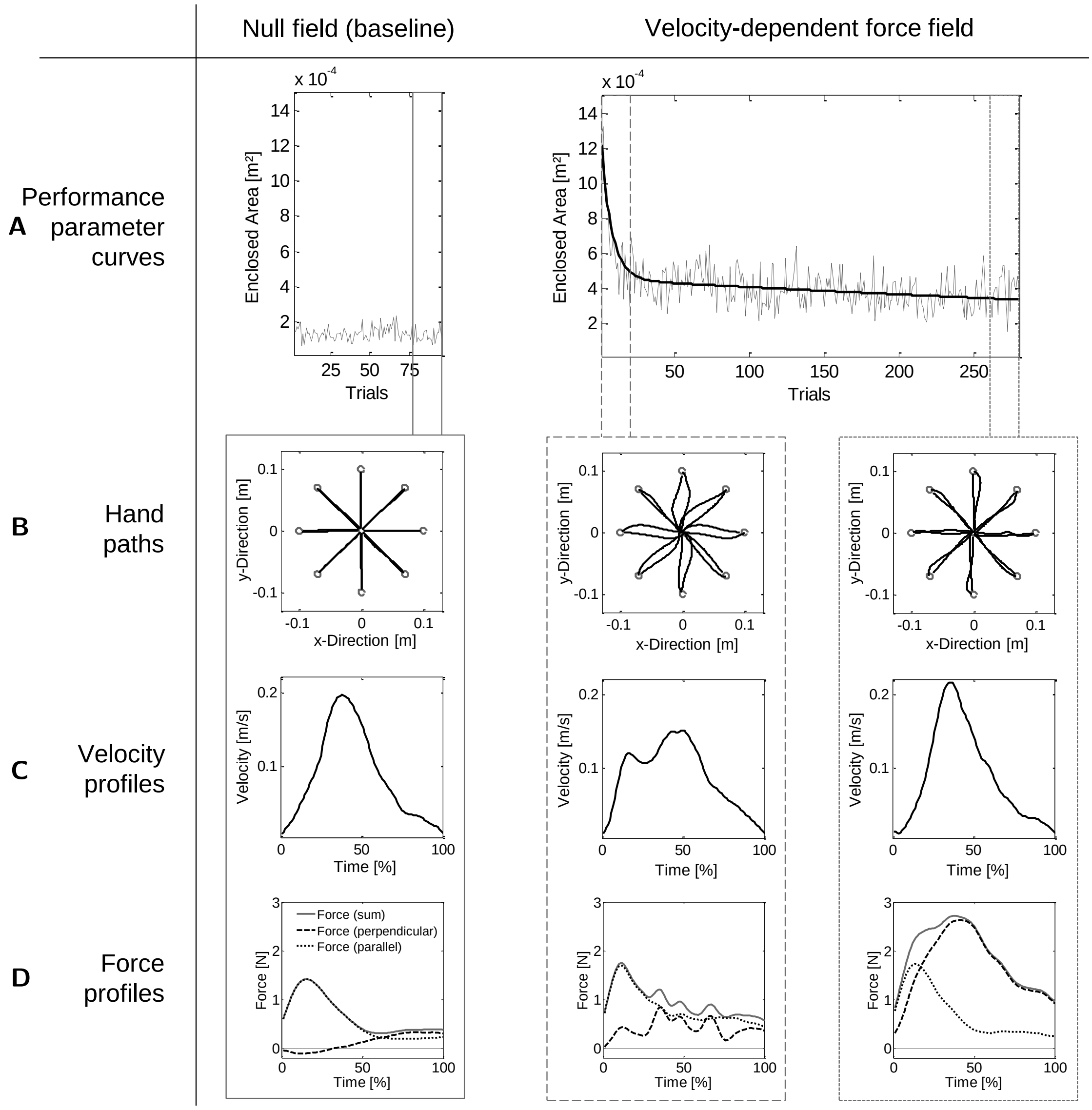


Figure 2.8: Visualization options demonstrated for a force field adaptation experiment. **A**, Mean performance parameter curves for a group of subjects illustrated by enclosed area of trial trajectory and straight line joining start and target point under null field (left) and force field conditions (right). **B**, Mean movement hand paths under null field conditions (left), for the first set of force field practice (middle), and within the last set of force field training (right). **C**,**D**, Mean velocity profiles and mean force profiles in the course of movement time under null field conditions (left), at the beginning of force field practice (middle), and at the end of force field practice (right).

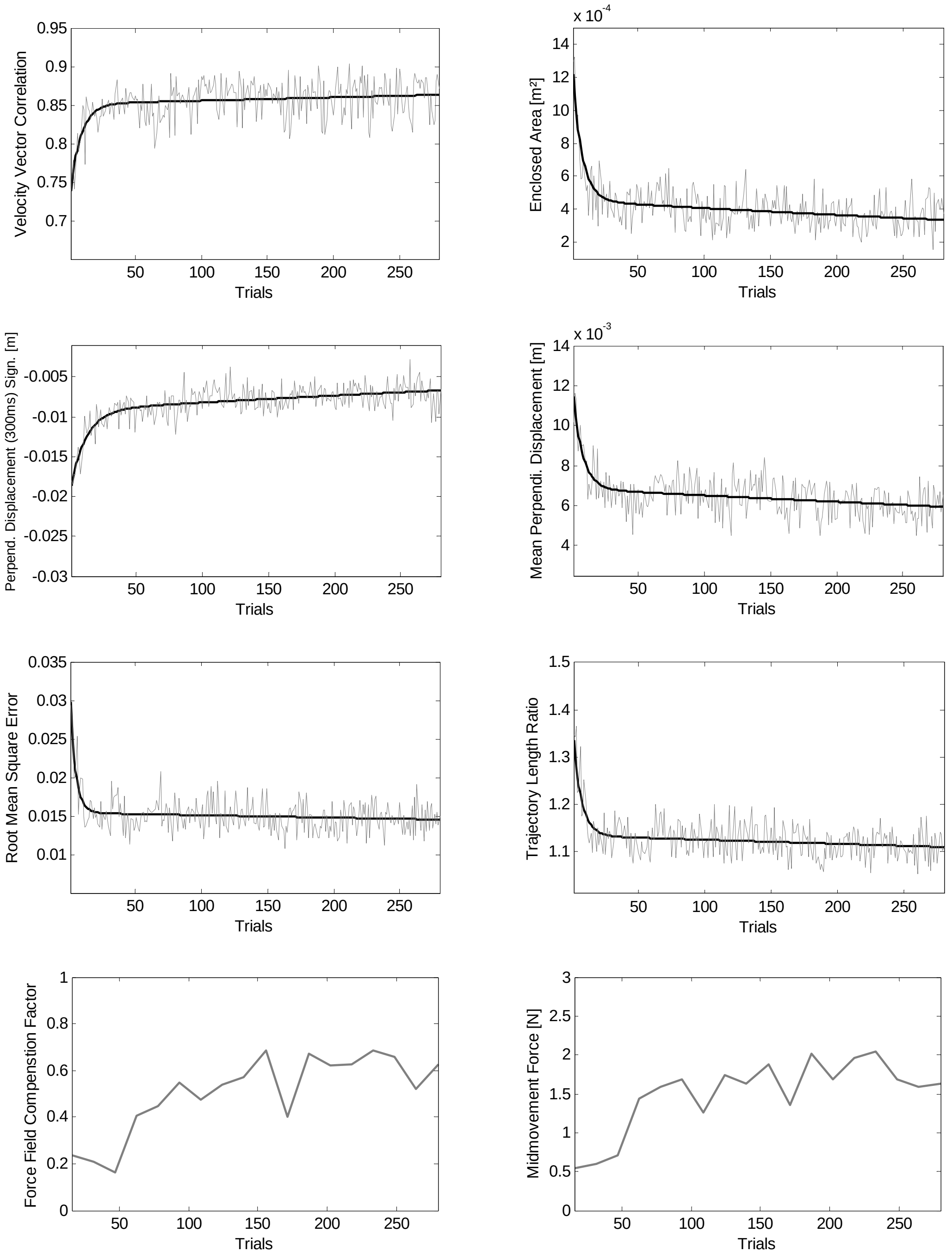


Figure 2.9: Visualization options illustrated by selected mean performance parameter curves as a function of trials. Underlying data is descended from a force field adaptation experiment: **A**, Velocity vector correlation coefficient between trial trajectory under force field conditions and baseline trajectories. **B**, Area enclosed by trial trajectory and straight line joining start and target point. **C**, Mean perpendicular displacement $\mathrm{PD}_{\mathrm{mean}}$ of trial trajectory from straight line joining start and target point. **D**, Perpendicular displacement 300 ms after movement start $\mathrm{PD}_{300\mathrm{ms}}$ as signed value. The negative results indicate dislocation of straight line in counterclockwise direction. **E**, Length ratio of trial trajectory and corresponding baseline trajectory. **F**, Root mean square error of trial trajectory and corresponding baseline trajectory. **G**, Force field compensation factor of randomly interspersed error clamp trials. **H**, Midmovement force evaluated within a time window of ±70 ms around time point of maximum velocity. The curves **A**-**F** are approximated by bi-exponential fitting curves whose shapes indicate adaptation to the force field condition with increasing number of trials, respectively.

2.4 Discussion

ManipAnalysis was developed for the analysis of force field experiments. Here, we first discuss the software's properties with respect to the previously stated general software quality requirements (functionality, reliability, usability, efficiency, maintainability, portability; ISO/IEC 9126, 2001). Afterwards, we discuss ManipAnalysis with regard to the initially mentioned research-specific requirements.

2.4.1 ManipAnalysis and general software quality requirements

ManipAnalysis was developed to manage all processing steps for the analysis of force field experiments. Therefore, only suited and approved processing procedures from computational neuroscience and human movement science were implemented. Those were deduced from common literature and our own practical experiences. Calculation algorithms were implemented by using MATLAB and relating MATLAB algorithms if existent. This enabled an easy and comparable implementation of algorithms. Moreover, MATLAB algorithms are well-proven, accurate, and numerically stable. For data export, well-established txt-files were chosen since these are supported by almost every other analytic software application that might be used in further processing steps. Altogether, requirements on functionality are satisfied.

Due to the use of a document-oriented database, all imported files as well as all intermediate and final calculation results of ManipAnalysis are consistently organized and centrally backed up. On the one hand, this enables several users to work simultaneously on the same data without being forced to use the same computer or to having to import the files several times. Hence, different users do not have to repeat previously conducted calculations since these are stored in the database. On the other hand, using a document-oriented database in combination with constant database backups provides complete recoverability of the data. Due to the fact that the application is relatively new, it is problematic to rank maturity and fault tolerance properties of the application. However, first experiences in analyzing large amount of data show that ManipAnalysis runs reliably.

In order to fulfill usability requirements, an easily operated user interface was implemented. A standard mode offers the most common analytic options with MATLAB running in the background. A debug mode provides detailed adjustments concerning all processing steps as well as access to the MATLAB workspace for manual calculations. Certainly, attractiveness of the application was of secondary importance within the development process. This is due to the fact that ManipAnalysis is a custom-made research-specific analytic tool. Nevertheless, the simple generation of movement trajectory plots or performance parameter values has positive influence on the application's attractiveness.

Since all mathematical calculations of ManipAnalysis are processed locally on the user's computer and subsequently backed up in the database, calculations only have to be computed once. Therefore, a perfect trade-off between performance and security is achieved. This leads to efficiency in time behavior and resource utilization.

Main benefit of the application's modular architecture is a high degree of maintainability and portability. If errors occur, only the corresponding module needs to be identified, tested, and remedied. Moreover, the application is adaptable and expandable in case of changes in calculation algorithms or research-specific changes like differing experimental setups. Thus, ManipAnalysis is not limited to the analysis of traditional two-dimensional center-out movements but might easily be adjusted to other tasks. Likewise, there is no limitation on experiments using dynamic perturbations. The analysis of experiments using kinematic perturbations (Krakauer et al., 2005) is possible as well. Most importantly, the application is compatible to arbitrary robotic manipulanda since recorded data of robotic manipulanda commonly contain the same type of information. In the event of a differing raw data structure, merely the import module needs to be adapted to use ManipAnalysis. For instance, ManipAnalysis processes data which is recorded using the self-developed robotic device BioMotionBot (Bartenbach et al., 2013) but also using the commercial device Kinarm EndPoint Lab (BKIN Technologies, Kingston, Canada, Scott, 1999). For the case of software adjustments, ManipAnalysis comprises an automatic deployment system. Thereby, updates are automatically installed using ClickOnce (Microsoft Corp., USA) technology.

Besides the need for the .NET framework, MATLAB, and connection to a MongoDB database, there are no limitations or requirements for the use of ManipAnalysis. Nor there are restrictions concerning co-existence with other applications.

2.4.2 ManipAnalysis and research-specific requirements

As outlined in this article, there exist diverse methodological approaches for the analysis of force field experiments. Likely, different analytic methods might lead to different conclusions. Therefore, it is important to know about the diversity of analytic methods and its particular characteristics. For instance, in order to evaluate movement trials most measures require the definition of a reference trajectory which is assumed to reflect an ideal pattern (e.g., straight line joining start and target point, individual baseline trajectories). However, it is debatable which trajectory does reflect ideality or whether such an ideality even exists.

Moreover, the type of data under consideration is crucial. Measures based on kinematic and dynamic data emphasize different aspects of motor performance. Dynamic measures that assess motor performance using error clamp trials evaluate motor performance in terms of feedforward mechanisms. In contrast, the above-stated kinematic measures evaluate motor performance with regard to feedforward, feedback, and reflex mechanisms as well as inertial properties of the subjects' arm (i.e., mechanical influence of forces on the human arm). Even within the class of kinematic measures, different aspects are emphasized. Kinematic measures based on hand paths (i.e., positional data) are easy to calculate and interpret, yet, neglecting temporal factors. In comparison, measures based on velocity data are more sensitive to aspects like smoothness of movement execution because they account for temporal factors.

Clearly, we cannot (and are not willing to) give instructions for the analysis of force field experiments. However, by implementing ManipAnalysis we offer a software application that supports all common measures of performance within the framework of force field experiments, thus enabling consideration of different aspects of motor performance.

2.5 Conclusion

The purpose of this article was to introduce the software application ManipAnalysis. This application was developed for the analysis of data gathered in force field experiments which are a common tool in the research of motor control and learning. General and research-specific software requirements were extracted from common literature and own practical experiences. The developed application only requires the .NET framework, MATLAB, and a MongoDB database. Due to its modular architecture, ManipAnalysis is expandable and adaptable in case of changing research-specific requirements. ManipAnalysis is neither limited to the analysis of classical two-dimensional center-out movement tasks nor there are restrictions concerning the used robotic manipulandum. ManipAnalysis handles all analytic steps beginning with the import and storage of data up to performance parameter calculation, visualization, and export. Altogether, ManipAnalysis fills the gap between acquisition and statistical analysis of data which is recorded during force field experiments. We presented diverse approaches to assess motor performance and outlined that these emphasize different aspects, e.g., different control mechanisms. Likely, usage of different analytic approaches leads to different concluding outcomes. Thus, we encourage researchers to chose their analytic approaches with caution bearing in mind the different mechanisms involved in motor control and learning.

3 Adaptation and Consolidation of Motor Memory

Published as

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Abstract

Force field studies are a common tool to investigate motor adaptation and consolidation. Thereby, subjects usually adapt their reaching movements to force field perturbations induced by a robotic device. In this context, so-called catch trials, in which the disturbing forces are randomly turned off, are commonly used to detect after-effects of motor adaptation. However, catch trials also produce sudden large motor errors that might influence the motor adaptation and the consolidation process. Yet, the detailed influence of catch trials is far from clear. Thus, the aim of this study was to investigate the influence of catch trials on motor adaptation and consolidation in force field experiments. Therefore, 105 subjects adapted their reaching movements to robot-generated force fields. The test groups adapted their reaching movements to a force field A followed by learning a second interfering force field B before retest of A (ABA). The control groups were not exposed to force field B (AA). To examine the influence of diverse catch trial ratios, subjects received catch trials during force field adaptation with a probability of either 0%, 10%, 20%, 30%, or 40%, depending on the group. First, the results on motor adaptation revealed significant differences between the diverse catch trial ratio groups. With increasing amount of catch trials, the subjects' motor performance decreased and subjects' ability to accurately predict the force field and therefore internal model formation was impaired. Second, our results revealed that adapting with catch trials can influence the following consolidation process as indicated by a partial reduction to interference. Here, the optimal catch trial ratio was 30%. However, detection of consolidation seems to be biased by the applied measure of performance.

3.1 Introduction

Motor learning is an important attribute of human life which refers to an improvement in execution of a motor behavior. Thereby, motor learning implies two distinct features: the ability to acquire new motor skills and the adaptation of existing motor skills to new environmental conditions (Huang & Krakauer, 2009; Krakauer & Mazzoni, 2011; Kitago & Krakauer, 2013). In neuroscience, motor learning has most often been studied in the context of adaptation of reaching movements. Thereby, subjects usually adapt their reaching movements to either kinematic perturbations (visuomotor rotations, Krakauer et al., 2005; prism-induced displacements, Held & Freedman, 1963) or dynamic perturbations (robot-induced forces, Shadmehr & Mussa-Ivaldi, 1994; rotation of body Lackner & DiZio, 2005; attached inertial loads, Krakauer et al., 1999). Here, we want to focus on motor learning in terms of adaptation of reaching movements to robot-induced forces. Thereby, subjects commonly interact with a robotic device that applies perturbing forces to the subjects' hands leading to changed dynamic conditions of the reaching movements. At the beginning of reaching under these changed dynamics, subjects' hand trajectories are deviated from desired straight hand paths showing a hooking pattern. This results in a motor error arising from the discrepancy between prediction and execution of the movement. When further exposed to this perturbation, subjects' performance initially improves rapid followed by a slower increase to steady state close to baseline performance (Shadmehr et al., 2010). This kind of fast trial-by-trial reduction of motor errors following an abrupt change in conditions is typically referred to as motor adaptation (Haith & Krakauer, 2013). When the dynamic perturbation is removed after adaptation and the subject is reaching under unperturbed conditions, hand trajectories are deviated again. Now, the hand trajectories show after-effects in a direction opposite to the initial deviation of the dynamic perturbation. This is taken as evidence that the sensorimotor system learned an internal model to specifically counteract the dynamic perturbation and did not simply increase arm stiffness (Shadmehr et al., 2010). To detect adaptation of such an internal model, usually error clamp trials or catch trials are interspersed. In error clamp trials, movements are constrained to a virtual channel and the subjects' forces against the channel wall are evaluated (Scheidt et al., 2000). In catch trials, the dynamic perturbation is randomly and without prior announcement removed (usually in 10–20% of the trials) and subjects reach under null field conditions. This allows detection of after-effects (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997). In contrast to error clamp trials, catch trials produce large motor errors that are fed back to the subject. As motor adaptation from one trial to the next was shown to be proportional to experienced motor error (Thoroughman & Shadmehr, 2000; Donchin et al., 2003), it is widely accepted that catch trials affect execution of immediately following movement trials (Thoroughman & Shadmehr, 2000; Scheidt et al., 2001; Karniel & Mussa-Ivaldi, 2002, 2003; Levy et al., 2010). However, the influence of catch trials on the overall motor adaptation process has not yet been investigated in detail.

Following adaptation, motor memory is transformed from an initially fragile state to a more robust and stable state and therewith gains resistance to interference. This time-dependent process is called consolidation and contributes to enhanced retest performance when exposed to the disturbance a second time (Robertson et al., 2004b; Krakauer & Shadmehr, 2006). In the context of force field experiments, numerous studies were able to detect enhanced retest performance of a learned force field A when exposed to this perturbation a second time (savings in AA-paradigm) (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Caithness et al., 2004; Overduin et al., 2006; Focke et al., 2013). Moreover, various studies investigated the consolidation process of force field adaptation using an ABA-paradigm. Thereby, consolidation following adaptation to force field A is interfered by learning a second force field B before retest of A (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Caithness et al., 2004; Focke et al., 2013). Some researchers found evidence for consolidation of force field A (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997), whereas others did not (Caithness et al., 2004; Focke et al., 2013). Most of these studies used catch trials without taking into account that these change the conditions of practice and may thus considerably influence the consolidation process. Indeed, Overduin et al. (2006) showed that subjects are able to consolidate a learned force field A in the ABA-paradigm when catch trials were interspersed during adaptation, whereas learning without catch trials did not lead to consolidation of force field A. Conversely, Focke et al. (2013) failed to confirm this finding for a more complex task, suggesting that not the presence of catch trials per se but the amount of induced catch trials might be crucial. Thus, consolidation also seems to be a practice-dependent process in which the effect of catch trials is insufficiently understood and needs to be further investigated.

Taken together, the detailed influence of catch trials on the overall motor adaptation process as well as on the following consolidation process remains unknown. Research in skill learning exhibited that variable practice schedules facilitate consolidation when learning closed tasks for which the environmental conditions are always similar and the movement can be planned in advance (Shea & Morgan, 1979; Shea & Kohl, 1991; Schmidt & Lee, 2011). Thereby, higher variability during practice leads to a poorer performance during learning but to a better performance at retest compared to lower variability during practice. Although, the relationship between motor adaptation and skill learning is far from clear (Yarrow et al., 2009), similar results may occur for motor adaptation and the following consolidation process. Therefore, the aim of our study was to investigate the influence of different catch trial ratios both on the motor adaptation process and on the consolidation process in force field adaptation. We hypothesized that increasing intermittence during practice operationalized with various catch trial ratios of up to 40% leads to a poorer performance during adaptation compared to lower intermittence during practice (e.g., 0% catch trials) but facilitates the consolidation process.

Table 3.1: Experimental paradigm and classification of subject groups.

Group		**Catch trial ratio [%]**	**Subjects**	**Paradigm**		
				Day 1 (Learning)	Day 2 (Interference)	Day 3 (Retest)
Control 0%	(C0)	0	n=11	F N A_0	–	A_0
Test 0%	(T0)		n=11	F N A_0	$B_0 = -A_0$	A_0
Control 10%	(C10)	10	n=11	F N A_{10}	–	A_{10}
Test 10%	(T10)		n=10	F N A_{10}	$B_{10} = -A_{10}$	A_{10}
Control 20%	(C20)	20	n=11	F N A_{20}	–	A_{20}
Test 20%	(T20)		n=9	F N A_{20}	$B_{20} = -A_{20}$	A_{20}
Control 30%	(C30)	30	n=11	F N A_{30}	–	A_{30}
Test 30%	(T30)		n=10	F N A_{30}	$B_{30} = -A_{30}$	A_{30}
Control 40%	(C40)	40	n=10	F N A_{40}	–	A_{40}
Test 40%	(T40)		n=11	F N A_{40}	$B_{40} = -A_{40}$	A_{40}

F: familiarization block in null field (25 sets, 400 trials); N: baseline block in null field (6 sets, 96 trials); A: clockwise velocity-dependent force field with different ratio of catch trials and force field trials 25 sets, 400 trials); B: counterclockwise velocity-dependent force field with different ratio of catch trials and force field trials (25 sets, 400 trials).

3.2 Materials and methods

3.2.1 Subjects

A total of 110 healthy subjects participated in this study (age 24.3±2.1 years; 46 female, 64 male; 103 right-handed, 7 left-handed). They all gave written informed consent and the test-protocol was reviewed and approved by the institutional review board. All subjects were naive to the experimental procedure (apparatus, paradigm, and purpose of the study) and had no known motor deficits or neurological impairments. Handedness was verified using Edinburgh Handedness Inventory (Oldfield, 1971).

The subjects were randomly assigned to ten groups, whereas five control groups (C0, C10, C20, C30, C40) and five corresponding test groups (T0, T10, T20, T30, T40) were defined (Table 3.1). To investigate consolidation patterns of motor memory, we considered all ten groups separately. To analyze motor adaptation to force field A during the learning session (day 1), we unified each two corresponding groups (e.g., C10 and T10) as the corresponding control and test groups passed the same experimental procedure on that day. We refer to the union of two such groups as the catch trial ratio groups 0%, 10%, 20%, 30%, and 40%.

Five subjects were excluded from the analysis because of technical reasons or lacking ability to adapt to the dynamics.

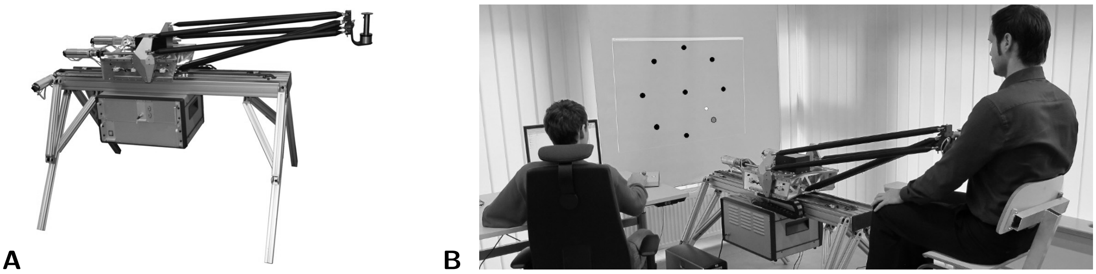

Figure 3.1: **A**, Robotic device BioMotionBot. **B**, Subject performing the horizontal point-to-point reaching task. The cursor corresponding to the position of the handle and the targets were displayed on a screen facing the subject.

3.2.2 Apparatus

Subjects grasped the handle of a robotic device (BioMotionBot; Figure 3.1A) that could exert forces (Bartenbach et al., 2013). The subjects' arms were not supported and all movements were restricted to the horizontal plane. Subjects had clear view of their hand throughout the whole experiment. They received full visual feedback of the targets as well as of the cursor corresponding to the position of the handle on a vertical screen mounted above the robotic device. Subjects sat on a chair, which was individually adjusted so that they were able to grasp the handle with their dominant hand and comfortable reach all target positions (Figure 3.1B). This individual seating position was reinstated in all following practice sessions. Position and force at the handle were recorded at a sampling rate of 200 Hz.

3.2.3 Procedure

Task

We used an experimental setup similar to that described by Focke et al. (2013). Subjects were asked to perform accurate goal-directed point-to-point reaching movements in the horizontal plane with their dominant hand using the robotic device. Starting from a center point, subjects had to reach for one of the eight peripheral target points which highlighted in a pseudo-randomized order. The subsequent movement was initiated from this point back towards the center point. Therefore, the end point of each movement was the starting point for the subsequent movement. The peripheral target points were uniformly arranged on a circle of 10 cm radius around the center point. Targets were red circles (1 cm diameter) and the cursor was a white circle (0.3 cm diameter) appearing on a black background. If a target had to be reached, it changed its color from red to yellow. To avoid target sequence specific phenomena, the target sequence differed for each subject.

We defined a set of movements as 16 trials eight outward and eight inward movements in which each peripheral target point occurred exactly once. All learning blocks were constructed as concatenation of such movement sets. This ensured the same amount of practice towards each target direction.

Subjects were requested to perform each movement within 500±50 ms. Additionally, subjects were told that reaction time was not important, i.e., after appearance of the new target they could wait as long as they wanted before starting the movement. Consequently, reaction time was excluded from the requested time interval. After completion of each movement, subjects received visual feedback about movement time on the screen. If the subjects reached the target within the required time, a green circle around the target appeared. If they moved too slowly, a red circle appeared and when moving too fast, an orange circle turned up. This visual feedback was provided throughout the whole experiment to ensure consistent movement speed.

Experimental design

To investigate the consolidation process of a learned task A, we used an ABA-paradigm whereby the practice sessions were distributed over three days with 24 h rest between each session (Table 3.1). To determine the adaptation process, we considered the learning block A on day 1.

On day 1, all subjects began with a familiarization block under null field conditions (F, no disturbing forces) for 25 sets (400 trials; Table 3.1). After performing this familiarization block, subjects were able to perform the movements at the requested speed. We did not further analyze this data. After 5 min of rest, subjects performed a baseline block for six sets (96 trials) under null field conditions (N). Based on these trials, we calculated baseline trajectories to evaluate null field performance and as reference to movement trials performed under force field conditions. After another 5 min of rest, subjects performed 25 sets (400 trials) in a velocity-dependent clockwise force field A. On day 2 (24 h rest), subjects of the test groups (T0,. . . ,T40) were exposed to a second interfering velocity-dependent counterclockwise force field B=–A for 25 sets. Subjects of the control groups did not attend the laboratory on day 2. On day 3, all subjects were retested for another 25 sets in force field A.

During force field adaptation, short breaks of 60 s were inserted after each five sets. Thereby, subjects could release their hand from the handle but remained seated. The sessions lasted approximately 60 min on day 1 and approximately 30 min on the subsequent practice days. Subjects were instructed to sleep at least 6 h between the test sessions.

Forces and catch trials

Within the force field adaptation blocks, the robotic device generated a velocity-dependent force field that applied forces perpendicular to the direction of movement according to the following equation:

$$\begin{pmatrix} F_x \\ F_z \end{pmatrix} = k \cdot \begin{pmatrix} \cos(\theta) & -\sin(\theta) \\ \sin(\theta) & \cos(\theta) \end{pmatrix} \cdot \begin{pmatrix} \dot{x} \\ \dot{z} \end{pmatrix} \tag{3.1}$$

Here, F_x and F_z are the robot-generated forces; $k = 20$ Ns/m is the force field viscosity; θ denotes the direction of the force field (force field A: $\theta = -90$ clockwise-directed, force field B: $\theta = 90$ counterclockwise-directed); $\dot{x}$ and $\dot{z}$ are the components of hand velocity in the horizontal plane.

During force field adaptation, catch trials were pseudo-randomly interspersed without prior announcement. Depending on the group, catch trials appeared with either 0%, 10%, 20%, 30%, or 40% probability. The catch trial ratio is indexed in the name of group and applied force field, respectively (e.g., C10: control group adapting to force field A10 with 10% catch trials; Table 3.1). Catch trials occurred in outward and inward movements and in some cases occurred one after another. If a catch trial occurred towards a specific direction, no force field trial was performed towards this direction during this set of movements. Catch trials were induced without replacement such that the number of force field trials differed between the catch trial groups but the total amount of performed movements retained (400 movements).

3.2.4 Data analysis

Preprocessing

All parameters were calculated using the custom-made software application ManipAnalysis (Stockinger et al., 2012). Raw data of hand trajectories were filtered using a fourth-order Butterworth low-pass filter (6 Hz cut-off frequency). Afterwards, movement velocities were numerically computed using central difference method. Next, data sets were segmented. For position data, movement start was defined as the time-point when the cursor left the starting point and movement termination was marked when the cursor reached the target point. For velocity data, movement onset (or end) was defined as the time at which velocity exceeded (or fell under) 10% of maximal velocity of that movement. Finally, the data sets were time-normalized using cubic spline interpolation to make them comparable.

We calculated baseline trajectories and baseline velocity profiles for each of the 16 movement directions by respectively averaging corresponding movements of the last five sets recorded in the baseline block under null field conditions (N) (Stockinger et al., 2012).

Performance measurement

Velocity vector correlation coefficient
To quantify movement performance under force field conditions, we calculated a velocity vector correlation coefficient. This widely used measure only considers force field trials and quantifies motor performance by estimating the similarity between the velocity profiles of force field movements and corresponding baseline movements (Shadmehr & Brasher-Krug, 1997; Caithness et al., 2004; Overduin et al., 2006; Stockinger et al., 2012).

Perpendicular displacement
To specifically evaluate catch trial movements, we calculated the signed perpendicular displacement ($\mathrm{PD}_{\mathrm{catch}}$) of hand trajectory from the straight line joining start and target point 300 ms after movement start (Shadmehr & Brasher-Krug, 1997; Donchin et al., 2002). This measure allowed us to gauge both the magnitude and the direction of the

deviation. For instance, a subject who adapted to a clockwise-directed force field A will predictively generate additional forces in counterclockwise direction to cancel out the expected disturbing forces (Shadmehr & Mussa-Ivaldi, 1994). Consequently, we would expect the perpendicular displacement on a catch trial to be counterclockwise-directed. We indicate such after-effects appropriate to force field A with negative sign. In contrast, we indicate after-effects appropriate to force field B with positive sign.

Moreover, the perpendicular displacement was calculated for force field trials ($\mathrm{PD}_{\mathrm{field}}$) to calculate a learning index as described in the following paragraph. Other measures of trajectory displacement (e.g., maximal perpendicular displacement, mean perpendicular displacement, perpendicular displacement 200 ms after movement start) yielded qualitatively similar results and are therefore not presented in this paper.

Learning index

To relate force field trials and catch trials, we calculated a learning index (LI). This learning index allows quantification of force field learning with respect to after-effects during catch trials (Donchin et al., 2002; Overduin et al., 2006). When subjects adapt to the force field conditions, trajectories should become straight-lined and therefore show gradually decreasing perpendicular displacement values in force field trials. However, in catch trials there should be increasing after-effects to the opposite direction with ongoing learning (Shadmehr & Mussa-Ivaldi, 1994). Based on this idea we calculated the learning index as follows:

$$\mathrm{LI} = \frac{\overline{\mathrm{PD}}_{\mathrm{catch}}}{|\overline{\mathrm{PD}}_{\mathrm{field}}| + |\overline{\mathrm{PD}}_{\mathrm{catch}}|} \in [-1, 1] \tag{3.2}$$

Thereby, PD denotes the perpendicular displacement of hand trajectory as defined above in either force field trials ($\mathrm{PD}_{\mathrm{field}}$) or catch trials ($\mathrm{PD}_{\mathrm{catch}}$). The learning index was calculated using perpendicular displacement mean values ($\overline{\mathrm{PD}}$) of force field and catch trials for each set (16 trials) of movements.

Early in the adaptation period, subjects should show a learning index near zero because in catch trials small after-effects and in force field trials large displacements should appear. With ongoing practice, the absolute value of the learning index should increase because after-effects in catch trials increase and deviations in force field trials decrease (Donchin et al., 2002). A subject who resists the disturbing forces by increasing the stiffness of the arm may perform an accurate movement showing only small deviations during force field trials. Nevertheless, this leads to a low-valued learning index because perpendicular displacements are also small in catch trials. Thus, the learning index is a good measure to quantify force field prediction and thus internal model formation (Overduin et al., 2006).

The learning index is a relative measure of performance with a theoretical limit of 1 (absolute value). It is signed as the numerator includes the signed perpendicular displacement of catch trials. This allows distinction of learning the two opposing force fields A and B. Thereby, learning of the clockwise-directed force field A was indicated with a negative value, whereas learning of the counterclockwise-directed force field B had positive sign.

The learning index was not calculated for the 0% catch trial groups (C0, T0) as these groups did not receive any catch trials that indicate after-effects.

We conducted the statistical analyses for velocity vector correlation coefficient, learning index as well as the perpendicular displacement. We did this for several reasons. First, velocity vector correlation is a well-established and frequently used measure to quantify force field learning (e.g., Shadmehr & Brasher-Krug, 1997; Caithness et al., 2004; Overduin et al., 2006). This enables comparison to most former force field studies. Second, velocity vector correlation allowed us to quantify performance of the 0% catch trial group which is impossible when using the learning index. Third, we additionally used the learning index based on the perpendicular displacement because it also considers catch trials and therefore more emphasizes the internal model prediction and the direction of force prediction than the velocity vector correlation. Furthermore, the perpendicular displacement is an intuitively accessible and frequently used measure of motor error (e.g., Shadmehr & Brasher-Krug, 1997; Donchin et al., 2002).

Difference values

To assess performance changes between two distinct points in time, we calculated the difference value of performances between these two points in time. Thereby, increase (or decrease) of performance within the considered period was indicated with positive (or negative) sign. Using this difference value we were able to compare performance changes across different groups.

The term “initial performance” always refers to the mean score of the first set of movements (16 trials) within the considered period. Accordingly, “end performance” always refers to the mean score of the last set of movements (16 trials) within the considered period.

Statistics

To test for differences within groups, we used paired t-tests. Adaptation on day 1 was confirmed by comparing initial and end performance of the learning session for each group. To check for consolidation of force field A of a specific group, we compared initial performance of the learning session (day 1) and retest session (day 3) of that group.

To test for differences between groups, we conducted one-way ANOVAs with between subject factor *group*. Hereby, differences in initial or end performance were determined. To compare the degree of adaptation between groups, we considered the difference value of initial and end performance in force field A of the learning session (day 1).

To test for differences in consolidation between the pairs of groups, we conducted a two-way ANOVA with the between subject factors *catch trial ratio* [0%, 10%, 20%, 30%, 40%] and *interference* [control group, test group]. Therefore, we compared the difference values calculated from initial performance of the learning session (day 1) and retest session (day 3) between the different groups. This allowed evaluation of the influence of different catch trial ratios on the consolidation of force field A with respect to the interference of force field B. To evaluate after-effects, we used one-sample t-tests to compare given mean values to zero.

All statistical analyses were conducted using IBM SPSS software (v.21). All data are presented as mean values and 95% confidence intervals. For all statistical tests, the level of significance was a priori set to $p = 0.05$. If one-way ANOVAs revealed significant differences, Bonferroni Post-hoc analysis was used. Effect sizes were determined using partial eta squared η_p^2 (small effect: $\eta_\mathrm{p}^2 = 0.01$; medium effect: $\eta_\mathrm{p}^2 = 0.06$; large effect: $\eta_\mathrm{p}^2 = 0.14$) or Cohen's d (small effect: $d = 0.20$; medium effect: $d = 0.50$, high effect: $d = 0.80$) (Cohen, 1992). All correlation coefficients were transformed using Fisher z-transform before statistical analyses were conducted. All presented data of velocity vector correlation refers to the retransformed z-values.

3.3 Results

The initial performance of the learning session (day 1, first set) did not differ significantly between the ten groups (one-way ANOVA, factor: *group* [C0,...,C40, T0,...,T40]). This holds for the velocity vector correlation ($F_{(9,95)} = 1.30$, $p = 0.249$), perpendicular displacement ($F_{(9,95)} = 1.58$, $p = 0.135$), and learning index ($F_{(7,75)} = 0.92$, $p = 0.493$). Furthermore, we found no significant differences in initial (first set) or end performance (last set) between corresponding control and test groups which received the same amount of catch trials (pairwise independent t-tests). These findings hold for velocity vector correlation, perpendicular displacement, and learning index. Thus, we can unify corresponding control and test groups to analyze the adaptation process during the learning session (day 1) as subjects received the same protocol on that day. Similarly to the ten separated groups, we found no significant differences in initial performance of the learning session (day 1) when considering the five different catch trial ratio groups (one-way ANOVA, factor: *catch trial ratio* [0%,...,40%]; unification of each two corresponding control and test groups) for velocity vector correlation ($F_{(4,100)} = 1.42$, $p = 0.234$), perpendicular displacement ($F_{(4,100)} = 1.42$, $p = 0.222$), and learning index ($F_{(3,79)} = 0{,}68$, $p = 0.568$). Therefore, we act on the assumption that all groups and all catch trial ratio groups started with similar initial conditions.

In the following, we first present results of the adaptation process of the learning session (day 1) considering the five unified catch trial ratio groups. Afterwards, we present results of the consolidation of force field A. The test groups were exposed to a second interfering force field B on day 2 before retest of force field A on day 3, whereas the control groups were retested in force field A on day 3 without interference. Therefore, in consolidation analysis, we consider all ten control and test groups separately (Table 3.1). Additionally, we present results of the after-effects detected during catch trials.

3.3.1 Adaptation

Hand trajectories and velocity profiles

On day 1, all subjects showed the expected adaptation pattern when exposed to force field A. At the beginning of force field adaptation, subjects' hands were considerably disturbed. This resulted in distinctively curved trajectories compared to the null field condition (Figure 3.2A,B). The force field disturbance was also indicated by a change in the hand velocity profiles. Under null field conditions, subjects produced typical bell-shaped velocity profiles with a single peak (Figure 3.2D). At the beginning of force field adaptation, however, subjects' velocity profiles were noticeably disturbed (Figure 3.2E). With practice, subjects were able to counteract the forces resulting in straight-lined trajectories and velocity profiles similar to those profiles in baseline movements (Figure 3.2C,F).

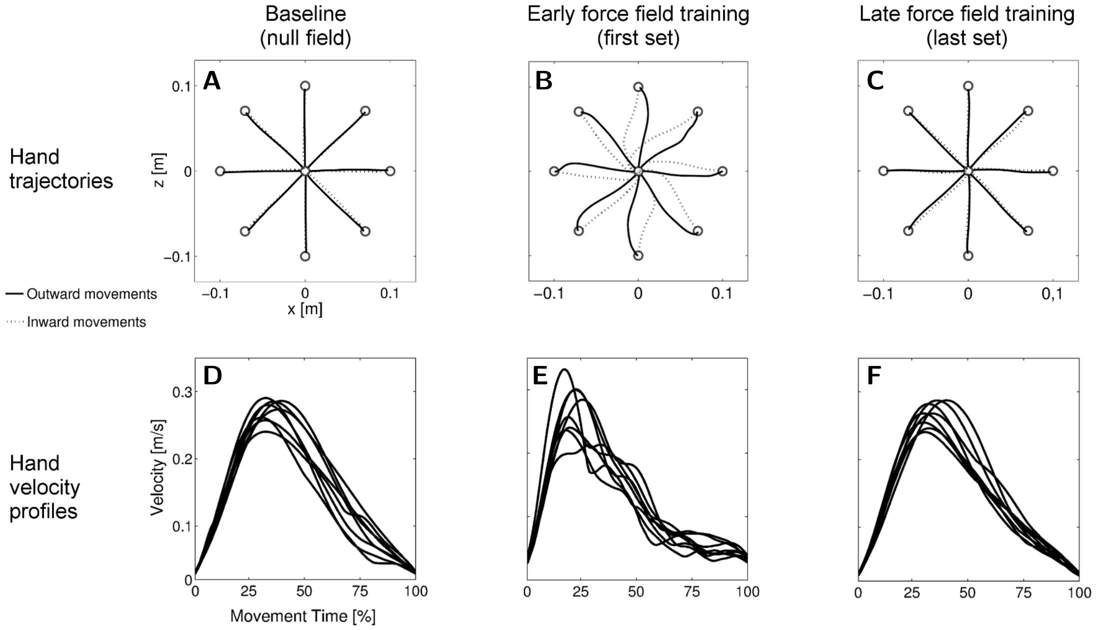

Figure 3.2: Representative mean hand trajectories and mean hand velocity profiles (outwards movements only) of one group. **A**, Straight-lined baseline trajectories. **B**, Disturbed trajectories at the beginning of force field adaptation (first set). **C**, Reshaped straight-lined trajectories at the end of force field adaptation (last set). **D**, Smooth bell-shaped, single-peak baseline velocity profiles. **E**, Disturbed velocity profiles at the beginning of force field adaptation. **F**, Velocity profiles at the end of force field adaptation showing bell-shaped, single-peak profiles.

Velocity vector correlation coefficient and perpendicular displacement

The time course of velocity vector correlation coefficient and perpendicular displacement demonstrate the progress of adaptation to force field A for all groups (Figure 3.3, left; Figure 3.4, left). Adaptation is illustrated by a distinct improvement of motor performance during force field learning. Initially, all groups show rapid improvements in performance. With further practice, the rate of performance improvement decreases. Finally, performance output reaches plateau.

We statistically confirmed adaptation to force field A for each catch trial ratio group. Thereby, all groups showed significantly higher end performance compared to the initial performance (paired *t*-test: $p < 0.001$ for all five groups). Moreover, we found differences

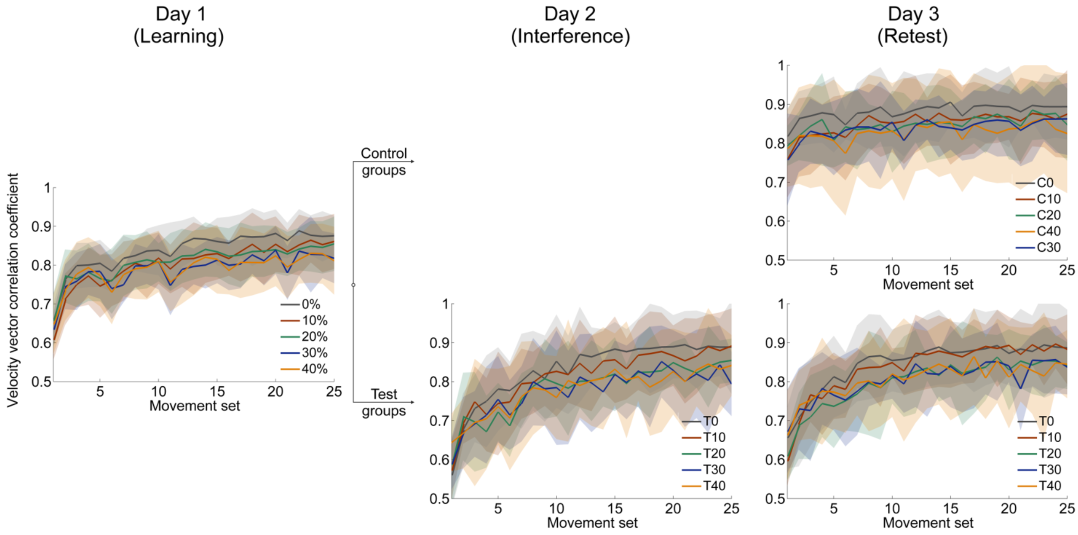

Figure 3.3: Mean time courses of velocity vector correlation coefficient for all three days. After learning force field A on day 1 (left), subjects of each catch trial ratio group were divided into control and test groups. Test groups adapted to an interfering force field B=-A on day 2 (mid). On day 3, all groups were retested in force field A (right). On all three days, subjects were able to adapt to the changed dynamic conditions indicated by increasing correlation coefficients. All data is presented as mean values ±95% confidence intervals.

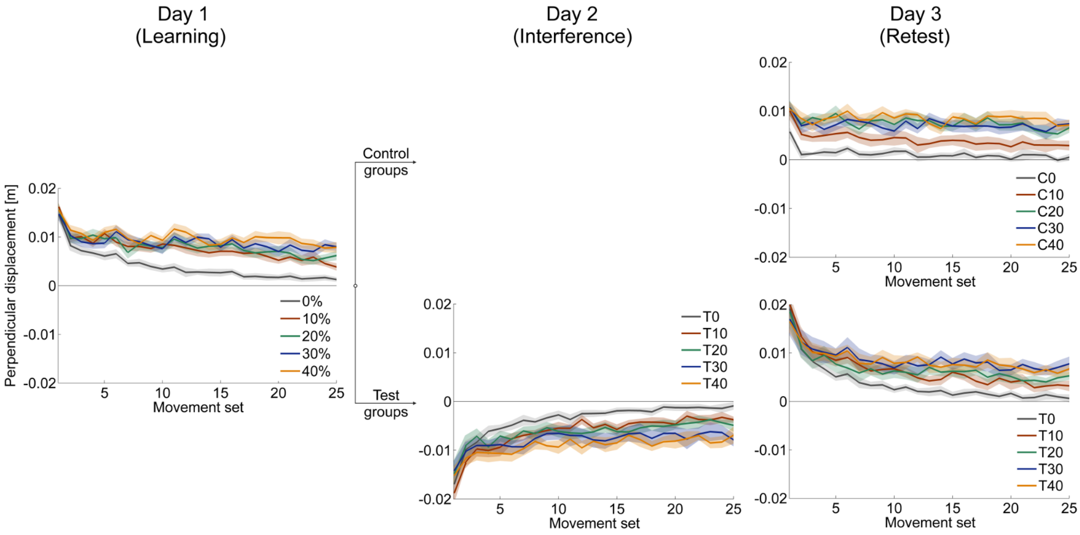

Figure 3.4: Mean time courses of signed perpendicular displacement 300 ms after movement start in force field trials. Positive (negative) values indicate deviations in clockwise (counterclockwise) direction caused by disturbance of force field A (force field B). On all three days, subjects were able to adapt to the changed dynamic conditions leading to decreased errors. All data is presented as mean values ±95% confidence intervals.

in the degree of adaptation between the five catch trial ratio groups: The performance improvement value assessed by subtracting initial performance from end performance showed significant differences between the five groups. All these findings hold for both velocity vector correlation (one-way ANOVA: $F_{(4,100)} = 6.70$, $p < 0.001$; Figure 3.6A) and perpendicular displacement (one-way ANOVA: $F_{(4,100)} = 24.64$, $p < 0.001$; Figure 3.6B). For the velocity vector correlation, Bonferroni Post-hoc analysis revealed significant differences between 0% and 30% catch trial ratio ($p = 0.015$), 0% and 40% catch trial ratio ($p = 0.001$), 10% and 30% catch trial ratio ($p = 0.015$), as well as between 10% and 40% catch trial ratio ($p = 0.015$). For the perpendicular displacement, Bonferroni Post-hoc analysis revealed significant differences between 0% and 20% catch trial ratio ($p < 0.001$), 0% and 30% catch trial ratio ($p < 0.001$), 0% and 40% catch trial ratio ($p < 0.001$), 10% and 20% catch trial ratio ($p = 0.002$), 10% and 30% catch trial ratio ($p < 0.001$), 10% and 40% catch trial ratio ($p < 0.001$), as well as between 20% and 40% catch trial ratio ($p = 0.024$).

Additionally, we conducted the same analyses comparing the performance at the time point at which all groups had performed a total of 240 force field trials, i.e., same amount of force field trials. We found similar results, i.e., significant worse degree of adaptation with increasing catch trial ratio for velocity vector correlation (one-way ANOVA: $F_{(4,100)} = 3.31$, $p = 0.014$) and perpendicular displacement (one-way ANOVA: $F_{(4,100)} = 13.35$, $p < 0.001$). Thus, the reported differences between the catch trial ratio groups were not because of the different amount of performed force field trials. Therefore, sensorimotor adaptation, as quantified by the velocity vector correlation coefficient and perpendicular displacement, worsened as the catch trial ratio increased.

Learning index

To determine the degree of force field learning with respect to catch trials, we conducted the same adaptation analyses as above for the four groups that received catch trials using the learning index. All four groups improved rapidly at the beginning of adaptation (Figure 3.5, left). This rapid improvement decayed with ongoing practice and finally reached plateau for all groups. All groups were able to adapt to the force field conditions when considering the learning index. This was exhibited by a significant improvement from first set to last set (paired t-test: $p < 0.001$ for all four groups).

To gauge differences in the improvement of learning index during adaptation, we compared the difference values (initial vs. end of adaptation) of learning index and found significant differences between the four groups (one-way ANOVA: $F_{(3,79)} = 2.85$, $p = 0.043$). Bonferroni Post-hoc analysis revealed significant differences between 10% and 30% catch trial ratio ($p = 0.032$) as well as between 10% and 40% catch trial ratio ($p = 0.016$) (Figure 3.6C). These differences also hold, when evaluating the learning index at the time point at which all groups had performed 240 force field trials (one-way ANOVA: $F_{(3,79)} = 3.53$, $p = 0.019$). Therefore, sensorimotor adaptation, as quantified by the learning index, worsened as the catch trial ratio increased. These results are in accordance to the results of velocity vector correlation and perpendicular displacement mentioned above.

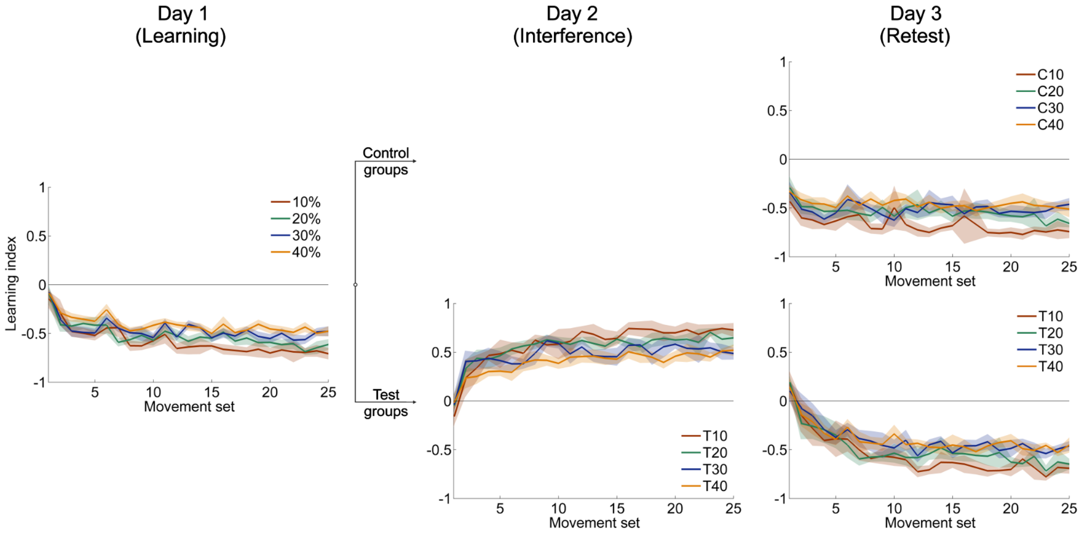

Figure 3.5: Mean time courses of learning index which relates catch trials and force field trials. Learning of the clockwise-directed force field A is indicated with negative values, learning of the counterclockwise-directed force field B has positive sign. All data is presented as mean values ±95% confidence intervals.

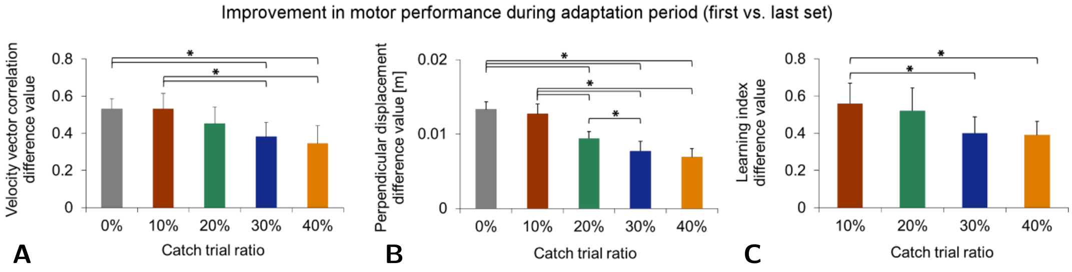

Figure 3.6: Comparison of degree of adaptation between catch trial ratio groups using velocity vector correlation coefficient (**A**), perpendicular displacement (**B**), and learning index (**C**). All three performance measures indicate a significantly decreasing degree in force field adaptation with increasing catch trial ratio. All data is presented as mean values ±95% confidence intervals; asterisks indicate significant differences between catch trial ratio groups.

Adaptation to the interfering force field

On day 2, all test groups were exposed to the interfering force field B and followed the same protocol as on day 1, respectively. Thus, these groups received different amounts of catch trials. We found differences in the degree of adaptation to force field B between the test groups: The performance improvement value assessed by subtracting initial performance from end performance showed significant differences between the five test groups for all measures (one-way ANOVA: velocity vector correlation: $F_{(4,46)} = 7.564$, $p < 0.001$; perpendicular displacement: $F_{(4,46)} = 11.407$, $p < 0.001$; learning index: $F_{(3,36)} = 7.561$, $p < 0.001$). For the velocity vector correlation, Bonferroni Post-hoc analysis revealed significant differences between T0 and T30 ($p = 0.001$), T0 and T40 ($p = 0.007$), T10 and T30 ($p = 0.002$), as well as between T10 and T40 ($p = 0.009$). For the perpendicular displacement, Bonferroni Post-hoc analysis revealed significant differences between T0 and T20 ($p = 0.019$), T0 and T30 ($p < 0.001$), T0 and T40 ($p = 0.001$), T10 and T30 ($p < 0.001$), as well as between T10 and T40 ($p = 0.006$). For the learning index, Bonferroni Post-hoc analysis revealed significant differences between T10 and T30 ($p = 0.001$) and between T10 and T40 ($p = 0.001$). Therefore, the test groups' attained level of adaptation to force field B decreased with increasing catch trial ratio which is in line with the findings on the adaptation to force field A on day 1.

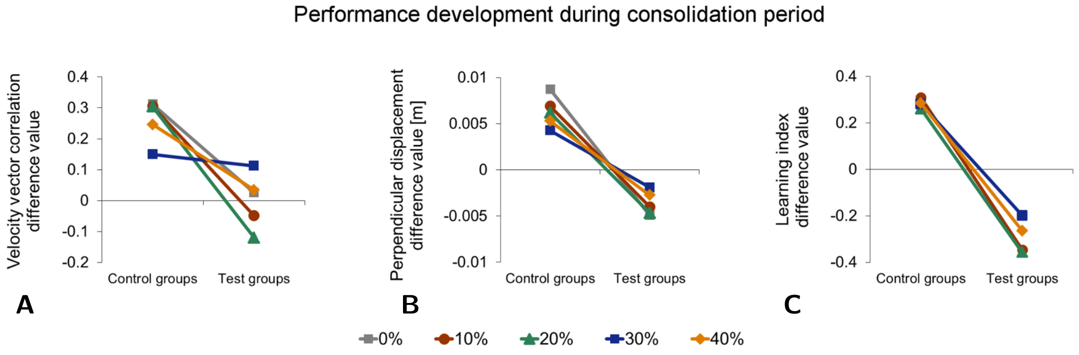

Figure 3.7: Comparison of development in initial performance from learning session (day 1) to retest (day 3) of force field A measured by velocity vector correlation (**A**), perpendicular displacement (**B**), and learning index (**C**). Positive values indicate a performance improvement, whereas negative values indicate a decreased initial retest performance compared to naive performance. In general, test groups show impaired consolidation compared to corresponding control groups indicated by a significant effect of interference [control, test]. For velocity vector correlation (**A**) and perpendicular displacement (**B**), there is also a significant interaction of interference and catch trial ratio, indicating different consolidation depending on the catch trial ratio. Thereby, consolidation is least impaired for 30% catch trial test group. All data is presented as mean values ±95% confidence intervals.

3.3.2 Consolidation

Velocity vector correlation coefficient and perpendicular displacement

As expected, all control groups exhibited savings of force field A from learning on day 1 until retest on day 3. This was indicated by a significant increase of the initial performance (mean score of first set) measured by velocity vector correlation from learning session (day 1) to retest (day 3) of force field A for all control groups (paired t-test: $p < 0.010$ for all five groups). In particular, we found no significant differences in this increase between the five control groups (one-way ANOVA: $F_{(4,49)} = 2.31$, $p = 0.073$) when comparing the difference value of initial performance on day 1 and day 3, i.e., the consolidation processed similarly for all control groups.

The aim of our study was to investigate the influence of different catch trial ratios on the consolidation process in the ABA-paradigm, in particular on resistance to interference of force field B learning. To assess the influence of catch trials on the consolidation process with respect to the interference of force field B, we conducted a two-way ANOVA (between subject factors: *catch trial ratio* [0%,. . . ,40%] and *interference* [control group, test group]) analyzing the difference values of initial performances of the learning session and retest of each catch trial ratio group (Figure 3.7A). We found a significant interference effect ($F_{(1,95)} = 65.90$, $p < 0.001$, $\eta^2_\mathrm{p} = 0.41$) and a significant interaction between interference and catch trial ratio ($F_{(4,95)} = 5.11$, $p = 0.001$, $\eta^2_\mathrm{p} = 0.18$). Thus, in general, exposure to the interfering force field B on day 2 had an effect on the consolidation process. However, for different catch trial ratio groups, consolidation progressed differently. Post-hoc analysis (pairwise independent t-tests between corresponding control and test groups) revealed significant differences between groups C0 and T0 ($t_{(20)} = 5.79$, $p < 0.001$, $d = 2.47$), C10 and T10 ($t_{(19)} = 4.68$, $p < 0.001$, $d = 2.06$), C20 and T20 ($t_{(18)} = 6.27$, $p < 0.001$, $d = 2.85$) as well as between C40 and T40 ($t_{(19)} = 2.74$, $p = 0.013$, $d = 1.18$) indicating a significant effect of the exposure to the interfering force field B, respectively. However, we found no significant differences between C30 and T30 ($t_{(19)} = –0.02$, $p = 0.983$, $d = 0.01$). Thus, the consolidation process of subjects receiving 30% catch trials was not significantly influenced by the interfering force field B when measured by velocity vector correlation. Taken together, for the catch trial ratio groups 0%, 10%, and 20% the difference values comparing initial performance of the learning session (day 1) and retest (day 3) differed significantly between control and test groups. Thereby, test groups performed worse. This significant difference did not appear for a catch trial ratio of 30%. In case of a further increase of the catch trial ratio up to 40%, control and test groups showed significant differences again.

We conducted the same analyses for the performance values assessed by the perpendicular displacement (Figure 3.7B). The two-way ANOVA (between subject factors: *catch trial ratio* [0%,. . . ,40%] and *interference* [control group, test group]) analyzing the difference values of initial performances of the learning session and retest revealed a significant interference effect ($F_{(1,95)} = 179.21$, $p < 0.001$, $\eta^2_\mathrm{p} = 0.65$) and a significant interaction between interference and catch trial ratio ($F_{(4,95)} = 3.10$, $p = 0.019$, $\eta^2_\mathrm{p} = 0.12$). In general, this indicates an effect of exposure to force field B and differing consolidation progression for the diverse catch trial ratios which is in line with the findings of the velocity vector correlation. In contrast, Post-hoc analysis (pairwise independent t-tests), showed significant differences between all corresponding control and test groups, respectively (0%: $t_{(20)} = 7.96$, $p < 0.001$, $d = 3.39$; 10%: $t_{(19)} = 7.13$, $p < 0.001$, $d = 3.12$; 20%: $t_{(18)} = 6.10$, $p < 0.001$, $d = 2.71$; 30%: $t_{(19)} = 4.28$, $p < 0.001$, $d = 1.86$; 40%: $t_{(19)} = 4.49$, $p < 0.001$, $d = 1.97$). Therefore, exposure to force field B significantly impaired the consolidation process of all test groups. However, this impairment depended on the catch trial ratio and was least for the 30% catch trial ratio test group compared to its control group (Figure 3.7B).

Thus, the consolidation process, as measured by the velocity vector correlation, was influenced by catch trials, suggesting most resistance to interference of force field B for 30% catch trials. Consolidation, in terms of absence of interference and as quantified by the perpendicular displacement, could not be detected for any catch trial ratio. However, the consolidation process was least impaired for 30% catch trial ratio suggesting partial resistance to interference.

Learning index

We also considered the progress of learning index from the learning session (day 1) to the retest session (day 3). All control groups showed significantly higher initial learning index values at retest than at the learning session (paired t-test: $p < 0.015$ for all four groups). In particular, we found no significant differences in this increase between the four control groups when comparing the difference value of initial performance on day 1 and day 3 (one-way ANOVA: $F_{(3,39)} = 0.08$, $p = 0.970$), i.e., the consolidation processed similarly for all control groups. This is in accordance to the findings of the velocity vector correlation and perpendicular displacement. However, the two-way ANOVA (between subject factors: *catch trial ratio* [10%,. . . ,40%] and *interference* [control group, test group]) revealed only a significant effect of interference ($F_{(1,75)} = 129.59$, $p < 0.001$, $\eta_p^2 = 0.63$; Figure 3.7C) but no significant interaction between interference and catch trial ratio ($F_{(3,75)} = 0.59$, $p = 0.625$, $\eta_p^2 = 0.02$). Therefore, exposure to force field B had a significant influence on the consolidation process for all considered catch trial ratios. Thus, in contrast to the results of velocity vector correlation and perpendicular displacement, the catch trial ratio had no significant influence on the consolidation process as quantified by the learning index.

After-effects

Figure 3.8 illustrates after-effects of force field adaptation in catch trials that occurred during all sessions. For all catch trial ratio groups, after-effects are initially small but increase with ongoing practice and reach plateau. At the end of each day, the catch trial groups' after-effects differed significantly in magnitude (one-way ANOVAs: $p \leq 0.001$ for all three days). Thereby, with increasing catch trial ratio, subjects showed significantly smaller after-effects.

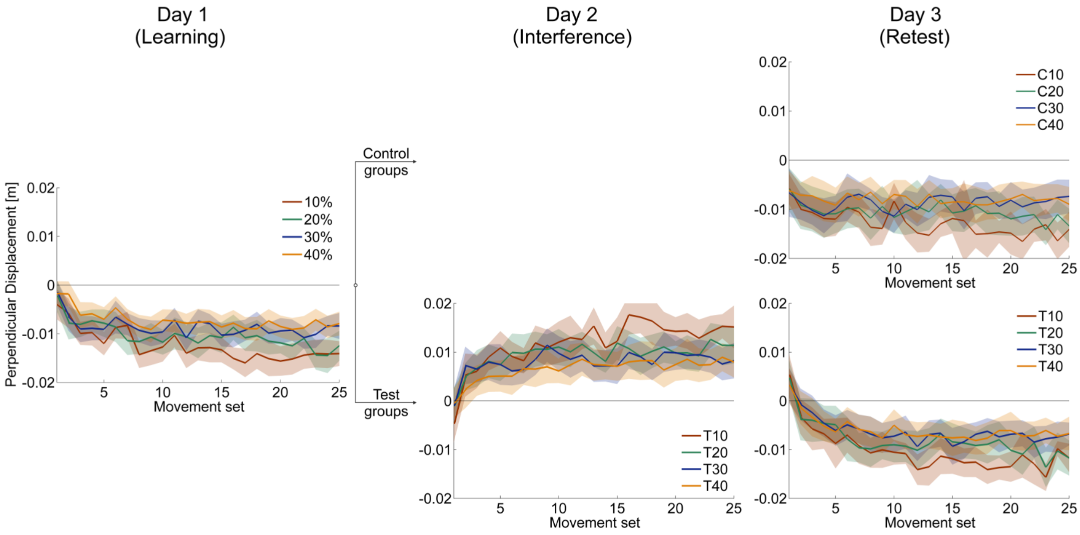

Figure 3.8: Mean time courses of after-effects measured by signed perpendicular displacement during catch trials. Negative (positive) values indicate deviations in counterclockwise (clockwise) direction and therefore after-effects appropriate to force field A (force field B). The magnitude of after-effects increases with ongoing practice and is least for subjects receiving 30% and 40% catch trials. All data is presented as mean values ±95% confidence intervals.

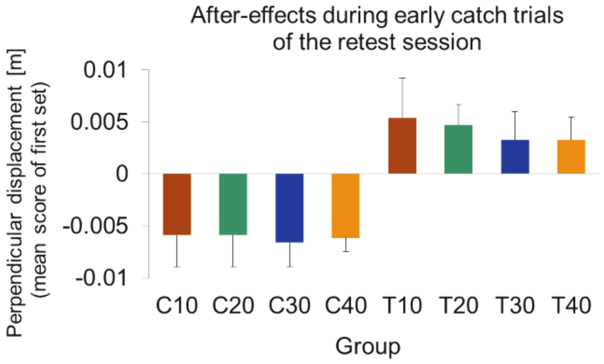

Figure 3.9: Mean values of signed perpendicular displacement in catch trials of the first movement set at retest of force field A (day 3). All control groups show significant negative after-effect values indicating predictive force compensation appropriate to force field A. Test groups show significant positive after-effect values indicating predictive force compensation appropriate to force field B. All data is presented as mean ±95% confidence intervals.

To investigate after-effects of force field B adaptation onto retest of force field A, we considered catch trials at the beginning of the retest session (day 3). We calculated the mean values of perpendicular displacements in catch trials of the first set of movements. This allowed us to quantify the magnitude and the direction of after-effects. Comparison of after-effects based on only the first catch trial, which occurred for all groups on the third or fourth trial, lead to similar results.

At the beginning of the retest session, all control groups showed significant negative mean perpendicular displacements (one-sample t-test vs. zero; C10: $t_{(10)} = –3.72$, $p = 0.004$; C20: $t_{(10)} = –3.73$, $p = 0.004$; C30: $t_{(10)} = –5.58$, $p < 0.001$; C40: $t_{(9)} = –9.38$, $p < 0.001$; Figure 3.9). Thus, subjects of all control groups started retest of force field A with a force field prediction appropriate to force field A. We found no significant differences of these after-effects between the control groups (one-way ANOVA: $F_{(3,39)} = 0.65$, $p = 0.578$).

The test groups, however, all showed significant positive perpendicular displacements in catch trials at the beginning of retest (one-sample t-test vs. zero; T10: $t_{(9)} = 2.74$, $p = 0.023$; T20: $t_{(8)} = 4.87$, $p = 0.001$; T30: $t_{(9)} = 2.37$, $p = 0.042$; T40: $t_{(10)} = 2.90$, $p = 0.016$; Figure 3.9). Thus, subjects of all test groups started retest of force field A with a force field prediction appropriate to force field B. We found no significant differences of these after-effects between the test groups indicating similar after-effects of force field B adaptation onto retest of force field A (one-way ANOVA: $F_{(3,36)} = 0.68$, $p = 0.542$).

3.4 Discussion

Our study was designed to investigate the influence of catch trials on the overall motor adaptation process as well as on the following consolidation process. We hypothesized that increasing intermittence during practice – operationalized with various catch trial ratios – leads to a poorer performance during adaptation compared to constant practice but facilitates consolidation. Against the background of these hypotheses, we separately discuss the results on motor adaptation (Subsection 3.4.1) and consolidation (Subsection 3.4.2). Finally, we relate our results to findings from research on skill learning (Subsection 3.4.3).

3.4.1 Catch trials influence internal model formation and motor performance during adaptation

Our results on motor adaptation showed that increased intermittence by interspersed catch trials lead to poorer performance during adaptation. We assume that the catch trial induced intermittences impair the ability to form an internal model and therewith impair accurate compensation for the dynamic perturbation.

In accordance to former studies (e.g., Shadmehr & Mussa-Ivaldi, 1994), our results showed that all groups were able to adapt to the changed dynamic conditions induced by the disturbing force field (Figures 3.3, 3.4, 3.5). Though, the degree of adaptation depended on the amount of induced catch trials. This finding holds for all considered performance measures (Figures 3.3, 3.4, 3.5). Overduin et al. (2006) did not find an influence of catch trials on the performance development during adaptation. But they solely compared 0% and 20% catch trial ratio groups using the velocity vector correlation. However, we tested a wider range of catch trial ratios and performance measures demonstrating that, in general, motor adaptation depends on the catch trial ratio. These differences in the degree of adaptation are not attributed to the different amount of performed force field trials but seem to be distinctively caused by the catch trial induced intermittences.

We assume that subjects of different catch trial ratio groups had formed internal models of different quality. As mentioned above, the learning index is a good measure of force field prediction (Donchin et al., 2002; Overduin et al., 2006). Subjects receiving less catch trials (10%, 20%) demonstrated learning curves that suggest better force field prediction compared to the 30% and 40% catch trial ratio groups (Figure 3.5, left). Accordingly, the higher learning index for low catch trial groups contributes to an appropriate internal model formation that enables accurate movement generation using a feedforward control strategy (Franklin et al., 2008; Donchin et al., 2002; Overduin et al., 2006). In contrast, the learning index values of the catch trial ratio groups 30% and 40% suggest an impaired ability to form an appropriate internal model. This would cause inaccurate prediction of perturbing forces and require reaction using muscular co-contraction to perform the movement (Overduin et al., 2006). Maybe, subjects receiving a high amount of catch trials relied more on an impedance control strategy by increasing arm stiffness (Schabowsky et al., 2007). Former research already proposed coexistence of forward model prediction and impedance control strategy (Milner & Franklin, 2005; Osu et al., 2003; Takahashi et al., 2001). Since we tested adaptation using various catch trial ratios, we propose that the ability to form an appropriate internal model changes gradually with altered conditions of practice. This might explain the order of attained performance level according to the amount of induced catch trials which is reasonable as with increasing catch trial ratio the interference and the uncertainty increase which prevents the sensorimotor system of accurately predicting the disturbing forces (Franklin et al., 2008; Osu et al., 2003; Takahashi et al., 2001). In contrast, internal model formation is more emphasized for subjects receiving constant force field perturbations. For such constant perturbations, it was previously assumed that appropriate internal model formation is the main reason for high movement performance at the end of the learning session (Shadmehr et al., 2010).

3.4.2 Consolidation depends on catch trial ratio and performance measure

For the consolidation process following motor adaptation, we found differing results for the considered performance measures suggesting a different sensibility to detect consolidation. Considering the velocity vector correlation, we found that the consolidation process can be positively influenced by catch trials. When subjects learned a second interfering task in-between, consolidation was least impaired for a catch trial ratio of 30%. This was demonstrated by a similar performance development during the consolidation period of corresponding control and test groups for 30% catch trial ratio (Figure 3.7A). For lower catch trial ratio (0%, 10%, 20%), however, consolidation was impaired when learning an interfering second task as indicated by significant differences in the consolidation between corresponding control and test groups. Similarly, for 40% catch trial ratio such significant difference in the consolidation between control and test group occurred. Therefore, learning with an optimal amount of catch trials seems to make the subsequent consolidation process more resistant to interference compared to learning without catch trials or learning with an immoderate amount of catch trials. For the perpendicular displacement, we also found an influence of catch trials on the consolidation process (Figure 3.7B). We detected differences in the degree of impairment of the consolidation process between the various catch trial ratios showing strongest resistance to interference for 30% catch trial ratio. However, for this measure, there was no complete resistance to the interference caused by force field B for any test group. Furthermore, we did not find consolidation when considering the learning index suggesting a disruption of the consolidation process when adapting to an interfering force field B, regardless of the induced amount of catch trials (Figure 3.7C).

To our best knowledge, Overduin et al. (2006) provided the only study which also considered both the velocity vector correlation and the learning index. They observed consolidation for subjects receiving 20% catch trials for both measures. Shadmehr and Brashers-Krug (1997) also used catch trials (approx. 17%) and found consolidation within the ABA-paradigm. However, they only computed velocity vector correlation coefficients. The fact that we detected a reduced interference on the consolidation process using this measure merely for a higher catch trial ratio of 30% might be explained by the higher complexity of our reaching task. In contrast to the mentioned studies, we did not support the subjects' arms. This results in more degrees of freedom within shoulder and elbow joints to be controlled and thus in an increased task complexity. Maybe, an increase of the catch trial ratio up to 30% further emphasized its positive effects on the consolidation process, compensated for our increased task complexity, and therewith facilitated consolidation. However, a further increase of catch trial ratio up to 40% seems to impair consolidation as it increases uncertainty about the task.

The missing detection of consolidation as measured by the perpendicular displacement and learning index might be due to a lower sensitivity of these measures compared to the velocity vector correlation. In this connection it is noteworthy that Overduin et al. (2006) also detected a trend toward a difference between their 20% catch trial control and test groups which, however, turned out not to be statistically significant. It remains the question, why there should be a differing sensitivity between the considered measures. The underlying computations offer a possible explanation because the measures are based on different types of information. The perpendicular displacement and the learning index depend on positional data. The velocity vector correlation, however, uses velocity data and therefore also considers temporal factors. Moreover, the velocity vector correlation is a similarity measure which compares fielded movements to baseline movements recorded under null field conditions, whereas the perpendicular displacement and the learning index are measures of difference.

Irrespective of methodological factors, the question remains, why test groups revealed differences in the reduction of interference that impaired the consolidation process. Former studies that investigated consolidation in ABA-paradigms discussed anterograde interference effects that might have avoided detection of consolidation (Brashers-Krug et al., 1996; Shadmehr & Brasher-Krug, 1997; Caithness et al., 2004). Anterograde interference describes the influence of the interfering force field B onto the recall of force field A. Therefore, anterograde interference might cover the consolidation of force field A (Robertson et al., 2004b). We were able to detect anterograde interference for all test groups that received catch trials by considering the after-effects of learning force field B onto retest of force field A on day 3. Thereby, all considered test groups showed similar after-effects indicating anterograde interference of similar magnitude (Figure 3.9). Former studies using catch trials could not be sure about the relative magnitude of anterograde interference effects because only one catch trial group was given and for the 0% catch trial groups detection of after-effects was not possible. Certainly, we were not able to measure anterograde interference effects for our 0% catch trial test group T0 either. However, the similar after-effects of the catch trial test groups T10, T20, T30, and T40 allow extrapolation to the 0% catch trial group T0 and provide strong evidence for similar effects for all five test groups. Thus, anterograde interference effects do not depend on the induced catch trial ratio during adaptation. Therefore, anterograde interference cannot entirely explain the lacking consolidation. In our experimental design, test groups adapted to force field B on day 2 following the same protocol as on day 1. Thus, these groups received different amounts of catch trials leading to significant different attained end performances in force field B. This might have influenced the formation of an internal model appropriate to force field B. Therefore, the observed differences in the resistance to interference between catch trial ratios might be caused by the different types of interference induced via force field B. For the reason of comparability, our experimental protocol was designed similar to those of former studies presenting catch trials on day 2 (Shadmehr & Brasher-Krug, 1997; Overduin et al., 2006). To further enhance understanding of consolidation processes, future studies should keep the interfering task fixed.

As outlined above, subjects' attained end performance in force field A on day 1 decreased with increasing amount of catch trials. Nevertheless, all control subjects started with a similar level of initial performance at retest independent of the end performance on day 1. This finding emphasizes the importance to separate acquisition performance from retention performance (learning-performance distinction; Kantak & Winstein, 2012). Accordingly, challenging practice schedules with high variability induce difficulties for the learner which might impair acquisition performance but facilitate long-term retention and consolidation processes, referred to as the contextual interference effect (Schmidt & Lee, 2011). Research suggests, that variable practice schedules influence motor memory formation causing deeper cognitive processing and therefore stronger and more elaborate motor memory representations (Kantak & Winstein, 2012; Robertson et al., 2004b). This positive effect is supposed to occur because variable practice induces more contrasting inter-trial comparisons than constant practice (Kantak & Winstein, 2012). In our design, catch trials produced variable practice schedules that led to impaired acquisition performance but a potentially stronger internal model representation of force field A enhancing long term retention. Altogether, there is strong evidence that the practice structure affects consolidation of motor memory (Robertson et al., 2004b; Tanaka et al., 2009; Kantak et al., 2010; Kantak & Winstein, 2012). Moreover, in variable and constant practice, different neural substrates seem to be critical for consolidation (Tanaka et al., 2009; Kantak et al., 2010). Tanaka et al. (2009) further supposed that motor memories, which are encoded in variable practice schedules, are stored more quickly and become more rapidly stabilized and resistant compared to constant practice. These suggestions provide possible explanations for our findings on differing resistance to interference when learning with catch trials compared to constant force field practice. Yet, we suppose that for our specific task, not the presence of catch trials per se is important. Rather there seems to be an optimal amount of catch trial induced variability that facilitates the consolidation process.

3.4.3 Comparison of motor adaptation and skill learning

At the outset of this article we argued that motor adaptation and skill learning need to be considered as two distinct features of motor learning (Huang & Krakauer, 2009; Krakauer & Mazzoni, 2011) and that the relationship between motor adaptation and skill learning is far from clear (Yarrow et al., 2009). In our view, comparing our results to the results from skill learning reveals some parallels.

Results in research on variability of practice showed that variable practice schedules in learning a single motor skill (McCracken & Stelmach, 1977) or multiple motor skills (Shea & Morgan, 1979) can lead to an impaired motor performance during the acquisition phase compared to constant practice schedules. These findings correspond to our results on motor adaptation. Hereby, groups with high variability induced by a high amount of catch trials showed a poorer performance at the end of the learning phase than groups with less or no catch trials. Taken together, in both cases, schedules with high variability that cause interferences lead to poorer performance at the end of the learning phase compared to groups that practiced under constant conditions.

As mentioned above, it is important to separate acquisition performance from retention performance (Kantak & Winstein, 2012). Again, this was shown when learning a single motor skill (Shea & Kohl, 1991) and multiple motor skills (Shea & Morgan, 1979). In our study, we observed a similar phenomenon, since groups practicing in intermittent practice schedules (high amount of catch trials) revealed impaired performance at the end of adaptation phase but the induced variability partly facilitated consolidation. However, the results of our study indicate that for motor adaptation there seems to exist an optimal amount of such variability. Nevertheless, these parallels have to be considered with caution and further research comparing both features of motor learning is required.

3.5 Conclusion

In this paper we investigated the influence of catch trials on the overall motor adaptation process as well as on the consolidation process. We found that in motor adaptation, subjects show different ability to form an internal model depending on the amount of catch trials. These findings demonstrate a substantial influence of catch trials on the adaptation process. The consolidation process following motor adaptation further seems to be influenced by variable practice schedules suggesting an effect on the reduction of interference. For our specific task, a catch trial ratio of 30% was most beneficial indicating the existence of an optimal amount of catch trials. However, we cannot state a total absence of interference for any catch trial ratio. Moreover, the detection of consolidation seems also to be biased by the applied measure of performance. Therefore, further studies should account for the characteristics of used analytical methods. Comparing our results to results from motor skill learning (e.g., Schmidt & Lee, 2011) revealed similarities indicating that the processes of motor adaptation and skill learning possibly follow similar principles. However, similarities and differences between these two processes of motor learning should be focused in future studies to gain a more comprehensive understanding of human motor learning.

4 Adaptation and Generalization of Motor Memory

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Abstract

Intermanual transfer, i.e., generalization of motor learning across hands, is a well-accepted phenomenon of motor learning. Yet, there are open questions regarding the characteristics of this transfer, particularly the intermanual transfer of dynamic learning. In this study, we investigated intermanual transfer in a force field adaptation task concerning the direction and the coordinate frame of transfer as well as the influence of a 24 h consolidation period on the transfer. We tested 48 healthy human subjects for transfer from dominant to non-dominant hand and vice versa. We considered two features of transfer. First, we examined transfer to the untrained hand using force channel trials that suppress error feedback and learning mechanisms to assess intermanual transfer in the form of a practice-dependent bias. Second, we considered transfer by exposing the subjects to the force field with the untrained hand to check for faster learning of the dynamics (interlimb savings). Half of the subjects were tested for transfer immediately after adaptation, whereas the other half was tested after a 24 h consolidation period. Our results showed intermanual transfer both from dominant to non-dominant hand and vice versa in extrinsic coordinates. After the consolidation period, transfer effects were weakened. Moreover, the transfer effects were negligible compared with the subjects' ability to rapidly adapt to the force field condition. We conclude that intermanual transfer is a bidirectional phenomenon that vanishes with time. However, the ability to transfer motor learning seems to play a minor role compared with the rapid adaptation processes.

4.1 Introduction

Interlimb transfer refers to a generalization of motor learning from one limb to another. This transfer is a well-documented phenomenon and is of high interest for both practical and theoretical reasons (Magill, 2007). Most frequently, interlimb transfer is investigated for arm movements (i.e., intermanual transfer). Thereby, subjects usually adapt their reaching movements to either kinematic or dynamic perturbations and are subsequently checked for transfer to the contralateral untrained arm. Yet, it is assumed that adaptations to kinematic and dynamic perturbations at least partly involve different memory systems (Krakauer et al., 1999; Donchin et al., 2012) and that transfer of kinematic and dynamic features follows different principles (Sainburg, 2002). Previous research mostly concentrated on intermanual transfer following kinematic adaptation (e.g., Sainburg, 2002; Sainburg & Wang, 2002; Taylor et al., 2011; Mostafa et al., 2014). In contrast, fewer studies investigated intermanual transfer of learned dynamics (e.g., Criscimagna-Hemminger et al., 2003; Joiner et al., 2013). Yet, basic characteristics regarding intermanual transfer of dynamic adaptation are far from clear. Here, we focus on intermanual transfer of dynamic learning.

For instance, there are open questions on a-/symmetry and magnitude of this transfer. Previous studies that investigated intermanual transfer in force field adaptation tasks reported a unidirectional transfer, asymmetric in particular, only from the dominant to the non-dominant arm (Criscimagna-Hemminger et al., 2003; Wang & Sainburg, 2004; Galea et al., 2007). However, it remains unclear why transfer should be exclusively unidirectional. It was assumed that force field adaptation with the dominant arm yields a more proficient internal model compared with the non-dominant arm and that this internal model is fundamental for the transfer to the contralateral arm (Wang & Sainburg, 2004). In contrast to this elaborate internal model formation of the dominant arm controller, the non-dominant arm controller was suggested to rely more on an impedance control rather than feedforward motor control (Duff & Sainburg, 2007; Schabowsky et al., 2007). Hence, the non-dominant arm controller lacks in “knowledge” that could be transferred to the contralateral arm. However, the detailed connection between internal model formation during adaptation and intermanual transfer remains unclear.

Moreover, there are diverging results when the coordinate frame of transfer is considered. Transfer could occur in an extrinsic (Cartesian-based) coordinate frame meaning that for a certain movement the forces on the left and the right hand should be similar. Transfer might also occur in intrinsic (joint-based) coordinates. Thereby, if the workspace is near the midline, transfer would lead to the same joint torques, resulting in mirror symmetric force profiles (for details, see Criscimagna-Hemminger et al., 2003). Criscimagna-Hemminger and colleagues (2003) as well as Malfait and Ostry (2004) found transfer within an extrinsic coordinate frame. On the contrary, Wand and Sainburg (2004) as well as Galea and colleagues (2007) found transfer within an intrinsic coordinate frame. From a theoretical point of view, knowledge about the coordinate frame of transfer offers valuable information about the internal representation of motor actions and might help to improve computational models of motor control and learning.

After learning a motor task, the motor memory formed is stabilized by processes of consolidation (Robertson et al., 2004b). For force field adaptation tasks, plenty of studies have demonstrated such motor memory consolidation on a behavioral level (Brashers-Krug et al., 1996; Caithness et al., 2004; Overduin et al., 2006; Focke et al., 2013; Stockinger et al., 2014). Moreover, functional imaging has shown that after practice, the brain engages new regions to perform the task suggesting a change of newly formed neural representations (Shadmehr & Holcomb, 1997). In particular, sleep seems to play a major role in memory formation and consolidation (Rasch & Born, 2013). Accordingly, sleep supports generalization processes by structural reorganization and consolidation of more general motor memory representations (Rasch & Born, 2013; Censor, 2013). However, it is still unclear whether consolidation processes may also facilitate intermanual transfer of dynamic adaptation.

The aim of this study was to investigate intermanual transfer characteristics in a force field adaptation task. First, we hypothesized that motor adaptation is more elaborate with the dominant compared with the non-dominant hand. We further hypothesized that intermanual transfer only occurs from dominant to non-dominant hand. For this purpose, we considered two distinct features of transfer (practice-dependent bias, interlimb savings). Moreover, we examined the coordinate frame of this transfer. Finally, we hypothesized that processes of consolidation (including nocturnal sleep) facilitate intermanual transfer.

4.2 Materials and methods

4.2.1 Participants

A total of 48 healthy human subjects (18–29 years; 10 female, 38 male) participated in the study. All subjects gave written informed consent, and the test protocol was reviewed and approved by the KIT ethics committee. All subjects were right-handed (Edinburgh Handedness Inventory; Oldfield, 1971) and were naive to the experimental procedure (apparatus, paradigm, and purpose of the study). They were instructed to sleep at least 6 h in the nights prior to the test sessions and asked not to consume any alcohol or drugs during the test days.

4.2.2 Apparatus

We used a robot-assisted experimental paradigm (Shadmehr & Mussa-Ivaldi, 1994). Thereby, subjects grasped the handle of a robotic device (Kinarm End-Point Lab, BKIN Technologies, Kingston, Canada) that could exert forces. The subjects' arms were not supported and motion of the robot's handle was restricted to the horizontal plane. Subjects had clear view of their hand throughout the whole experiment. They received full visual feedback of the targets as well as of the cursor corresponding to the position of the handle on a vertical monitor, approximately centered at eye level. Subjects sat on a chair such that they were able to comfortably grasp the handle with either hand and reach all target positions. The robot was centrally positioned in front of the subjects such that the center position of the robot handle was located in the subjects' midsagittal plane. Position and force at the handle were recorded at a sampling rate of 200 Hz.

4.2.3 Task

Subjects were asked to perform accurate goal-directed 2d point-to-point reaching movements using the robot handle. Starting from a center point, subjects had to reach for one of three peripheral target points which appeared in a pseudo-randomized order. The subsequent movement was initiated from this peripheral point back toward the center point. Therefore, the end point of each movement was the starting point for the subsequent movement. The peripheral target points appeared in 10 cm distance from the center point in forward (0°), forward-leftward (45° left of straight line), or forward-rightward (45° right of straight line) direction (Criscimagna-Hemminger et al., 2003). If a target had to be reached, it appeared as a light gray circle (1 cm diameter) on a black background. The cursor representing the position of the handle was displayed as white circle (0.35 cm diameter).

We defined a set of movements as six trials (three outward and three inward movements) in which each peripheral target point occurred exactly once and, thus each of the possible six movements had to be performed once. All learning blocks were constructed as concatenation of such movement sets and were equal for all subjects. This ensured the same amount of practice towards each target direction.

Subjects were requested to perform each movement within 500±50 ms. Subjects were told that reaction time was not important – i.e., after appearance of the new target they could wait as long as they wanted before initiating the movement. After completion of each movement, subjects received visual feedback about movement time on the screen. If the subjects reached the target within the required time, its color changed to green. If they moved too slowly, it became red, and if moving too fast, it became blue. This visual feedback was provided throughout the whole experiment to ensure consistent movement speed.

4.2.4 Experimental design

To test for transfer in both directions, participants were divided in two main groups (*left-to-right*: LR, *right-to-left*: RL; Table 4.1). To assess the influence of a consolidation period on transfer, we further subdivided the groups. One half was tested for transfer immediately after the training block (*immediate* transfer groups: LRi, RLi). The other half was tested for transfer following a consolidation period of 24 h (*consolidation* transfer groups: LRc, RLc). Thus, there were four different groups to which subjects were randomly assigned (LRi, RLi, LRc, RLc; twelve subjects per group). Note that each two groups that were tested for the same transfer direction (LRi and LRc; RLi and RLc) followed the same basic timetable but differed only in the break between force field training and transfer test. Similarly, the groups that were tested for different transfer direction but same transfer

Table 4.1: Subject groups and experimental setup.

Transfer direction	**Group**	**Familiarization**	**Baseline**					**Training**	**Break**	**Transfer bias**	**Transfer savings**
		[NF]	[NF,EC,FF_{CT}]	[NF]	[EC]	[NF]	[EC]	[FF,EC]		[EC]	[FF,EC]
		54, 54	54, 54, 54, 54	6	6	6	6	168		6	168
LR	LRi	L R	L R L R	R	R	L	L	L	–	R	R
	LRc	L R	L R L R	R	R	L	L	L	24 h	R	R
RL	RLi	R L	R L R L	L	L	R	R	R	–	L	L
	RLc	R L	R L R L	L	L	R	R	R	24 h	L	L
			6 randomized EC; 6 randomized FF_{CT} (1 per hand & direction)					∼10% EC; 30 s break after 84 trials			∼10% EC; 30 s break after 84 trials

R: right, L: left, i: immediate transfer, c: consolidation transfer;
NF: null field trial, FF: force field trial, EC: error clamp trial, CT: catch trial

test type (LRi and RLi; LRc and RLc) followed the same basic timetable but differed only in the hand used to perform each block. In particular, the target sequences for the groups were mirrored and therefore similar with reference to the body midline. Thus, for instance, when the LRi and LRc groups had to perform a forward-leftward movement, the RLi and RLc groups had to perform a forward-rightward movement.

During the experiment, three different trial types were used: null field trials (NF, no perturbing forces), force field trials (FF, perturbing forces), and error clamp trials (EC, force channel trials).

On null field trials, the subjects could reach without perturbing forces as the robot's motors were turned off.

On force field trials, the robot generated a velocity-dependent force field that applied forces to the subjects' hand via the robot handle. A clockwise-directed curl force field pushed the handle perpendicular to the direction of movement:

$$\mathbf{F} = \begin{pmatrix} F_x \\ F_y \end{pmatrix} = \begin{pmatrix} 0 & k \\ -k & 0 \end{pmatrix} \cdot \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix},$$

(F_x and F_y are the robot-generated forces, $k = 15$ Ns/m is the force field viscosity, and x and y are the components of hand velocity). This force field was used to alter the dynamic conditions of the movements and therewith provoke subjects' adaptation of reaching movements (Shadmehr & Mussa-Ivaldi, 1994).

On error clamp trials, the robot generated a virtual force channel (wall stiffness 6000 N/m, wall viscosity 25 Ns/m) that restricted the movement to a straight line toward the target point, thus counteracting all movements perpendicularly to the target direction (Scheidt et al., 2000; Joiner et al., 2013). These trials were used to measure the forces at the handle that subjects produced perpendicular to the movement direction. These forces served as indicator for predictive force field compensation. Because on these trials the motor errors were clamped to zero and the force field that had to be learned was not present, these trials allowed measurement of motor adaptation with respect to feedforward adaptation without overlapping error feedback or learning mechanisms (Scheidt et al., 2000; Joiner et al., 2013).

The experiment consisted of a familiarization block, a baseline block, a force field training block, and a transfer test block (Table 4.1). The familiarization block consisted of 54 null field trials for each hand.

The baseline block consisted of two cycles of 54 trials per hand which consisted mostly of null field trials but also contained six pseudo-randomly interspersed error clamp trials and force field catch trials per hand (one trial per movement direction and hand). The baseline block finished with another set of null field trials followed by a set of error clamp trials for each hand, respectively (one trial per movement direction and hand). The error clamp trials during the whole baseline block (two error clamp trials for each hand and each movement direction) served as baseline trials. The force field catch trials (one trial for each hand and each movement direction) served as force field baseline to assess the arm stiffness and the impact of the force field to the arms.

The force field training block (168 trials) consisted mainly of force field trials which were performed with the training hand only. To assess performance, error clamp trials were randomly interspersed with a probability of approximately 10%.

In the transfer test block, we tested for two different features of transfer: practice-dependent bias and interlimb savings (Table 4.1). First, we defined *practice-dependent bias* as a change in the prediction of the environmental conditions when reaching with the untrained hand caused by the previous contralateral force field adaptation. To assess this practice-dependent bias, we used six error clamp trials (one trial per movement direction) (Joiner et al., 2013). Second, we considered whether force field adaptation with the training arm facilitated subsequent force field adaptation with the transfer arm. For this purpose, subjects also performed a force field training block (168 trials) with their transfer hand equivalent to the initial force field training block (Criscimagna-Hemminger et al., 2003). We refer to this kind of transfer as *interlimb savings* (Joiner et al., 2013). Note that both features refer to the ability to transfer learning. The practice-dependent bias would lead to changes in the prediction about the dynamics, whereas interlimb savings would lead to the ability to adapt faster when the previously experienced learning stimulus is presented.

Throughout the whole experiment, there were short breaks of 30 s each time subjects had to change the reaching hand as well as after 84 trials (14 sets) in the force field training blocks.

4.2.5 Data Analysis

Preprocessing

All data was processed using the custom-made software application ManipAnalysis (Stockinger et al., 2012). Thereby, raw data were filtered using a fourth-order Butterworth low-pass filter with a cut-off frequency of either 6 Hz (positional data) or 10 Hz (force data). Movement velocities were numerically computed using the central difference method. Next, data sets were segmented. Movement start (or end) was defined as the time point at which hand speed exceeded (or fell below) 10% of maximal speed of that movement. Finally, data sets were time-normalized using cubic spline interpolation.

Performance measurement

Subjects had to learn to compensate forces in the perpendicular direction because the force field was acting perpendicularly to the movement direction. Therefore, we concentrated on the analysis of forces (on error clamp trials) and deviations (on force field trials) in the perpendicular direction.

As dynamic performance measure, we considered the forces that subjects produced against the virtual channel wall during error clamp trials. During the baseline block, we recorded two such force profiles for each hand and each movement direction. By averaging these force profiles, we assessed a baseline force profile for each hand and each movement direction, respectively. As a performance measure, we computed a force field compensation factor (Joiner et al., 2013). This factor was found by linear regression of the actually measured perpendicular force profile on the error clamp trial and the ideal perpendicular force profile (forces necessary to cancel the force field if it had occurred; determined by $\mathbf{F}_{\text{ideal}} = (F_{\text{ideal},x}, F_{\text{ideal},y})^\top = (0, 15\ \text{Ns/m}; -15\ \text{Ns/m}, 0) \cdot (\dot{x}_{\text{actual}}, \dot{y}_{\text{actual}})^\top$) according to:

$$\mathbf{F}_{\text{actual}} = a_0 + a_1 \cdot \mathbf{F}_{\text{ideal}}(t) + \epsilon(t).$$

Thereby, ϵ is an additive error term, a_0 is the intercept, and the parameter a_1 serves as the force field compensation factor (Joiner & Smith, 2008; Joiner et al., 2013).

In addition, we calculated the midmovement force as the average perpendicular force produced against the channel wall during error clamp trials within a time window ranging from 70 ms before to 70 ms after maximum speed of that movement (Joiner et al., 2013). The statistical analyses using this measure yielded results similar to the force field compensation factor. Thus, these results are not presented in this article.

The performance measurement using error clamp trials is a good indicator for the performance of the feedforward controller, because it is not confounded by error feedback and learning mechanisms. This allows analyses of the adaptation of the feedforward controller by formation of an internal model of the task.

As a kinematic performance measure, we considered force field trials and computed the perpendicular displacement of hand path from straight line joining the start and target points at maximum hand speed (PD_{vmax}) (Pekny et al., 2011; Mattar & Ostry, 2007). The produced hand path results from the superposition of several control mechanisms (feedforward control, feedback control, impedance control) and therefore reflects net motor performance. In addition, we fit the adaptation curves obtained by the kinematic error (PD_{vmax}) to an exponential function:

$$f(t) = a \cdot \exp(-t/\tau) + \beta$$

(mean R^2-value across all subjects was 0.65), whereby, we analyzed the time constant τ, which represents the rate of adaptation (e.g., Davidson & Wolpert, 2004).

To evaluate magnitude and direction of forces or deviations, all measures were computed as signed values. Thereby, for outward (inward) directed movements, a positive sign indicates force compensation or perpendicular deviation in counter-clockwise direction (clockwise direction).

Statistics

Normal distribution of the data was checked using Kolmogorov-Smirnov test. Homoscedasticity was checked using Levene's test. Results of these tests were not in conflict with the respective parametric statistical tests used. If ANOVAs revealed significant differences, Tukey's honestly significant difference (or Tukey-Kramer method in unbalanced cases) Post-hoc tests were used.

For all statistical tests, the level of significance was set a priori to $p = 0.05$. When multiple analyses were conducted addressing the same research question, Holm-Bonferroni procedure (sequentially rejective Bonferroni test; Holm, 1979) was used to adjust the level of significance. All results that are reported as statistically significant comply with this α-level adjustment. Effect sizes were determined using partial eta squared η_p^2 (small effect: $\eta_\mathrm{p}^2 = 0.01$; medium effect $\eta_\mathrm{p}^2 = 0.06$; large effect: $\eta_\mathrm{p}^2 = 0.14$) or Cohen's d (small effect: $d = 0.20$; medium effect $d = 0.50$; large effect: $d = 0.80$; Cohen, 1988). All data are presented as mean values and 95% confidence intervals. All statistical analyses were conducted using IBM SPSS software (v.22).

4.3 Results

4.3.1 Adaptation to the force field condition

The subjects' hand paths reflected the typical adaptive behavior (Figure 4.1). Under null field conditions, hand paths were unperturbed and almost straight-lined (Figure 4.1A,D). When exposed to the force field, hand paths initially showed high deviations (Figure 4.1B,E) but straightened with training (Figure 4.1C,F).

We used two different approaches to assess adaptation to the force field condition. We calculated a dynamic performance measure that represents subjects' predictive behavior and a kinematic endpoint error measure that represents net motor performance (Figure 4.2).

Before performing the analysis of adaptation to the force field condition, we considered the impact of the force field on the subjects' arms before any learning occurred. Therefore, we analyzed motor performance under null field conditions and on force field catch trials, i.e., null field and force field baseline (Figure 4.2A, left). A repeated-measures ANOVA (*condition* [null field baseline, force field catch trial]; *hand* [L, R]) of these baseline values revealed a significant effect of hand ($F_{(1,46)} = 84.8$, $p < 0.001$, $\eta_\mathrm{p}^2 = 0.65$), a significant effect of the force field condition ($F_{(1,46)} = 1918.2$, $p < 0.001$, $\eta_\mathrm{p}^2 = 0.98$), and a significant interaction of hand and force field condition ($F_{(1,46)} = 14.8$, $p < 0.001$, $\eta_\mathrm{p}^2 = 0.24$). Under null field conditions, movements of both arms tended to be curved inward (as indicated

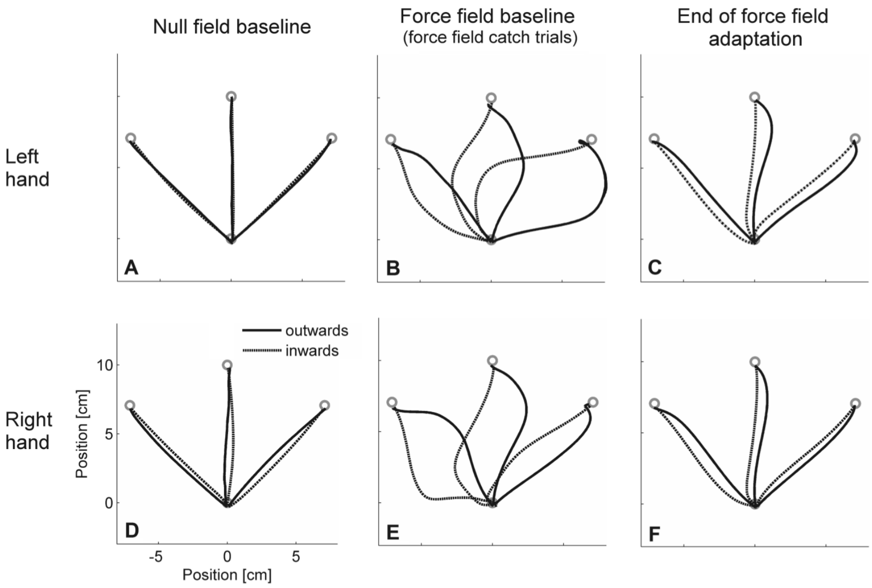

Figure 4.1: Mean plots of reaching movements with left (**A**-**C**, LR group) and right (**D**-**F**, RL group) hand: null field baseline (**A**,**D**), force field catch trials (**B**,**E**), and movement trials at the end of the training block under force field conditions (**C**,**F**). In comparison to the right hand, left hand movements are straighter under null field conditions, but are more deviated by the force field (Note: All illustrations are in extrinsic coordinates).

by the positive sign of the deviations). Thereby, left arm produced significantly lower deviations ($t_{(47)} = 8.22$, $p < 0.001$, $d = 1.81$). On force field catch trials, the left arm showed significantly higher deviations compared with the right arm ($t_{(47)} = 10.85$, $p < 0.001$, $d = 2.07$). Thus, the force field had significant impact on both hands. However, the impact of the force field on the left hand was higher than on the right hand.

To preclude that the assessed differences in force field catch trials are due to dissimilar error feedback mechanisms of the two hands (which might occur earlier than the time point of maximum speed at which the hand path was evaluated), we conducted the same analysis comparing the perpendicular displacement 80 ms and 150 ms after movement onset. Thereby, we found qualitatively similar results indicating a larger impact of the force field to the left hand compared with the right hand ($p < 0.001$, in both cases).

Consideration of the adaptation to the force field condition revealed that subjects were able to reduce the kinematic endpoint error during force field training until reaching a performance plateau for both hands (Figure 4.2A, right). When the degree of performance improvement between hands was compared using a repeated-measures ANOVA (*time* [force field catch trials, end of adaptation]; *hand* [L, R]), the results showed a significant effect of time ($F_{(1,46)} = 880.8$, $p < 0.001$, $\eta_{\mathrm{p}}^2 = 0.95$) and hand ($F_{(1,46)} = 43.0$, $p < 0.001$, $\eta_{\mathrm{p}}^2 = 0.48$) as well as a significant interaction of time and hand ($F_{(1,46)} = 18.0$, $p < 0.001$, $\eta_{\mathrm{p}}^2 = 0.28$). This indicates significantly higher overall error reduction of the left hand compared with the right hand (caused by the initial differences). Consideration of the motor performance at the end of adaptation (mean of last eight sets) revealed no significant difference between the left and right hands ($t_{(46)} = 1.04$, $p = 0.304$, $d = 0.54$).

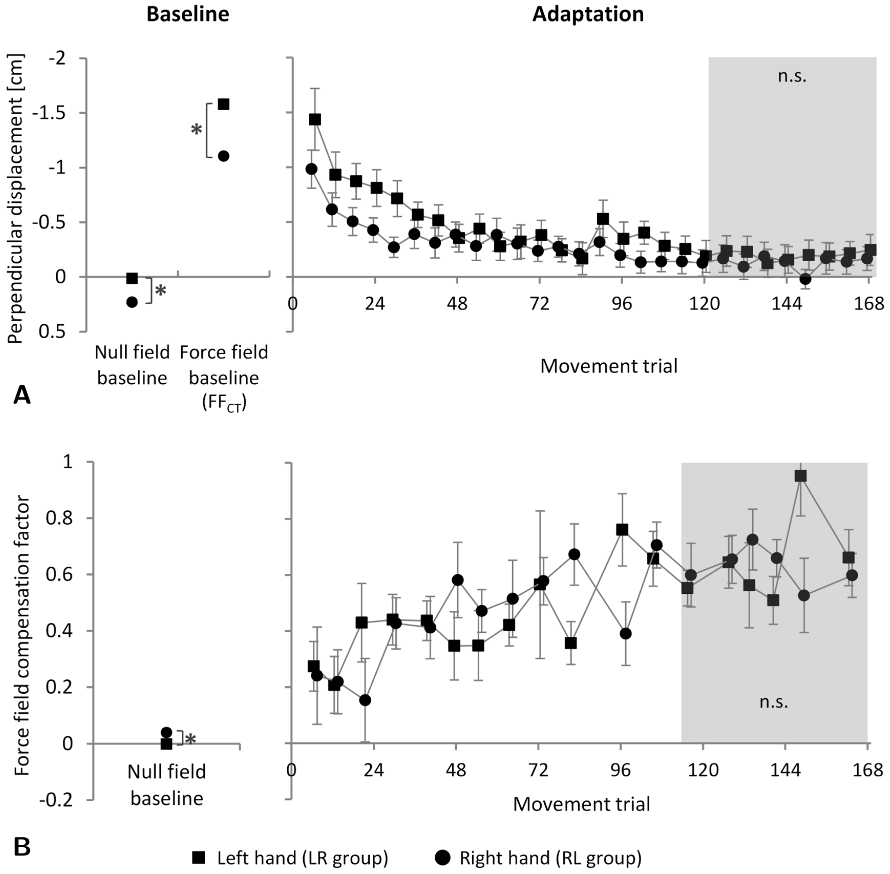

Figure 4.2: Baseline measurements and adaptation progression (mean±95% CI) for left and right hand as measured by the kinematic end point error (perpendicular displacement, **A**) and the force field compensation factor (**B**). After 84 trials, a break of 30 s was given. Asterisks indicate statistically significant differences.

Thus, motor adaptation ended up on a similar performance level for both hands. Moreover, consideration of the time constants of adaptation revealed no significant differences between the left and right hands ($\tau_{\mathrm{L}} = 3.9$, $\tau_{\mathrm{R}} = 4.9$; $t_{(46)} = 1.52$, $p = 0.223$, $d = 0.32$), indicating similar adaptation capacities for both hands.

Consideration of the force field compensation factor yielded similar results for the adaptation to the force field condition (Figure 4.2B; Figure 4.3). A repeated-measures ANOVA (*time* [baseline, end of adaptation], *hand* [L, R]) revealed a significant effect of time ($F_{(1,46)} = 999.5$, $p < 0.001$, $\eta_{\mathrm{p}}^2 = 0.96$). The effect of hand ($F_{(1,46)} = 0.6$, $p = 0.447$, $\eta_{\mathrm{p}}^2 = 0.01$) and the interaction of time and hand ($F_{(1,46)} = 3.1$, $p = 0.086$, $\eta_{\mathrm{p}}^2 = 0.06$) were not statistically significant. Under null field baseline conditions, we found significantly higher forces produced against the channel wall for the right hand compared with the left hand ($t_{(47)} = 4.27$, $p < 0.001$, $d = 0.89$; Figure 4.2B, left). This is in line with the aforementioned higher deviations of right hand paths under null field conditions. When exposed to the force field, subjects adapted their motor output by producing additional perpendicular forces. At the end of the training block (last six error clamp trials, one per

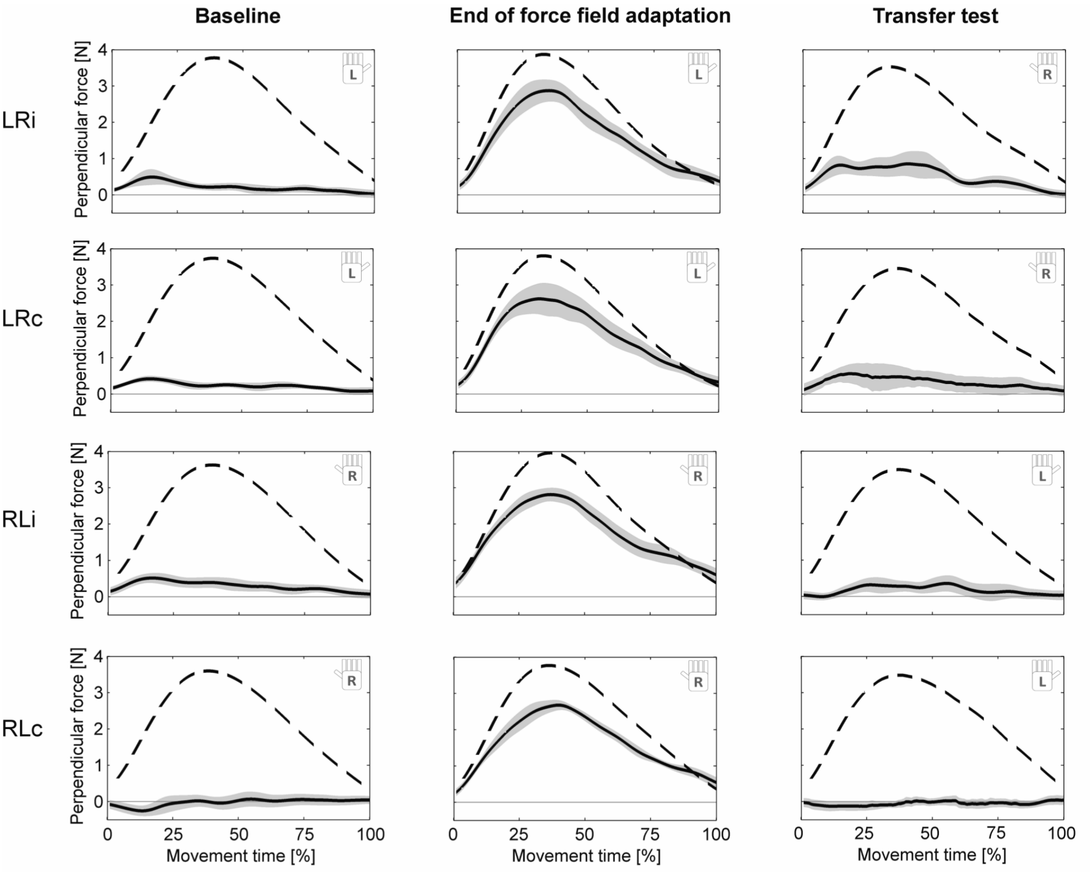

Figure 4.3: Ideal (dashed) and measured (solid) perpendicular force profiles on error clamp trials during baseline, at end of force field adaptation, and in the transfer test block (mean±95% CI). At the end of the training phase, all subject groups learned to produce additional compensatory forces in perpendicular direction. On the transfer tests, the groups LRi, LRc, and RLi show transfer in form of increased perpendicular forces compared with baseline conditions (practice-dependent bias).

movement direction), subjects learned to produce additional compensating perpendicular forces to counteract the force field. At the end of the training block, subjects compensated, on average, 64.8±4.5% (left) and 62.8±5.3% (right) of the force field. This did not differ between hands ($t_{(46)} = 0.56$, $p = 0.580$, $d = 0.16$). Therefore, left and right hands showed similar ability to adapt their motor output by predicting the force field.

Combining the results of kinematic and dynamic measures of performance shows that both left and right hands were able to adapt to the changed dynamic conditions by predicting the force field resulting in reduced kinematic reaching error. The applied force field had a higher impact on the left hand, causing a higher overall reduction of motor error during the training block. However, the motor error progression indicated a comparable rate of adaptation between hands. Similarly, feedforward motor adaptation was comparable between hands.

4.3.2 Transfer of learning

To assess transfer of learning, we considered two different transfer features. First, we considered the practice-dependent bias as measured on error-clamp trials. This allowed analysis of the subjects' predictions about the dynamic conditions with the transfer hand without previously being exposed to the force field with that hand (Joiner et al., 2013). Second, we considered the interlimb savings, i.e., subjects' ability to adapt to the force field condition with their transfer hand when exposed to the contralaterally experienced force field (see *Materials and Methods*).

Practice-dependent bias

Figure 4.3 illustrates the perpendicular forces on error clamp trials applied by the subjects at the end of adaptation as well as in the transfer test immediately after training (LRi, RLi) and after the 24 h consolidation period (LRc, RLc). As shown in Figure 4.4, transfer occurred in extrinsic coordinates as indicated by the positive sign of the force field compensation factor (which was defined relative to the forces necessary to counter the force field).

To simplify presentation of the results and make the two hands comparable, all further reported results of the force field compensation factor base on baseline-subtracted force profiles. To assess if transfer in terms of a practice-dependent bias occurred, we considered error clamp trials immediately after adaptation. Thereby, we found transfer of learning both from left to right arm (one-sample t-test vs. 0; LRi: $t_{(11)} = 4.33$, $p = 0.001$) and from right to left arm (RLi: $t_{(11)} = 3.39$, $p = 0.006$) as indicated by an increased lateral force compared with baseline (i.e., zero value; Figure 4.4). On average, this corresponded to 23.7% (LRi) and 20.0% transfer (RLi). After the 24 h consolidation period, only the LRc group showed significant transfer to the contralateral arm of, on average, 12.8% (LRc: $t_{(11)} = 4.27$, $p = 0.001$; RLc: $t_{(11)} = 0.55$, $p = 0.592$).

To test if the amount of transfer differed between transfer conditions, we conducted a 2×2 ANOVA (*transfer direction* [LR, RL], *transfer type* [immediate, consolidation]). Thereby, we found a significant effect of transfer direction ($F_{(1,44)} = 6.22$, $p = 0.016$, $\eta_p^2 = 0.12$) and of transfer type ($F_{(1,44)} = 12.79$, $p = 0.001$, $\eta_p^2 = 0.23$) but no significant interaction of these two factors ($F_{(1,44)} = 0.64$, $p = 0.43$, $\eta_p^2 = 0.014$).

Altogether, immediately after adaptation, transfer of learning in terms of practice-dependent bias occurred in both directions. After the consolidation period, these transfer effects declined and only occurred from the left to right hand.

Interlimb savings

To assess interlimb savings, subjects were exposed to the force field with their transfer hand. Consideration of the randomly interspersed error clamp trials during the force field block allowed analysis of subjects' predictive behavior. The progression of the force field compensation factor for naive subjects and transfer subjects is shown in Figure 4.5A and 4.5B for each hand, respectively. Accordingly, the progression of net motor performance as quantified by the perpendicular displacement is depicted in Figure 4.5C and 4.5D.

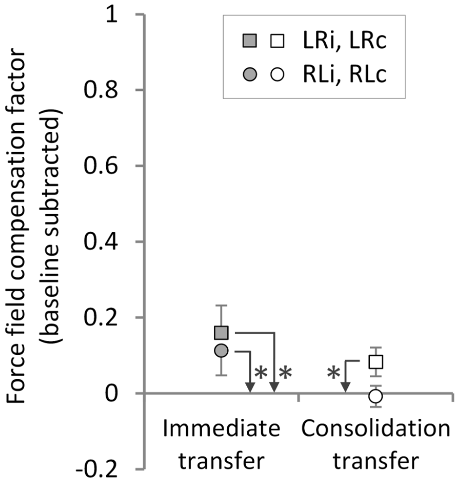

Figure 4.4: Transfer of learning by means of practice-dependent bias as measured by the force field compensation during error clamp trials for all four groups (mean±95% CI). Asterisks indicate statistically significant differences vs. zero (baseline).

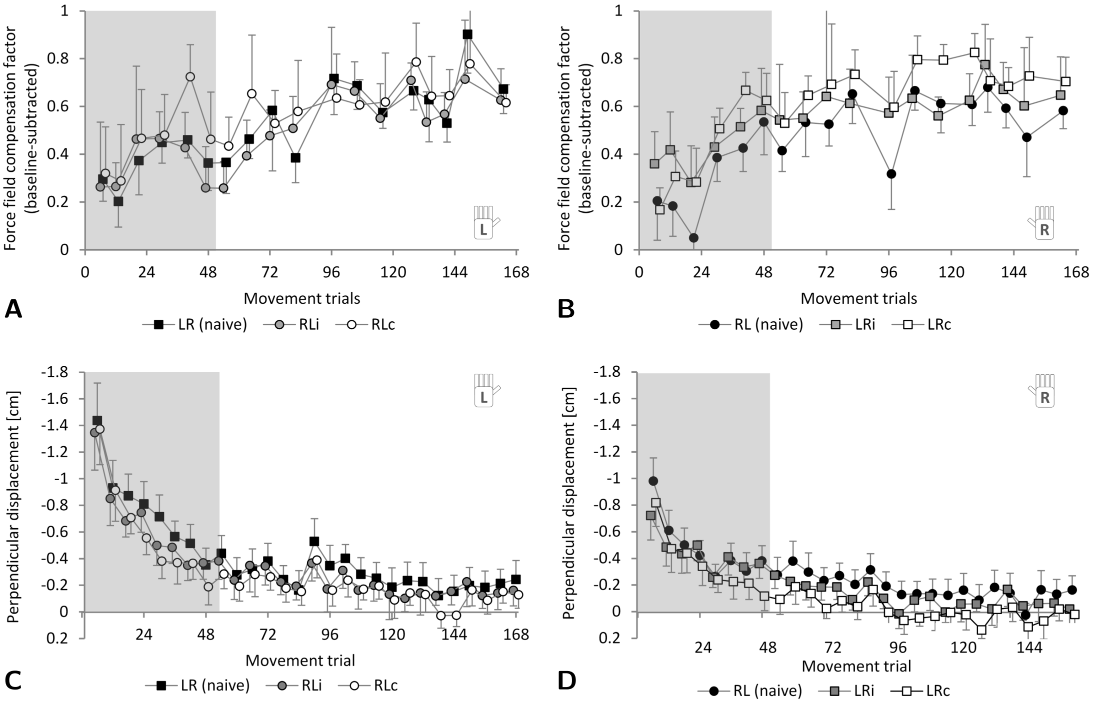

Figure 4.5: Intermanual transfer by means of interlimb savings as comparison of adaptation progression between novices (black) and transfer groups (gray, white) on error clamp trials (**A**,**B**) and the kinematic endpoint error on force field trials (**C**,**D**) (mean±95% CI). **A**,**C**: left-hand novices vs. right-to-left transfer groups; **B**,**D**: right-hand novices vs. left-to-right transfer groups. After 84 trials, a break of 30 s was given.

For statistical analyzes, we considered the first eight sets of movement trials (48 movements, containing six error clamp trials) because these comprise the initial adaptation phase before performance reaches plateau. Within this time window, we compared performance between transfer and control subjects using one-way ANOVAs. For instance, for the transfer groups LRi and LRc - i.e., transfer from left to right hand - the pooled RL group (RLi and RLc) served as control group because its subjects were naive to the force field when reaching with their right hands. Moreover, to assess differences in the rate of adaptation, we compared the time constants of adaptation between groups as assessed by fitting to exponentials (see *Materials and Methods*).

For the right-to-left direction (*group* [LR, RLi, RLc]; Figure 4.5A,C), there were no statistically significant differences between groups. This holds for the force field compensation factor measured on error clamp trials ($F_{(2,45)} = 2.56$, $p = 0.088$, $\eta^2_{\mathrm{p}} = 0.10$) as well as for the mean values of perpendicular displacement measured on force field trials ($F_{(2,45)} = 1.75$, $p = 0.185$, $\eta^2_{\mathrm{p}} = 0.07$) and for the time constants of adaptation ($\tau_{\mathrm{LR}} = 3.9$, $\tau_{\mathrm{RLi}} = 3.0$, $\tau_{\mathrm{RLc}} = 3.9$; $F_{(2,45)} = 0.85$, $p = 0.433$, $\eta^2_{\mathrm{p}} = 0.04$).

For the left-to-right direction (*group* [RL, LRi, LRc]; Figure 4.5B,D), there were differences between groups ($F_{(2,45)} = 4.05$, $p = 0.024$, $\eta^2_{\mathrm{p}} = 0.153$) when the force field compensation factor was considered. Thereby, the control group tended to show less force field compensation compared with the transfer groups. However, after α-level adjustment using to Holm-Bonferroni method, these differences were not statistically significant. Similarly, the performance assessed by the perpendicular displacement did not reveal any statistically significant differences between groups when the mean values ($F_{(2,45)} = 2.00$, $p = 0.146$, $\eta^2_{\mathrm{p}} = 0.082$) or the time constants of adaptation ($\tau_{\mathrm{RL}} = 4.4$, $\tau_{\mathrm{LRi}} = 5.2$, $\tau_{\mathrm{LRc}} = 5.8$; $F_{(2,45)} = 0.93$, $p = 0.401$, $\eta^2_{\mathrm{p}} = 0.04$) were considered.

Even when considering only the forces measured during the first randomly interspersed error clamp trial (which occurred on the seventh trial), we did not detect any differences between groups. This holds both for right-to-left transfer direction (one-way ANOVA: *group* [LR, RLi, RLc], $F_{(2,45)} = 0.19$, $p = 0.829$, $\eta^2_{\mathrm{p}} = 0.01$) as well as left-to-right transfer direction (one-way ANOVA: *group* [RL, LRi, LRc], $F_{(2,45)} = 1.17$, $p = 0.320$, $\eta^2_{\mathrm{p}} = 0.05$).

Taking all results together, for all considered measures of performance, we failed to detect clear transfer effects by means of interlimb savings immediately after adaptation as well as after the consolidation phase in either direction. Thus, transfer effects were quite weak compared with the fast initial performance improvements caused by adaptation mechanisms.

4.4 Discussion

This study revealed three main findings: (1) the ability to adapt to the force field condition did not differ between hands; (2) intermanual transfer in form of a practice-dependent bias occurred both from dominant to non-dominant hand and vice versa in extrinsic coordinates; and (3) a consolidation phase (incl. nocturnal sleep) after adaptation did not foster but rather weakened transfer effects.

4.4.1 Adaptation does not differ between hands

Our results showed that subjects are able to adapt their reaching movements to a changed dynamic environment with either hand. During training, the left hand reduced motor error more than the right hand when absolute values were considered. This, however, was mainly attributed to the higher impact of the force field on the left hand and therewith to higher deviations at the beginning of force field exposure. Accordingly, the adaptation rate did not differ between hands. Most interestingly, we did not detect differences between hands in the ability to predict the force field at the end of adaptation when considering the force field compensation factor, which is a measure of feedforward control mechanisms. Thus, we did not detect better adaptation competence of the dominant right hand compared with the non-dominant left hand. We rather assume that both the dominant and non-dominant arm controllers are able to form an elaborate internal model of the task dynamics.

This result is in contrast to the findings of Duff and Sainburg (2007). In their study, only the dominant, not the non-dominant, arm showed increased motor errors during after-effect trials following the adaptation to an attached inertial load (Duff & Sainburg, 2007). This was taken as evidence for a more elaborate predictive control during dominant compared with non-dominant arm movements. On the other hand, Sainburg (2002) found after-effects for both dominant and non-dominant arm movements following adaptation to an inertial load. However, these initial after-effects were not statistically evaluated for potential differences but appear to be of similar magnitude for either hand (see Figure 2B in Sainburg, 2002). Similarly, a closer look at the results of Criscimagna-Hemminger et al. (2003) indicates that their subjects did not show a better adaptation competence when using the dominant compared with the non-dominant arm (consider control groups in their Figures 3B vs. 4B or Figure 5A vs. 5B). Unfortunately, Criscimagna-Hemminger and colleagues (2003) did not statistically test for this issue either, because this was not part of their research question. Thus, one can only speculate about this disparity. Yet, our findings contradict the assumption that the non-dominant arm controller is generally less proficient in forming an appropriate internal model for feedforward control (Wang & Sainburg, 2004; Sainburg, 2002). Likewise, we cannot support the idea that the non-dominant arm controller relies more on an impedance control than on feedforward control during reaching under changed dynamic conditions (Sainburg, 2002; Schabowsky et al., 2007). Moreover, the left hand's higher deviations during force field catch trials challenge the assumption that the non-dominant arm generally relies more on impedance control and therefore makes use of higher arm stiffness (Schabowsky et al., 2007).

4.4.2 Intermanual transfer of dynamic learning is bidirectional

Our second main finding is that dynamic learning can transfer both from dominant to non-dominant hand and vice versa. Former research reported only unidirectional transfer from dominant to non-dominant hand (Criscimagna-Hemminger et al., 2003; Wang & Sainburg, 2004; Galea et al., 2007). This unidirectional transfer was explained by the above-discussed potential different abilities of the dominant and non-dominant arm controller to form an appropriate internal model of the task dynamics (Wang & Sainburg, 2004). Accordingly, the formation of such an internal model is critical for intermanual transfer. However, for methodological reasons, the aforementioned studies were not able to measure solely internal model formation without overlap of learning or feedback mechanisms or increased arm stiffness due to impedance control. Therefore, in these studies, effector specific differences in the attained feedforward adaptation level and acquired motor memory were not specifically assessed. Nevertheless, we also suggest that the formation of an internal model is mandatory for intermanual transfer. However, we propose that this can be accomplished for either arm in comparable quality and serve as the basis for bidirectional transfer.

We found that subjects learned, on average, 63% (right) and 65% (left) of the force field, and we found intermanual transfer of 20% (right-to-left) and 24% (left-to-right) immediately after adaptation in the form of a practice-dependent bias. For a similar learning schedule and the same performance measure, Joiner and colleagues (2013) found that subjects learned, on average, 77% of the force field and they assessed intermanual transfer of 9% (right-to-left). Maybe, the small differences in the attained adaptation level and amount of transfer are attributed to slight differences in the experimental setup (arm support, amount of targets). In any case, our quantitative results are more similar to those of Joiner and colleagues (2013) than to the 50% intermanual transfer reported by Malfait and Ostry (2004). These quantitative differences might be explained by the used performance measure, as discussed previously by Joiner and colleagues (2013). They argued that the feedforward adaptation, which is of interest, is overlapped by feedback control and increased stiffness when measuring transfer using force field trials. Moreover, measuring transfer using force field trials also induces learning processes as the learning stimulus is presented. It becomes apparent that learning the considered task proceeds at a very high rate when comparing our results on practice-dependent bias and interlimb savings. We found significant transfer in the form of practice-dependent bias on error clamp trials. In contrast, we did not detect this clear transfer when subjects were exposed to the force field and their initial performance was compared with naive subjects (interlimb savings). In our opinion, this is attributed to the rapid initial learning processes induced by force field exposure which complicates detection of transfer. Maybe, former studies were subject to this methodological issue and, thus potential bidirectional transfer remained hidden. However, note that we only found clear bidirectional transfer in terms of practice-dependent bias but we did not detect such clear transfer in terms of interlimb savings. At this point, we were not able to replicate the findings of Criscimagna-Hemminger and colleagues (2003) who detected interlimb savings in direction from dominant to non-dominant hand which suggests that the aforementioned methodological issues (e.g., feedforward adaptation overlapped by feedback control, measuring transfer while adapting to the force field) may not be the only reason for the asymmetrical transfer observed in previous studies.

We found that transfer occurred in extrinsic coordinates. This is in line with findings of Criscimagna-Hemminger et al. (2003) as well as Malfait and Ostry (2004) and contrasts the findings of Wand and Sainburg (2004) and Galea et al. (2007) who found transfer within an intrinsic (joint-based) coordinate frame. It is possible that intermanual transfer (in terms of interlimb savings) would have occurred in intrinsic coordinates if we specifically tested it by presenting a counter-clockwise force field in the transfer test. However, it is unlikely that subjects, who showed the reported transfer (practice-dependent bias) in extrinsic coordinates on error clamp trials, would immediately afterwards switch their prediction and show transfer by means of interlimb savings in intrinsic coordinates.

These diverging results on the coordinate frame of transfer indicate that the internal representation of movements is highly specific to the task and the experimental setup. For instance, the coordinate frame of transfer might depend on whether the same object is handled with both arms (e.g., one robot handle; Criscimagna-Hemminger et al., 2003; Malfait & Ostry, 2004) or whether two different objects are handled (e.g., two robotic handles; Galea et al., 2007) or additional loads are attached to either hand Wang & Sainburg (2004). When one single object is handled with both hands (present study; Criscimagna-Hemminger et al., 2003; Malfait & Ostry, 2004), transfer may occur preferentially in extrinsic coordinates as the changed dynamics are rather linked to the external object than to the limb dynamics. In the latter cases (Galea et al., 2007; Wang & Sainburg, 2004), transfer may have occurred preferentially in intrinsic coordinates. This would match with findings by Cothros et al. (2006) who suggested the acquisition of a distinct internal model of the dynamics of an object separate from internal models used to control limb dynamics. Another influencing factor might be the workspace in which movements are performed. Research suggests that reaching near or across the midline implies different motor control features compared with reaching in the ipsilateral hemispace (e.g., Bryden et al., 2011). Potentially, intermanual transfer might also be influenced by the workspace in which the original task is learned. Practice near the midline, as in our study, preferentially yielded to transfer in extrinsic coordinates (Criscimagna-Hemminger et al., 2003; DiZio & Lackner, 1995) whereas movements that were performed in ipsilateral hemispace were rather shown to be transferred in intrinsic coordinates (Wang & Sainburg, 2004). Furthermore, visual feedback of the own arm or the cursor representing the end-point being controlled as well as if the visual feedback is aligned vs. non-aligned might influence the internal representation of a task and therewith the coordinate frame of transfer (Parmar et al., 2015). Moreover, as supposed by Galea et al. (2007), the coordinate frame of transfer might also be attributed to the type of observed motor error and the visual cues providing this information.

Presumably, the internal representation of movements and, therefore the coordinate frame of intermanual transfer is a combination of different coordinate frames which is modulated by diverse task specifications. Recent investigations suggest such a mixture of internal representations underlying both intramanual (Berniker et al., 2014; Parmar et al., 2015) and intermanual generalization (Parmar et al., 2015).

Taking these findings together, we found bidirectional intermanual transfer in terms of practice dependent bias that occurred in extrinsic coordinates. Yet, the magnitude of transfer and the coordinate frame of transfer appear to be influenced by diverse task specifications. However, the observed transfer effects seem to play a minor role compared with the fast initial adaptation processes. Because transfer characteristics are of high interest from a theoretical point of view and give insights to fundamental motor learning mechanisms, future studies should account for the methodological difficulties in detecting transfer. Moreover, further research should examine whether transfer in more complex motor tasks has more robust features giving transfer subjects a substantial advantage in performance compared with naive subjects.

4.4.3 Intermanual transfer effects weaken with time

Despite the found bidirectional intermanual transfer of motor memory immediately after adaptation, transfer of motor memory declined with time. After the 24 h consolidation period, transfer from non-dominant to dominant hand decreased and, in the case of dominant to non-dominant hand, even vanished. Considering the initially mentioned importance of consolidation and sleep on motor memory formation (Censor, 2013; Rasch & Born, 2013), this finding is surprising.

Transfer in terms of practice-dependent bias decreased with the consolidation period. On error clamp trials after the consolidation period, we only detected a small amount of transfer from the non-dominant to the dominant hand (LRc group). Generally, a decrease of motor performance and therewith a decrease of transfer effects after a consolidation period could be caused by a warm-up decrement. This phenomenon refers to a decrement in performance caused by temporary factors rather than memory loss, e.g., loss of internal states that are critical for the motor action (Schmidt & Lee, 2011; Kantak & Winstein, 2012). Yet, potential transfer should have been detectable in our interlimb savings test block despite warm-up decrement because the internal set was reinstated. However, even when exposed to the force field, subjects did not show interlimb savings. Thus, processes of consolidation did not facilitate intermanual transfer in the considered task, but rather weakened transfer effects. Plenty of former studies found consolidation of motor memory for this specific task when the retest was performed with the training hand (Brashers-Krug et al., 1996; Shadmehr & Holcomb, 1997; Caithness et al., 2004; Overduin et al., 2006; Focke et al., 2013; Stockinger et al., 2014). This indicates that motor memory underlying the considered task is, in principle, sensitive to consolidation. Possibly, the consolidation period only fosters the stabilization of an effector-specific internal representation rather than a more generalized internal representation.

4.4.4 Neural processes and models of intermanual transfer

Previous research proposed several potential neural processes underlying transfer and generalization of motor memory. In the context of intermanual transfer, the most common explanations are the cross-activation model and the bilateral access model (for review, see Ruddy & Carson, 2013). According to the cross-activation model, unilateral practice causes bilateral adaptation by increasing motor activity in the contralateral hemisphere, which controls the arm, but also in the ipsilateral hemisphere. Thereby, during adaptation, an inferior motor program is built in the contralateral hemisphere, which is used on the transfer test. The bilateral access model states that motor adaptation occurs in neural regions which are involved in the control of the trained hand but also are accessible to the untrained hand (Ruddy & Carson, 2013; Anguera et al., 2007). Regarding the bidirectional transfer in our experiment, both models may account for our findings. However, our study was not designed to examine intermanual transfer on a neural level. For the purpose of a more elaborate theory of neural processes underlying the transfer, further studies using functional imaging techniques are needed.

5 General Discussion and Conclusion

This thesis aimed to investigate motor control and learning with special consideration of motor memory adaptation as well as its consolidation and generalization. For this purpose, the experimental paradigm of robot-assisted force field experiments was used. More precisely, the aim of this thesis was to address unresolved research issues concerning (1) the development of materials and methods – particularly, aspects of processing and analyzing data gained during motor adaptation experiments as well as assessment of motor performance, (2) the influence of unstable practice schedules in motor adaptation on motor memory consolidation, and (3) generalization characteristics of dynamic adaptation – particularly, direction (asymmetry/symmetry) and coordinate frame of intermanual transfer as well as the influence of a consolidation period on this transfer.

This final chapter summarizes and discusses the main findings on these issues, considers implications for future research, and finally closes with a general conclusion.

5.1 Approaches to analyze motor adaptation experiments

Chapter 2 considered methodological aspects of robot-assisted learning experiments in order to develop a stable methodological basis for the subsequently reported experiments. Although robot-assisted learning experiments are widely-used, no standards for the use of materials and methods existed. Accordingly, neither software applications nor standards for data processing and analysis of such experiments existed. Unfortunately, researchers often miss to report detailed information concerning the used methods. In particular this holds for data processing procedures and algorithms. For these reasons, the reported tailor-made software application ManipAnalysis was developed to serve as a common framework for the analysis of robot-assisted adaptation experiments and was successfully utilized in subject experiments (cf. Chapters 3, 4; Focke et al., 2013; Thürer et al., 2016; Taubert et al., in review).

As illustrated, multiple approaches exist to define and assess motor performance in robot-assisted adaptation experiments. The presented software application ManipAnalysis supports the most common performance measures – both based on kinematic and dynamic data. Even though these analytic approaches target at the same main aspect, researchers need to take their different emphases into consideration. Within this section, the properties of common motor performance assessment approaches, their controversies, and challenges shall be discussed.

5.1.1 The choice of a reference trajectory

To assess motor performance, it is intuitive and common to consider kinematic data of movement trials. Most often, goal-directed reaching movements are evaluated with respect to some pre-defined reference trajectory. Thereby, performance is either quantified by a correlation coefficient determining the similarity to that reference trajectory or by an error measure, i.e., deviation from the reference trajectory (see Section 2.3.2).

Often the reference trajectory is individually determined for each subject in baseline measurements under null field conditions (baseline trajectories; e.g., Shadmehr & Mussa-Ivaldi, 1994; Gandolfo et al., 1996). On the one hand, such individual determination of the reference trajectory has the advantage of respecting subject-specific preferences and factors (e.g., handedness, segment lengths). On the other hand, this procedure is labor-intensive because it requires additional measurements and calculations for each single subject.

In another prevalent approach, movements are compared to a universal reference trajectory. In case of point-to-point reaching, one often considers the direct line joining start and target point as the ideal hand path and a bell-shaped (Gaussian-like) speed profile as an ideal hand velocity function. At first glance, this approach seems oversimplified. However, it is supported by diverse computational and behavioral studies (e.g., Flash & Hogan, 1985; Shadmehr & Mussa-Ivaldi, 1994). From a computational point of view, the sensorimotor system has to select one specific motor command out of an infinite number of possible motor commands. This refers to an optimization problem of minimizing a cost function (Jordan, 1996). The most commonly considered cost function in the context of point-to-point reaching is hand jerk[1] (Hogan, 1984; Flash & Hogan, 1985). Such an ideal minimum hand jerk movement produces straight-lined hand paths as well as symmetric and bell-shaped hand speed profiles (Shadmehr & Wise, 2005). In behavioral experiments, these patterns repeatedly occurred (e.g., Flash & Hogan, 1985; Shadmehr & Mussa-Ivaldi, 1994) such that minimum hand jerk optimization is frequently used for modeling and simulation purposes (e.g., Bhushan & Shadmehr, 1999; Thoroughman & Shadmehr, 2000; Donchin et al., 2003). Notably, subjects keep these patterns irrespective of the direction or the scale of the movement (within a comfortably reachable workspace; Moraso, 1981; Wolpert et al., 2013) as well as in the absence or presence of perturbations (Haith & Krakauer, 2012). Taken together, evaluation of a performed goal-directed arm movement with respect to a minimum hand jerk trajectory – in particular, to a straight-lined hand path – is reasonable both from behavioral and computational perspective.

These two possibilities to define a reference trajectory are the most common ones in current research. However, the implicit assumption that reaching movements underlie an invariant optimization criterion, which is valid under perturbed and unperturbed conditions, is debatable (Donchin et al., 2003; Izawa et al., 2008; Ito et al., 2013). Similarly, the pure existence of a desired trajectory that serves as reference is subject of controversial discussion (Todorov & Jordan, 2002; Cisek, 2005). These issues should be addressed in future research.

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[1] Jerk, $\dddot{x}$, is the third time derivative of position, x. Thus, a minimum jerk optimization yields a maximization of smoothness.

5.1.2 Kinematic and dynamic data to assess motor control mechanisms

Measures based on kinematic data

To evaluate movement trials in dynamic adaptation tasks, most frequently kinematic data is used. The main reason for this choice is twofold. First, kinematic data is easy to analyze and comprehensible. Second, if the experimental setup does not utilize robotic devices to induce dynamic perturbations but attached inertial loads (e.g., Krakauer et al., 1999) or rotating environments (e.g., Lackner & DiZio, 1994), dynamic data is difficult or impossible to record and analyze.

Even within the class of kinematic performance measures, different aspects of motor control and learning are emphasized. For instance, measures based on hand paths (e.g., perpendicular displacement, enclosed area) only consider spatial factors, whereas measures based on velocity data (e.g., velocity vector correlation) can also account for temporal factors or smoothness of the performed movement. The study reported in Chapter 3 revealed that these different particularities can lead to different conclusions. Therein, motor performance assessed using a velocity vector correlation coefficient revealed different outcomes compared with a displacement measure based on the hand path. Obviously, the two measures emphasized different aspects of of motor control and learning.

As pointed out in Section 2.2, motor performance on force field trials can simply be evaluated using kinematic data. When subjects perform movements under altered dynamics, the motor control system may use different control strategies. On the one hand, feedforward control (predictive control) can be used to predict the dynamics of the task. On the other hand, feedback mechanisms (reflexes, corrections due to sensed errors) and impedance control strategies (increased stiffness by muscular co-contraction) can be used to stabilize the movements (Franklin & Wolpert, 2011; Wolpert et al., 2011). Impedance control is particularly important to gain stability at initial stages of learning (Thoroughman & Shadmehr, 1999; Milner & Franklin, 2005) or when facing uncertain or unstable conditions (Burdet et al., 2001; Takahashi et al., 2001; Osu et al., 2003). It is assumed that movements are controlled by a combination of these strategies (Franklin et al., 2003; Osu et al., 2003) resulting in the observable net motor performance. The reliance on the respective strategy seems to depend on the environmental stability and the quality of the task-related information (Takahashi et al., 2001; Osu et al., 2003). Thus, impedance control is a valuable strategy but makes feedforward motor control hard to uncover. Therefore, it is important to bear in mind that movement trials during force field exposure represent net motor performance rather than merely feedforward motor control mechanisms.

Often, one is interested in feedforward motor control mechanisms because these reflect internal model properties. To assess these feedforward mechanisms different approaches are possible. First, consideration of movements under force field exposure is justified when the time point of evaluation is set before reflex mechanisms and/or corrective motor commands affect the movement. To catch predominantly feedforward control mechanisms, the according time point should not be later than approximately 150 ms after movement onset (e.g., $\mathrm{PD}_{100\mathrm{ms}}$, de Xivry et al., 2011) because reflexes and voluntary corrective reactions may occur thereafter (responses to sensed perturbations: short-latency reflexes [20–45 ms], long-latency reflexes [45–100 ms], voluntary reactions [120–180 ms]; Pruszynski et al., 2008). Moreover, mechanical factors influence the magnitude of deviations on force field trials. The effect of perturbing forces on the subject's arm depends on its inertial properties (arm's mass, segment lengths, limb configuration) but also on its stiffness and viscosity properties.

Another way to gauge information about feedforward motor control in dynamic learning is the induction of (null field) catch trials. On these trials the dynamic perturbation is unexpectedly removed and allows the detection of after-effects. These after-effects reflect a subject's prediction about the dynamic conditions and would not occur if the subject merely increased arm stiffness to resist the environmental perturbation. For this reason, after-effects indicate feedforward motor control (Shadmehr & Mussa-Ivaldi, 1994). However, similarly to the assessment of motor performance on force field trials, this approach is also confounded by feedback mechanisms because after-effects induce large sudden errors that are fed back to the sensorimotor system. Similarly, the problematic with respect to inertial properties, stiffness, and viscosity of the arm arises and may affect the magnitude of after-effects. Furthermore, when detecting after-effects using a block of null field catch trials, subjects will return their force outputs to baseline level quite fast because null field catch trials cause unlearning (Thoroughman & Shadmehr, 2000). This is due to the high motor errors that are fed back to the sensorimotor system signifying that force field compensation is unnecessary (Smith et al., 2006). But most importantly, as the study reported in Chapter 3 revealed, random induction of catch trials in the practice schedule significantly influences motor adaptation as well as consolidation of motor memory.

Measures based on dynamic data

A more recent way to detect feedforward motor control mechanisms – and therewith a subject's ability to form an internal model of the task dynamics – uses error clamp trials (force channel trails; Scheidt et al., 2000; Section 2.2). On these trials, the hand path is constrained by virtual walls to the straight line towards the target point. Measurement of a subject's forces at the handle that are applied against the channel wall reveal information about predictive force field compensation and enable evaluation of motor performance in terms of feedforward mechanisms (Shadmehr et al., 2010). In contrast to force field trials or null field trials, the motor errors are clamped to zero such that error feedback is suppressed. Contrary to null field catch trials, error clamp trials preserve the adapted behavior from unlearning because the force field and error signals that could promote or wash out prior learning are absent (Criscimagna-Hemminger & Shadmehr, 2008; Scheidt et al., 2000). Accordingly, the random integration of error clamp trials is assumed to keep the overall learning schedule unaffected. Indeed, absence of motor errors for many trials by inducing large blocks of error clamp trials yields a return of motor output towards baseline level. However, this processes at comparably low rate (Smith et al., 2006; Criscimagna-Hemminger & Shadmehr, 2008; Vaswani & Shadmehr, 2013).

Altogether, besides kinematic data, recent research considers dynamic data to assess motor performance. Kinematic measures mostly encompass feedforward motor control features as well as mechanical factors (stiffness, viscosity, inertia of subject's arm) and feedback motor control mechanisms (reflexes, corrective reactions). In combination with error clamp trials, dynamic measures predominantly gauge feedforward motor control features. Thus, despite the same intention, kinematic and dynamic measures pronounce different aspects of motor control and learning. Likely, different analytic approaches lead to different concluding outcomes. For these reasons, profound knowledge of the mechanisms underlying motor control and learning is a premise to perform sophisticated research.

5.2 Characteristics and mechanisms of motor memory adaptation and its consolidation

The previous section discussed concepts for the analysis in motor adaptation experiments. Herein, the utilization of catch trials was considered. Originally, catch trials were induced in learning schedules as an analytic tool in order to detect after-effects of motor learning and to gain insights into feedforward motor adaptation (e.g., Brashers-Krug et al., 1996) but their potential influence on the learning process was neglected. As mentioned above, catch trials cause sudden large motor errors that are fed back to the sensorimotor system. This alters the conditions of practice and potentially influenced motor control and learning features. Despite their wide-spread use, the detailed influence of catch trials on motor control and learning remained elusive. The study reported in Chapter 3 considered this issue in detail to bridge the gap between prior investigations that tried to unravel the potential effects of catch trials but found differing results (Overduin et al., 2006; Focke et al., 2013).

5.2.1 Unstable practice conditions affect adaptation and consolidation of motor memory

Instability affects internal model formation during adaptation

We found that unstable practice conditions, caused by inducing catch trials, impair motor adaptation. More precisely, an increased instability due to an increased catch trial ratio led to a poorer motor performance during adaptation. Thus, catch trials had a significant effect on the motor learning process.

First, these results underpin the importance of the methodological issues discussed in the previous section. Obviously, the considered motor learning paradigm is highly sensitive to methodological factors.

Second, with regards to content, the results indicate that subjects had an impaired ability to form an appropriate internal model of the task dynamics when catch trials were induced. To cope with the induced instability, subjects utilized both feedforward prediction and impedance control strategies in hybrid fashion. This is suggested by previous investigations considering reaching movements under unstable environmental conditions

(Takahashi et al., 2001; Osu et al., 2003; Franklin et al., 2003). To our best knowledge, the study reported in Chapter 3 is the first to investigate dynamic adaptation across a wide range of different environmental conditions allowing detection of gradual changes in motor adaptation. With increasing instability – i.e., increasing catch trial ratio – subjects tended to rely more on impedance control. This indicates a gradual transition of control strategies in relation to the environmental instability. Therewith, the results extend prior studies investigating motor control and learning under unstable conditions (e.g., Scheidt et al., 2001; Takahashi et al., 2001; Osu et al., 2003; Franklin et al., 2003) and contribute to a more profound understanding of motor control and learning features.

Instability can foster consolidation of motor memory

We found that unstable practice conditions impaired subjects' ability to adapt to the dynamics but fostered subsequent offline consolidation processes. This yielded a stabilized motor memory representation because the interfering effect of learning a second task was reduced. Therefore, we found evidence that consolidation of human motor memory following motor adaptation is not exclusively time-dependent but also practice-dependent. This is in line with investigations showing that the neural substrates of motor memory consolidation depend on the practice structure (Kantak et al., 2010). Yet, not instability per se is important to foster consolidation processes but rather there seems to exist an optimal amount of instability facilitating consolidation of motor memory. When the instability was too high, its positive effect diminished. That offers a possible explanation for the diverging findings of Overduin et al. (2006) and Focke et al. (2013). Overduin et al. (2006) found consolidation within an ABA-paradigm when inducing 20% catch trials, whereas our group was not able to (completely) reproduce this finding for a more complex task (Focke et al., 2013). The experimental setup of the study reported in Chapter 3 was similar to that of Focke et al. (2013). Here, we found that unstable practice can also facilitate consolidation processes in this more complex task, yet, with an optimal catch trial ratio of 30%.

There is evidence that the practice schedule modulates the neural substrates of motor memory consolidation (Robertson et al., 2004b; Tanaka et al., 2009; Kantak et al., 2010). This would explain different consolidation processes of variable compared to constant practice. The study reported in Chapter 3 supports these assumptions and underpins the importance of the practice schedule on motor memory consolidation.

Taken together, motor memory consolidation processes can be fostered by unstable practice conditions. The optimal extent of instability and its positive effects seem to depend on the task specification, in particular, on the task complexity.

5.2.2 Computational models and neural correlates of motor adaptation and consolidation

Computational models of motor adaptation under unstable conditions

The findings reported in the study of Chapter 3 are also interesting from a computational point of view. The behavioral findings may contribute to advances in the modeling of motor control and learning processes. In this context, so-called state-space models have been extensively used (Smith et al., 2006; Lee & Schweighofer, 2009). The basis of state-space models is the assumption that the subjects' internal models implement the task dynamics with respect to the system's state rather than rote memorization of a forces or torques when performing a motor action (Conditt et al., 1997). In reaching movements, the state may be described by the position and velocity of the limb (Shadmehr & Wise, 2005). Using the state-space model approach, one can model motor adaptation as trial-by-trial adjustment of the internal model by iterative motor error reduction. This idea is derived from dynamic systems theory in the style of a feedback control approach. Such an iterative process of motor error reduction accounts for the empirical finding that the motor error on trial n is linearly correlated to the change in motor output on trial $n+1$ (Thoroughman & Shadmehr, 2000; Donchin et al., 2003). Altogether, using state-space models one can describe internal model adaptation and therewith adjustments in feedforward motor control, i.e., prediction of the task conditions.

As outlined above, when subjects are exposed to unstable conditions, they seem to use an impedance control strategy in addition to a feedforward motor control strategy. We recently conducted a computational study accounting for the different control mechanisms in order to reproduce the subjects' adaptive behavior reported in Chapter 3 (Stockinger, 2014). Therein, we implemented adaptive subject controllers which were embedded in a state-space model framework. These controllers were designed to adapt their motor output using a supervised error learning algorithm and were trained in the scenarios of Chapter 3. Under unstable conditions, two control processes were required to reproduce subject behavior: one process that forms an internal model of the task dynamics (feedforward controller) and a second process that stabilizes the limb around the desired trajectory (impedance control). With increasing instability, the feedforward controller had difficulties in building an appropriate internal model of the task dynamics. To ensure movement goal achievement, the modeled controller tended to rely more on the impedance controller. Thus, both control strategies were used in parallel but the reliance on the two strategies gradually changed with the environmental instability. Under stable dynamic perturbations, the modeled subject controller relied almost exclusively on internal model formation and only made use of impedance control at the initial phase of adaptation.

These findings are in accordance to former computational studies that considered different motor control strategies under uncertain environmental conditions (e.g, Burdet et al., 2006; Mitrovic et al., 2010; Kadiallah et al., 2012). Moreover, we were able to extend these previous findings by validating our model with respect to a larger range of environmental conditions and demonstrating a gradual change in utilized motor control strategies.

Neural correlates of motor adaptation and consolidation

Besides the behavioral and computational consideration of motor control and learning, it is interesting to ask which neural correlates are involved. Previous research revealed an important role of the cerebellum in motor control and learning suggesting that the cerebellum computes internal models. Yet, it is under debate whether these internal models refer to inverse or forward internal models (Izawa et al., 2012; Haith & Krakauer, 2013). Evidence for a cerebellar involvement comes from patient studies showing that damage to the cerebellum impairs the ability to adapt movements to perturbations (Maschke et al., 2004; Smith & Shadmehr, 2005; Rabe et al., 2009; Donchin et al., 2012). Similar evidence for the importance of the cerebellum comes from neuroimaging studies (Nezafat et al., 2001; Krebs et al., 1998) or studies using stimulation techniques such as transcranial direct current stimulation (tDCS) or transcranial magnetic stimulation (TMS) (Galea & Celnik, 2009; Grimaldi et al., 2014; Celnik, 2015). In order to test for a cerebellar involvement when learning the task considered in this thesis, our group recently performed a tDCS experiment in a similar experimental setup as reported in Chapter 3. Therein, we modulated error processing during motor adaptation by applying tDCS to the cerebellum and found that tDCS during adaptation accelerated forgetting in the movement set breaks, whereas the continuous learning-related motor error reduction was preserved (Taubert et al., in review).

Besides the cerebellum, the motor cortex is known to be involved in motor control and learning (Diedrichsen et al., 2005; Herzfeld et al., 2014). The primary motor cortex (M1) was shown to be involved in motor learning as being sensitive to TMS (de Xivry et al., 2011) and tDCS (Galea & Celnik, 2009). Recently, also involvement of the premotor cortex in motor learning was discussed (Taylor & Ivry, 2014). Thus, motor learning is not restricted to the cerebellum. Rather, different neural substrates seem to contribute to adaptation and consolidation of motor memory at different stages (Shadmehr & Holcomb, 1997; Diedrichsen et al., 2010).

Presumably, motor memory is reorganized after its adaptation and the brain engages new regions to perform the motor task. Such reorganization by consolidation processes may contribute to increased functional stability (Shadmehr & Holcomb, 1997; Krebs et al., 1998). Our group recently investigated activity in the electroencephalography (EEG) over the prefrontal cortex in a consolidation paradigm similar to that depicted in Chapter 3. Following a period of consolidation, subjects showed an increased gamma band power over prefrontal areas at retest. In contrast, subjects whose consolidation period was interfered by learning a second task did not show this pattern (Thürer et al., 2016). Thus, consolidation processes seem to affect the brain areas involved during retrieval of motor memory.

Taken together, there is evidence that motor control and learning of the considered task depends on the cerebellum as well as the motor cortex and the prefrontal cortex. Yet, their detailed functions as well as their interplay in motor control and learning remain unresolved.

5.3 Characteristics and mechanisms of motor memory generalization

The aim of Chapter 4 was to investigate motor memory generalization in a force field adaptation task – in particular, direction and coordinate frame of intermanual transfer as well as the influence of a consolidation period on intermanual transfer.

5.3.1 Characteristics and different features of intermanual transfer

In order to gain a comprehensive understanding of transfer mechanisms, we defined two different features of transfer: practice-dependent bias and interlimb savings. Our results revealed intermanual transfer both from dominant to non-dominant hand and vice versa. However, the ability to transfer motor learning seems to play a minor role compared with the rapid adaptation processes because we found transfer by means of a practice-dependent bias but no clear transfer by means of interlimb savings. That means, prior adaptation changed the subjects' prediction about the dynamic conditions at the contralateral arm (practice-dependent bias) but did not result in significantly faster adaptation with the contralateral arm (interlimb savings). This is the first study dissociating and considering both these features of intermanual transfer. Most former studies investigated transfer only in terms of interlimb savings (Criscimagna-Hemminger et al., 2003; Wang & Sainburg, 2004; Galea et al., 2007) whereas only one study considered transfer in terms of practice-dependent bias (Joiner et al., 2013).

Intriguingly, we found that transfer of dynamic learning can occur in bidirectional manner, i.e., both from dominant to non-dominant and vice versa. This contrasts previous findings (Criscimagna-Hemminger et al., 2003; Wang & Sainburg, 2004; Galea et al., 2007). We also outlined that transfer is difficult to detect for methodological reasons which might have complicated detection of potential bidirectional transfer in former studies.

Moreover, the study depicted in Chapter 4 is the first to consider the influence of a consolidation period (incl. nocturnal sleep) on intermanual transfer of dynamic adaptation. Consolidation of motor memory – particularity in connection with sleep – is suggested to be an important aspect of motor learning because structural modifications and reorganizations occur (Rasch & Born, 2013; Censor, 2013). Against this background, it is surprising that transfer mechanisms were not fostered by a period of consolidation. Yet, further research is needed to gain more detailed insights into the relation of motor memory consolidation and intermanual transfer.

5.3.2 Models and neural correlates of intermanual transfer

Consideration of transfer mechanisms is revealing because it allows ratiocination of brain regions that are involved in the formation of an abstract movement representation during adaptation, regardless of the hand being used during adaptation. Based on behavioral studies two prominent models have been proposed to explain intermanual transfer: the bilateral access model and the cross activation model (Ruddy & Carson, 2013).

In the framework of the bilateral access model, motor memory formed during unilateral practice is not effector-specific but is encoded in more abstract form. This abstract motor memory can be utilized for motor control for both the trained and the untrained, contralateral limb (Ruddy & Carson, 2013). When transfer of learning occurs, the *untrained* hemisphere accesses this motor memory formed during initial contralateral practice.

One prominent example of such bilateral access offers the callosal access model (Taylor & Heilman, 1980). This model bases on the assumption that the left hemisphere plays a dominant role in movement control for both body sides and motor memory formation is lateralized to this dominant hemisphere (Liepmann, 1905; Serrien et al., 2006). However, the motor networks projecting to the untrained limb have access to this previously formed motor memory. Accordingly, interlimb transfer from the right to left hand would be accomplished by initial motor memory formation in the dominant (left) hemisphere and gained access by the motor networks projecting to the left hand. Thereby, the corpus callosum serves as mediator between the lateralized motor networks (Ruddy & Carson, 2013; Anguera et al., 2007; Takeuchi et al., 2012). This is supported, for example, by research on hominids showing that intermanual transfer performance is associated with the structural integrity of the motor and sensory regions of the corpus callosum (Phillips et al., 2013). Another possibility for bilateral access is that the established motor memory is located in cortical or subcortical areas which project bilaterally, i.e., which are accessible to the motor networks of both limbs (Ruddy & Carson, 2013).

The cross-activation model bases on the observation that in unilateral movement tasks there is increased excitability both in contralateral and ipsilateral cortical motor areas (Lee et al., 2010; Ruddy & Carson, 2013). Such bilateral cortical activity during unilateral practice indicates dual neural adaptations in both hemispheres (Ruddy & Carson, 2013). For instance, during right hand motor learning, a motor program is stored in the dominant hemisphere and an inferior duplicate of this motor program is stored in the non-dominant hemisphere. When performing the task with the untrained limb, the non-dominant motor areas use this inferior motor program independent of the superior motor program in the dominant motor areas (Anguera et al., 2007). In the intermanual transfer experiment depicted in Chapter 4, we found bidirectional transfer. This finding could be explained by both the bilateral access model and the cross activation model. However, in order to detect systematic differences in the strength of this transfer between both directions, further investigations are needed.

Criscimagna-Hemminger et al. (2003) considered intermanual transfer in a similar dynamic adaptation task as depicted in Chapter 4. These authors found intermanual transfer of motor learning for a split brain patient. This suggests interhemispheric connections independent of the corpus callosum. However, further statements about the neural mechanisms underlying intermanual transfer of dynamic learning would be speculation.

Another noteworthy finding of the intermanual transfer experiment in Chapter 4 is the coordinate frame of transfer. We found transfer in extrinsic coordinates which is in line with previous studies sharing a similar experimental setup (Criscimagna-Hemminger et al., 2003; Malfait & Ostry, 2004). Such transfer in extrinsic coordinates suggests an internal representation of the motor task in extrinsic coordinates. This is interesting from a cognitive and a computational perspective. First, such representation in extrinsic coordinates suggests that subjects related the motor task – i.e., learning a force field – with an external object rather than with respect to their own body. Second, from a computational perspective, this finding is in line with the previously discussed assumption that the subjects' controllers minimize a cost function that is defined in extrinsic coordinates (i.e., minimum hand jerk, Subsection 5.1.1) rather than in intrinsic coordinates (e.g., minimum torque change).

5.4 Implications for future research

The findings of this thesis comprise both methodological aspects and aspects with regard to adaptation of motor memory as well as its consolidation and generalization. Motor control and learning is a vital field of research which possesses valuable potential for theoretical and practical reasons. Thus, more studies are necessary to replicate and enhance the findings reported in this thesis. Based on the presented results future research should consider the following issues:

- consideration of the different mechanisms underlying the control of arm movements as well as further development of analytic approaches to assess these mechanisms;
- identification of further factors that facilitate consolidation of motor memory, e.g., type of feedback, structural learning schedules, or amount of practice;
- investigation of detailed relations between practice schedule, consolidation, and intermanual transfer in order to foster transfer processes;
- development of more elaborate computational models of motor learning that account for different control mechanisms and generalization characteristics;
- investigation of intermanual transfer using functional imaging techniques in order to identify the neural correlates underlying transfer;
- investigation of intermanual transfer mechanisms in more complex adaptation tasks in order to emphasize potential transfer effects in terms of interlimb savings;
- consideration of further similarities and differences between motor skill learning and motor adaptation in order to close the gap between these two types of motor learning and gain a more comprehensive understanding of motor learning in its entirety.

5.5 Conclusion

This thesis aimed to investigate motor control and learning mechanisms with special consideration of motor memory adaptation as well as its consolidation and generalization. These features are in the scope of current research because there are plenty of unresolved questions. To gain more detailed insights into the mechanisms underlying motor control and learning, we used the well-known experimental paradigm of force field adaptation. In essence, the current thesis revealed the following findings:

(1) The different analytic approaches for the assessment of motor performance, which are reported in the literature, emphasize different aspects of motor control and learning, e.g., different control mechanisms. Despite the same intention, usage of different analytic approaches can lead to different concluding outcomes. Potentially, diverging findings of prior investigations are caused by such methodological factors. For this reason, profound knowledge about the diversity of analytic methods and their characteristics is indispensable to perform sophisticated research. Thus, researchers are encouraged to chose their analytic approaches with caution bearing in mind the manifold nature of motor control and learning mechanisms.

(2) Unstable practice conditions impair internal model adaptation. Presumably, subjects use at least two different motor control strategies: feedforward control using internal model predictions and impedance control to modulate arm stiffness by muscular co-contractions. With increasing environmental instability the reliance on the motor control strategies gradually changes from feedforward to impedance control.

(3) Consolidation of motor adaptation is not only a time-dependent process but also a practice-dependent process. Unstable practice conditions can foster consolidation processes by increasing the resistance of the newly formed motor memory against interfering factors. Thereby, not instability per se is crucial to foster motor memory consolidation but rather there seems to exist an optimal amount of instability.

(4) Intermanual transfer of dynamic learning is a bidirectional phenomenon which occurs in extrinsic coordinates and weakens with passage of time. Intermanual transfer comprises two different features: practice-dependent bias (i.e., change in the prediction of the task conditions due to previous contralateral practice) and interlimb-savings (i.e., faster learning of the task due to previous contralateral practice). In particular, both the right and the left hand are capable of forming an appropriate internal model of the task when exposed to altered dynamic conditions.

These findings contribute to:

- our fundamental understanding of the mechanisms involved in motor control and learning as well as the internal representation of motor tasks;
- our understanding of motor memory consolidation and its dependence on the practice schedule and therewith to a basic understanding of how practice sessions in neurorehabilitation and sports should be designed;
- enhancements of computational models for motor control that can account for varying environmental conditions by using different control mechanisms; this contributes to designing robots with sophisticated control algorithms ensuring stable and safe operating.

Altogether, motor control and learning are vital fields of research which are interdisciplinary in nature. Therein, diverse disciplines like human movement science, neuroscience, and robotics contribute to an enhanced understanding of motor control and learning. Insights into the characteristics and mechanisms of the human sensorimotor system offer valuable information to compose effective practice schedules in neurorehabilitation and sports, for designing safer workplaces, better tools and prostheses, or to develop more sophisticated robots. Against this background, this thesis contributes to an enhanced understanding of human motor control and learning.

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Statutory Declaration

Hiermit erkläre ich, dass ich die vorliegende Dissertation mit dem Titel

> "Adaptation, consolidation, and generalization mechanisms in human motor control and learning – development of a methodological framework and conduction of psychophysical studies"

selbstständig angefertigt habe und keine anderen als die angegebenen Quellen und Hilfsmittel benutzt sowie die wörtlich oder inhaltlich übernommenen Stellen als solche kenntlich gemacht und die Satzung des Karlsruher Instituts für Technologie (KIT) zur Sicherung guter wissenschaftlicher Praxis beachtet habe.

Karlsruhe, den 02. November 2015