



DISSERTATION

Predicting habitual activities from bone architecture using a biomechanical approach

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Dipl.-Ing. Alexander SYNEK, MSc

Mat.Nr.: 1128857

Schönbrunnerschlossstraße 31A/21, 1120 Vienna, Austria

under the supervision of

Assoc. Prof. Dipl.-Ing. Dr. techn. Dieter H. Pahr

Institute of Lightweight Design and Structural Biomechanics, E317

reviewed by

Prof. Dipl.–Ing. Markus O. Heller, PhD	Prof. Marcus G. Pandy, PhD
Faculty of Engineering and the Environment,	Department of Mechanical Engineering,
University of Southampton, United Kingdom	University of Melbourne, Australia

Affidavit

I declare in lieu of oath, that I wrote this thesis and performed the associated research myself, using only literature cited in this volume. If text passages from sources are used literally, they are marked as such.

I confirm that this work is original and has not been submitted elsewhere for any examination, nor is it currently under consideration for a thesis elsewhere.

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Alexander Synek

Abstract

Motivation: Bone is a remarkable, living material which has the ability to adapt to its mechanical environment. As a result, the characteristic loading patterns of habitual activities shape the bone both externally and internally. While a lot of research focuses on predicting changes of bone architecture (i.e. external shape and internal structure) due to altered loading conditions or diseases, little was so far done to make use of the process of bone adaptation in a different way: Given a well-adapted bone architecture, it might be feasible to estimate its loading history and, ultimately, to make inferences about habitual activities of the respective individual.

Goals: The primary goal of this thesis was to investigate the feasibility of predicting habitual activities from bone architecture using a biomechanical approach. Considering bone loads as the intermediate link between activity and bone architecture, the subgoals were to investigate (1) the possibility of predicting bone loads from bone architecture and (2) the possibility of associating predicted bone loads with specific habitual activities.

Methodological approach: The feasibility of predicting activities from bone architecture was tested by predicting habitual manual activities of humans and non-human primates (manipulation/tool use, climbing/suspension, knuckle-walking) from metacarpal bone architecture. Two biomechanical methods were used to fulfil the subgoals of this thesis: (1) A micro-finite elementbased inverse remodelling algorithm was used to predict bone loads from bone architecture. The algorithm was first tested on human proximal femora to investigate its plausibility and robustness and then applied to primate metacarpal bones to detect activity-related differences of joint loads. (2) Musculoskeletal models of a human and bonobo finger were used to investigate the relation of habitual activities to bone loading. The models were first implemented and adjusted to in vitro experimental data and then used to predict differences of joint loads acting on the metacarpal bone by applying in vivo experimental data collected during various habitual activities.

Main results: (1) Application to the proximal femora showed that the inverse remodelling algorithm delivers coarse but plausible estimates of joint loads that are robust enough for interspecies comparisons. Application to the metacarpal bones revealed that the algorithm is sufficiently sensitive to detect activity-related differences of joint loads, although these differences were smaller than expected. (2) The adjustment of the human and bonobo musculoskeletal finger models to in vitro experimental data highlighted both the models' parameter sensitivity and the need for model optimization to obtain accurate predictions. The application of in vivo data

ABSTRACT

showed that differences of the magnitude and direction of joint loads acting on the metacarpal bone during the investigated habitual activities are evident but smaller than external loading and finger posture would suggest.

Conclusions: Taken together, the results suggest that the prediction of habitual activities from bone architecture is feasible with this biomechanical approach only if the respective differences of actual bone loads are large enough (e.g. knuckle-walking vs. manipulation/tool use activities). The fact that actual bone loads might deviate from expectations based on observations of external loading and posture warrants the use of musculoskeletal models for accurate functional interpretations of bone loads.

Kurfassung

Motivation: Knochen ist ein einzigartiges, lebendes Material, das sich an äußere Belastungen anpassen kann. Die durch tägliche Aktivitäten einwirkende Lasten prägen daher sowohl die Form als auch interne Struktur des Knochens. In der Vergangenheit hat sich die Forschung hauptsächlich mit der Vorhersage von Knochenadaption im Zuge von veränderten Lasten oder Krankheiten beschäftigt. Dabei blieb jedoch eine weiterer, spannender Nutzen der Knochenadaption außer Acht: Ausgehend von einem gut adaptierten Knochen sollte es theoretisch möglich sein, Lasten, die in der Vergangenheit auf ihn gewirkt haben, rückzurechnen und schlussendlich sogar Rückschlüsse auf alltägliche Aktivitäten des entsprechenden Individuums zu ziehen.

Ziele: Das primäre Ziel dieser Dissertation war es, die Machbarkeit der Rekonstruktion von alltäglichen Aktivitäten allein aus der Architektur eines Knochens (also seiner Form und internen Struktur) zu untersuchen. Unter der Annahme, dass Knochenlasten das Bindeglied zwischen Knochenarchitektur und Aktivitäten bilden, wurden zwei Unterziele definiert: (1) Die Untersuchung der Möglichkeit, Knochenlasten aus der Knochenarchitektur vorherzusagen und (2) die Untersuchung der Möglichkeit, Knochenlasten mit spezifischen Aktivitäten zu assoziieren.

Methodischer Ansatz: Die Machbarkeit der Rekonstruktion von Aktivitäten allein aus der Knochenarchitektur wurde in dieser Arbeit am Beispiel manueller Aktivitäten von Menschen und Menschenaffen (Manipulation/Werkzeugverwendung, Klettern, Knöchelgang) untersucht, die aus der Architektur eines Mittelhandknochens vorhergesagt werden sollen. Zwei biomechanische Methoden wurden hierbei verwendet, um die beiden Unterziele zu erfüllen: (1) Ein mikro-finite elemente-basierter inverser Remodellierungs-algorithmus wurde eingesetzt, um die Knochenlasten aus der Knochenarchitektur zu berechnen. Dieser Algorithmus wurde zuerst an humanen proximalen Femora getestet, um die Robustheit und Plausibilität der Vorhersagen zu untersuchen, und danach auf Mittelhandknochen angewendet um aktivitäts-bezogene Unterschiede von Gelenklasten zu identifizieren. (2) Muskuloskeletale Modelle vom Finger eines Menschen und eines Bonobos wurden dann verwendet, um den Bezug zwischen Knochenlasten und Aktivitäten zu untersuchen. Die Modelle wurden zuerst implementiert und anhand in vitro experimenteller Daten adaptiert und danach eingesetzt um anhand in vivo experimenteller Daten und eine Mittelhandknochen wirkenden Gelenklasten zu bestimmen.

Hauptergebnisse: (1) Die Anwendung des inversen Remodellierungs-algorithmus auf die proximalen Femora zeigte, dass die Vorhersagen der Gelenklasten grob aber plausibel sind und robust genug für einen Vergleich großer Lastunterschiede, wie sie bei Aktivitäten unterschiedlicher

KURZFASSUNG

Spezies zu erwarten sind. Die Anwendung auf Mittelhandknochen von Menschen und Menschenaffen konnte zeigen, dass der Algorithmus sensitiv genug ist, um aktivitäts-bezogene Unterschiede von Gelenklasten zu identifizieren; allerdings waren die Unterschiede geringer als erwartet. (2) Die Adaption der muskuloskeletalen Fingermodelle an die Daten der in vitro Experimente offenbarte die Parametersensitivität der Modelle und bestätigte die Notwendigkeit einer Modelloptimierung. Die Anwendung der in vivo Daten zeigte, dass die Unterschiede der Gelenklasten zwischen den hier untersuchten Aktivitäten zwar deutlich sind, aber geringer ausfallen als Gelenkstellung und externe Fingerlasten es vermuten ließen.

Schlussfolgerungen: Insgesamt legen die in dieser Dissertation erhaltenen Ergebnisse nahe, dass die Rekonstruktion von Aktivitäten allein aus der Knochenarchitektur prinzipiell möglich ist; allerdings nur wenn die Unterschiede der aus den untersuchten Aktivitäten resultierenden, tatsächlichen Knochenlasten ausreichend groß sind (hier beispielsweise zwischen Werkzeugverwendung und Knöchelgang). Die Tatsache, dass die tatsächlichen Knochenlasten von den Erwartungen basierend auf Gelenkstellung und externen Lasten abweichen können, rechtfertigt hierbei die Verwendung von muskuloskeletalen Modellen zur korrekten funktionellen Interpretation von Knochenlasten.

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List of abbreviations

2D 3D CoR CPU CS CT DI DoF DP EDC EMG EMG EDC EMG FDS FE IP LU MC MCP MP	 Two-dimensional Three-dimensional Centre of rotation Coefficient of variation Central processing unit Central slip Computed tomography Dorsal interosseus Distal interphalangeal Degree(s) of freedom Distal phalanx Extensor digitorum communis Electromyography Flexor digitorum profundus Flexor digitorum superficialis Finite element Interphalangeal Lumbrical Metacarpophalangeal Middle phalanx
	Elever digitorum superficialis
FDS EE	Einite element
IP	Interphalangeal
LU	
MC	Metacarpal
MCP	Metacarpophalangeal
MP	Middle phalanx
PI	Palmar interosseus
	Proximal interphalangeal
RB	
	Radial Interossues
	Region of interest
JED TC	Terminal clin
UB	
UI	Ulnar interosseus

Chapter 1

Introduction

1.1 Motivation

Bone is a remarkable material that stands out not only by its mechanical properties [45, 227], but also by its ability of self-repair [52, 128] and load-driven adaptation [102, 148]. The ability of bone to adapt to mechanical loading fascinated researchers since the 19th century [163] and was soon discovered to be the result of a self-regulatory process governed by bone cells which form bone where needed, and resorb bone where not needed [64, 87]. This process is driven by external mechanical loading engendered by habitual activites [6, 28] (see Figure 1.1, grey arrow) but also other factors such as genetics [130], hormone levels [31, 225], or calcium homeostasis [25]. A dysbalance of this sensitive regulatory mechanism might lead to excessive bone loss and, ultimately, fragile bones prone to fracture [77].

Consequently, the process of bone adaptation, also called bone remodelling, attracted the attention of many researchers. Numerous experimental [143] and computational studies [70] were conducted to investigate both mechanical and biological factors of bone adaptation. Mathematical models were developed that aim to describe different phenomena of bone remodelling [10, 89, 171, 204] and enabled predictions of the evolution of bone structure in response to changes of the mechanical environment, e.g. due to insertion of implants [67], or changes of biological factors such as hormone levels [36].

However, the fact that bone adapts to external loading also creates another, far less investigated possibility: Given a well-adapted bone architecture, it might be feasible to reconstruct its loading history, and, ultimately, the habitual activities of the respective individual. This approach would be useful in many biomechanical applications, e.g. predictions of fracture risk [197] or simulations of bone healing [43], without the need for musculoskeletal models, which require numerous subject specific parameters [121, 179], or highly invasive measurements with instrumented prostheses [13, 14]. Since only bone is required to perform such predictions, the method might also help to study the behaviour of extinct species more directly than possible with current morphometric analyses [102, 188, 201]. Attempts to solving this "inverse remodelling" problem were so far only presented by a handful of researchers. The complexity of these approaches ranges from simple estimations based on cross sectional area [65] to the application of machine learning to model the relation between bone loading and architecture [68, 235]. A particularly promising and simple idea was presented by Fischer et al. [56]: Utilizing existing mathematical models of bone remodelling, they tried to combine and scale multiple loads applied to a bone in a way such that no remodelling occurs. Although information about whole bone architecture was limited to 2D geometry and apparent density distributions in their studies, the results were encouraging [57–59]. With increasing computational power, Christen et al. [37] were able to adapt this concept and extend it to much more detailed 3D models with accurate representations of bone architecture down to the micro-scale. The approach was verified on small bone cubes [39], was shown to predict varying levels of uniaxial in vivo loading in mice vertebrae [37], and delivered reproducible results in distal radius sections [42].

Despite its potential, the above inverse remodelling method cannot be considered fully applicable to this date: the studies of Fisher et al. were compromised by small sample sizes and limited modelling details [57, 59]; Christen et al. mostly focused on applying simple load cases (e.g. section forces) [37, 39, 42] and only used small sample sizes in a study on whole bones with more complex load cases [41]. In preliminary studies, Bona et al. [18] and Christen et al. [41] also tried to infer habitual activities of humans and non-human species from bone architecture. However, sample sizes were as small as a single specimen for each group and the link between activity and bone loading was based on vague assumptions rather than biomechanical data. As a result, further research is required to investigate both the potential and limitations of predicting bone loads and, ultimately, habitual activities from bone architecture using inverse remodelling methods.

1.2 Goals

The *primary goal* of this thesis was to investigate the feasibility of predicting different types of habitual activities from bone architecture (see Figure 1.1, blue arrow). Considering bone loads as the intermediate quantity between activity and bone architecture, the *subgoals* (see Figure 1.1, orange arrows) were:

- (1) To investigate the possibility of predicting whole bone loading from bone architecture using an inverse remodelling approach, and
- (2) to investigate the link between bone loads and habitual activities using biomechanical methods to improve the functional interpretation of the inverse remodelling predictions.



Figure 1.1: Graphical abstract of this thesis. The primary goal was to test the feasibility of predicting habitual activities from bone architecture. The prediction was considered a two-step procedure: An inverse remodeling algorithm predicts bone loading from bone architecture (method 1), while musculoskeletal models should support the interpretation of bone loading in terms of habitual activities (method 2). MCP joint: metacarpophalangeal joint

1.3 Methodological approach

The feasibility of predicting habitual activities from bone architecture was tested by investigating whether habitual *manual* activities of humans and non-human primates (manipulation/tool use, suspension/climbing, knuckle-walking) can be predicted from *metacarpal* bones. The activities and species were selected to show whether at least large differences in the types of activities (e.g. tool use and locomotion) can be identified. Also, this test case may provide interesting biomechanical insights for anthropologists helping to better understand the evolution of the human hand [103]. Specifically metacarpal bones (dark grey in Figure 1.1, centre panel) were chosen because activity-related differences in bone architecture have already been documented [35, 201]. As joint loads were considered to dominate the loading experienced by the metacarpal bone, all methods focus on predicting metacarpophalangeal (MCP) joint loads (indicated by the black arrow labelled F in Figure 1.1, centre panel). The subgoals were addressed using two biomechanical methods:

- (1) An *inverse remodelling algorithm* was implemented and tested by assessing the robustness and plausibility of joint load predictions at the proximal femur where in vivo loading data are available in literature (Figure 1.1, 1a), and finally used to predict MCP joint loads from metacarpal bone architecture (Figure 1.1, 1b)
- (2) Musculoskeletal models of a human and a non-human primate finger were implemented and tested by comparing model predictions to in vitro experimental data (Figure 1.1, 2a), and finally used to investigate the relation of various types of activities to MCP joint loads (Figure 1.1, 2b)

1.4 Thesis outline

The thesis is structured in accordance with the subgoals and the methodological approach as described in the previous sections.

Chapter 2 presents the investigation of predicting bone loads from bone architecture using an inverse remodelling method. The background for this chapter comprises an introduction to functional bone adaptation and inverse remodelling (Section 2.1). An investigation of the plausibility and robustness of the predictions obtained with the inverse remodelling algorithm is presented in Section 2.2. The application of the algorithm to metacarpal bones of human and non-human primates to find activity-related differences is presented in Section 2.3.

Chapter 3 contains the investigation of linking habitual activities to bone loads using musculoskeletal models. The functional anatomy of the human and non-human primate finger as well as a brief literature review of musculoskeletal finger models is presented in Section 3.1. Section 3.2 provides a description of the implementation of the finger models and a comparison of the model predictions to in vitro experiments. Finally, the application of the models using in vivo data collected during various manual activities is presented to investigate the link between different types of activities and MCP joint loads (Section 3.3).

Chapter 4 synthesizes the results of Chapters 2 and 3 to judge the feasibility of predicting habitual activities from bone architecture both for the chosen test case and from a general perspective (Section 4.1). The chapter is finalized by an outlook highlighting questions to be addressed in future studies (Section 4.2) and an overall conclusion (Section 4.3).

Chapter 2

Inverse bone remodelling

The goal of this chapter is to investigate the possibility to predict bone loading from bone architecture (see Figure 2.1). The background section (Section 2.1) provides a brief overview of the literature describing the aspects of functional bone adaptation relevant to this thesis, followed by an introduction to approaches of inverse remodelling presented in literature. An inverse remodelling algorithm was implemented and tested towards its applicability to predict loads acting on whole bones (see Section 2.2). Finally, in Section 2.3, the inverse remodelling algorithm was applied to metacarpal bones of humans and non-human primates to investigate the feasibility of detecting differences of metacarpophalangeal (MCP) joint loads related to distinct types of activities.



Figure 2.1: Outline of this chapter in the context of the whole thesis as presented in Figure 1.1. MCP joint: metacarpophalangeal joint

2.1 Background

2.1.1 Functional adaptation of bone

Bone serves multiple purposes, both of mechanical and metabolic nature: it ensures mechanical protection of inner organs and allows locomotion in conjunction with muscles which attach to the skeleton, but also plays an essential role in calcium homeostasis [25, 45]. From an evolutionary perspective, bones must be both light to ensure energy-efficient locomotion but also strong enough to sustain both habitual and unusual loads (e.g. due to fall) [49, 204]. In that regard, it is not surprising that the shape and internal structure of bone appears to follow certain rules of optimal design (see Figure 2.2), such as highlighted in the work of Julius Wolff which became famous as "Wolff's law" [231]. As it was later recognized that bone adapts in a self-regulatory way rather than following fixed rules of optimal design [87], the term "functional adaptation" will be used in this thesis.



Figure 2.2: Cross section through a proximal femur displaying its bone architecture. Particularly the trabecular bone structure appears to be well-adapted to external loading (labelled F).

The goal of this section is to shed light on the process of bone functional adaptation, providing selected details from the broad body of literature which are relevant to this thesis. In particular, evidence for load-driven adaptation of mature bone and the basic underlying process will be explained, followed by a description of the influence of various parameters of the loading regime and non-mechanical factors on bone adaptation. For further details on functional bone adaptation that go beyond the scope of this thesis, the reader is referred to recent literature reviews of Kivell [102], Rosa et al. [166], Robling et al. [161], and the comprehensive book "Multiscale Mechanobiology of Bone Remodeling and Adaptation" of Pivonka et al. [148].

2.1.1.1 Evidence for load-driven adaptation of mature bone

Although the concept of functional bone adaptation is already well accepted in the field, there is still some debate about the role of mechanical loading as compared to genetic influence [1]. Some authors even claim that the effect of load adaptive response is minor compared to the "genetic blueprint", which would compromise functional inferences about loading or activity drawn from bone architecture [130]. However, far more studies provide evidence for the load adaptive response of bone to habitual bone loading even in the mature skeleton and will be described briefly in the following.

Simple phenomenological observations of bone adaptation were presented in retrospective clinical studies, which showed the general effect of activity or lack thereof on the shape and internal structure of bone. For instance, substantial increase of cortical bone thickness in the dominant arms of tennis players were reported [96], whereas low gravity environments such as during space flight led to considerable reduction of bone density and thinning of the cortex [110]. It was also shown that an increase in physical activity generally enhances bone mass or density [118, 136]. A more direct relation of activity or loading to bone shape and architecture was provided by controlled animal studies. In thoroughly designed experiments, Barak et al. [6] and Pontzer [150] tested the sensitivity of bone adaptation by exercising animals on slightly inclined treadmills for a period of approximately one month and comparing trabecular orientation to control groups. Both studies showed that activity-related differences are clearly reflected in the bone architecture. Moreover, trabecular bone orientation in proximity to the joint was found to closely correspond to differences of joint postures during peak loading.

Thus, even if genetics do provide the general blueprint for the bone shape and internal architecture, activity-related differences were found to be strongly reflected in the bone architecture. This warrants the effort of reconstructing bone loading and activity from bone architecture.

2.1.1.2 The process of load-driven bone adaptation

While it could be clearly shown that bone adapts to external loading, the process behind this adaptive response is still not entirely understood to this date. As mentioned above, Julius Wolff was one of the first who tried to explain bone adaptation, hypothesizing that bone follows rules of optimal mechanical design. Specifically, his "trajectorial hypothesis" stated that trabecular and compact bone structure follows the density and orientation of trajectories of principal stresses [163, 231]. However, it was soon discovered that the apparently optimal design of bone is the result of a biological self-regulatory process rather than caused by fixed design rules [87]. Likely the most famous model of this regulatory process is the "Mechanostat"

postulated by Frost [64, 66]. Based on the experimentally observed dependency of bone loss and gain on local peak strains, Frost defined four so-called usage windows (Figure 2.3): bone mass is lost in the disuse window (effective strains below 100-300 $\mu\varepsilon$), maintained in the adapted window (300-1500 $\mu\varepsilon$), gained in the mild overload window (1500-3000 $\mu\varepsilon$), and the bone is damaged until fracture in the pathologic overload window (fracture at roughly 25000 $\mu\varepsilon$).



Figure 2.3: Schematic diagram of the mechanostat theory, stating that loss and gain of bone mass is directly related to the magnitude of local strains. Strain values were taken from Frost [64, 66]. DW: disuse window; AW: adapted window; MOW: mild overload window; POW: pathologic overload window

For bone adaptation to function as proposed by the mechanostat theory, it is inevitable that bone possesses sensors of mechanical loading and effectors which can resorb and add bone. The effectors of the bone are two types of cells, namely osteoblasts (forming bone) and osteoclasts (resorbing bone) [64, 66]. While the effectors and their highly organized activity have long been recognized [79], there was some dispute about the cellular mechanosensors and the signal transduction in bone [23]. Today it is commonly accepted that the network of interconnected osteocytes inside the bone serves as the main sensory mechanism of the bone [89, 104]. The exact process of signal transduction, i.e. how the osteocytes perceive a mechanical signal and how this signal translates to bone formation or resorption by osteoblasts and -clasts, is still a topic of research [161].

Although many questions about the process of load-driven bone adaptation remain to be answered, numerous experimental studies support the mechanostat theory [62]. Moreover, the general concept of local adaptation of bone to the magnitude of mechanical loading was also confirmed in a recent in vivo study using high resolution computed tomography (CT) scans of human tibiae in which a relation between local mechanical loading and bone formation/resorption could be found [40].

2.1.1.3 Influence of the loading regime on bone adaptation

Frost's original mechanostat theory postulates that bone remodelling is mainly driven by local mechanical load magnitude and fixed thresholds governing bone loss and gain. However, several studies found evidence that other loading parameters such as loading rate, number of loading cycles, and rest periods also influence the load-adaptive response of bone. A selection of these parameter which were considered most relevant for this thesis will be described briefly in the following.

A very important finding is that bone only adapts to dynamic loading, irrespective of the load magnitude [62, 112, 204]. Experiments systematically evaluating the effect of load frequency and strain rate on the osteogenic response found a strong increase of bone formation rate at higher frequencies [73, 205]. However, the bone formation rate was also shown to reach a plateau at a loading frequency of about 10 Hz [224].

Similar to the loading rate, bone remodelling also seems to be threshold-driven in terms of load duration. In particular, already a few loading cycles were shown to elicit a substantial increase in bone formation, whereas further loading cycles merely cause a stronger osteogenic response [170, 208]. In contrast to Frost, who assumed that the number of load cycles plays a minor role in bone formation [64], Qin et al. [154] emphasized that the number of load cycles and load magnitude have to be considered in conjunction. In particular, they found that even very low strains, which would fall in the disuse window of Frost's mechanostat, are sufficient to maintain bone mass if applied long enough. An interesting consequence of this finding is that not only infrequent peak loading events, but also low magnitude loading, e.g. from stabilizing muscle activity in static postures, might influence the bone architecture [169].

Finally, also the rest periods in between loading bouts were shown to have a positive effect on bone formation. For instance, applying 4 bouts of 60 load cycles each increased the bone formation rate in rat tibiae by more than 50 % when compared to a single period of 360 load cycles [159]. Another experiment showed that loading with low magnitude strains may not elicit an osteongenic response when applied in a single loading period, but can substantially increase bone formation rates when rest periods are introduced [190]. These results were interpreted as a gradual desensitization of the bone with increased load duration, which can be restored after extended resting periods [160, 161].

2.1.1.4 Non-mechanical factors influencing bone adaptation

In his mechanostat theory, Frost already indicated that also non-mechanical factors influence bone adaptation by altering the otherwise fixed thresholds governing bone loss or gain [64].

Numerous studies provided evidence for the influence of these non-mechanical factors, including genetics, age, and dependency on anatomical sites. A brief overview of these studies will be presented in the following.

As mentioned before, genetics definitely play an important role for the bone structure as they provide the blueprint of the bone [1, 130]. This might also induce differences in bone architecture between species that are unrelated to skeletal loading [102, 172]. For instance, overall larger bone density was found in chimpanzees when compared to humans which might reflect genetic differences rather than those of habitual loading [203]. A hypothesis which is in line with these observations is that genetics might dictate the bone's mechanosensitivity [170], i.e. the thresholds governing bone loss or gain.

Variable mechanosensitivity could also explain the site-specificity of bone adaptation [187]. Robling et al. [161] argue that the mechanosensitivity is not only influenced by genetics, but also regulated by adaptations of the osteocyte cytoskeleton to habitual strains and changes of the extracellular microenvironment of the cell. As a result, the bone's sensory mechanism rather than it's architecture might adapt to habitual external loading as well [168].

Numerous other factors influencing bone adaptation remain to be mentioned. Age clearly influences bone adaptation, as indicated by increased osteogenic response during growth [100]. Also changes in hormone levels such as estrogen [162] or thyroid hormones [225] and diet [30] influence bone formation and resorption. Finally, the function of bone as calcium reservoir might introduce stochastic resorption of bone rather than site-dependent remodelling in response to mechanical loading [25].

2.1.1.5 Conclusions

The above introduction highlights that bone architecture clearly and sensitively adapts to habitual external loading, which supports the idea of functional interpretation of the bone architecture. The general concept of the mechanostat theory, i.e. local resporption or formation of bone in response to mechanical load magnitude, was confirmed by numerous experimental studies and provides a basis for estimating external loading from bone architecture. However, the mechanostat does not directly account for many other mechanical (loading rate, duration, and rest periods) and non-mechanical factors (genetics, age, hormone levels, and calcium homeostasis) that complicate direct functional interpretations of bone architecture.

2.1.2 Literature review of inverse bone remodelling

As described in the previous section, bone is able to adapt to external loading through a selfregulatory process. Numerous studies aimed to model this process of bone adaptation at different length scales using computer simulations [9, 89, 140]. Given a set of predefined external loading conditions, the goal of these "forward remodelling" simulations is to find the homeostatic or adapted bone structure, i.e. the bone structure where no net change of bone mass occurs (see Figure 2.4, solid arrow). In the inverse remodelling problem, the adapted structure is used as a starting point and the goal is to find the external loading conditions which most closely lead to remodelling equilibrium (see Figure 2.4, dashed arrow) [56, 68, 235].



Figure 2.4: Outline of the forward and inverse remodelling problem. The goal of the inverse remodelling problem is to find the external loading regime based on a given adapted bone architecture. Bone architecture is schematically visualized by the distribution of density within the bone.

This section briefly describes previously used approaches to solve this inverse remodelling problem. One of these approaches, the so-called optimization-based inverse remodelling, will be explained in more detail, including the theoretical background as well as applications at the continuum and tissue level. Again, this section focuses on aspects relevant to this thesis. Further reading on forward and inverse remodelling problems is provided in recent reviews, such as those of Gerhard et al. [70] or Zadpoor [234].

2.1.2.1 Overview of inverse remodelling approaches

There are two major categories of approaches to solve the inverse remodelling problem [234]: (1) optimization-based and (2) mapping-based inverse remodelling. Alternative approaches are limited to estimations of bone loads from cross sections and respective geometrical properties such as total area and second moment of area [65].

Optimization-based inverse remodelling [18, 37, 56] seeks to find the loading history of a given bone architecture by optimally combining a predefined set of load cases (e.g. joint loads in

different directions). The goal of the optimization is to minimize the difference between a computed local mechanical stimulus and a target mechanical stimulus within the whole bone tissue. The target mechanical stimulus lies in the adapted window (see Section 2.1.1 and specifically Figure 2.3), such that no net change of bone mass would occur and the bone is in remodelling equilibrium. The required computations are limited to determining the distributions of local mechanical stimuli once for each of the predefined load cases and the optimization procedure required to find their optimal combination.

Mapping-based inverse remodelling [26, 68, 235] aims to find the mapping function which relates the loading history to the bone architecture. This function is usually determined using machine learning approaches such as artificial neural networks or support vector machines. The required training set must contain known loading conditions and the respective bone architecture and is artificially generated using forward remodelling simulations. The advantage of this approach is that once the mapping function is established, predictions of loading histories are fast. However, these predictions are still specific for only a single bone and generating the training dataset represents a considerable computational effort.

Although the mapping-based approach might become valuable for fast predictions in clinical applications, e.g. in conjunction with statistical shape and appearance models [26, 234], the optimization-based approach was considered more suitable to fulfil the goals of this thesis, where joint load histories of bones with largely different shape and internal structure have to be determined. The remainder of this section will, therefore, focus on the optimization-based approach.

2.1.2.2 Optimization-based inverse bone remodelling

Theory

The theoretical foundation of optimization-based inverse remodelling was established by Fischer et al. [56] and is based on the forward remodelling algorithm presented by Beaupré et al. [9]. The theory is presented in a general way in this section to be consistent with the originally proposed algorithm as well as subsequent, modified versions (e.g. that of Christen et al. [37]).

The goal of optimization-based inverse remodelling is to find the loading history which caused a given, adapted bone architecture or density distribution (see Figure 2.4). It is assumed that the loading history consists of a finite set of n load cases L_i which are acting on the bone for m_i load cycles within an observed timeframe, e.g. within a day (see Figure 2.5).



Figure 2.5: Schematic depiction of the loading history. The loading history is decomposed into a finite number of load cases L_i which act for m_i load cycles within an observed timeframe. Each load case *i* is defined by a set of forces F_{ij} scaled by factors α_{ij} which are acting simultaneously on the bone.

Following the theory of Beaupré et al. [9], the loading history causes a cumulative stimulus ψ at location x within the bone:

$$\psi(\boldsymbol{x}) = \left(\sum_{i=1}^{n} m_i \cdot f(\mathbf{L}_i, \boldsymbol{x})^k\right)^{1/k}$$
(2.1)

where $f(\cdot)$ is a function that quantifies the local mechanical loading state for a given load case L_i at location x as a single scalar value (e.g. effective stress [56] or strain energy density [37]) and k is a calibration parameter that allows to adjust the influence of load magnitude and load cycle number.

In remodelling equilibrium, it is assumed that the local stimulus $\psi(x)$ equals the so-called stimulus attractor or equilibrium stimulus $\tilde{\psi}$ at each point x within the bone volume Ω :

$$\psi(\boldsymbol{x}) = \widetilde{\psi}, \ \forall \boldsymbol{x} \in \Omega \tag{2.2}$$

Combining Equation 2.1 with 2.2 leads to:

$$\widetilde{\psi} = \left(\sum_{i=1}^{n} m_i \cdot f(\mathbf{L}_i, \boldsymbol{x})^k\right)^{1/k}, \ \forall \boldsymbol{x} \in \Omega$$
(2.3)

Consequently, the goal of the optimization-based load estimation is to find the load cases L_i and loading cycle numbers m_i which fulfil Equation 2.3. In practice, it is convenient to represent

each load component j = 1, ..., l of load case L_i as the product of a unit load F_{ij} with a scaling factor α_{ij} (see Figure 2.5). F_{ij} is a vector which defines the direction of the load components j of load case i and the scaling factor α_{ij} scales its magnitude. This allows rewriting Equation 2.3 as follows:

$$\widetilde{\psi} = \left(\sum_{i=1}^{n} m_i \cdot f(\alpha_{i1} \boldsymbol{F}_{i1}, \dots, \alpha_{il} \boldsymbol{F}_{il}, \boldsymbol{x})^k\right)^{1/k}, \ \forall \boldsymbol{x} \in \Omega$$
(2.4)

Thus, given a set of n predefined load cases with l unit loads F_{ij} (e.g. as shown in Figure 2.5), Equation 2.4 can be solved for the unknown scaling factors α_{ij} and loading cycles m_i . However, since bone remodelling is not only influenced by functional adaptation to mechanical stimuli, but also by non-mechanical factors such as genetics, age, and hormone levels (see Section 2.1.1) it cannot be presumed that Equation 2.4 is exactly fulfilled at all locations x. Rather, it is assumed that a combination of external loading exists which minimizes the difference between the actual stimulus and the equilibrium stimulus. The inverse remodelling problem can therefore be restated as an optimization problem in the form:

$$\underset{\alpha_{ij},m_i}{\text{minimize}} \quad \int_{\Omega} \left[\widetilde{\psi} - \left(\sum_{i=1}^{n} m_i \cdot f(\alpha_{i1} F_{i1}, \dots, \alpha_{il} F_{il}, \boldsymbol{x})^k \right)^{1/k} \right]^2 \mathrm{d}\Omega$$
(2.5)

All optimization-based load estimation algorithms presented in literature are based on the above optimization problem but vary in terms of the chosen stimulus measure (e.g. effective stress or strain energy density), the chosen parameters (e.g. k) and the solution approach (e.g. the number of loading cycles m_i is often predefined and the problem is only solved for scaling factors α_{ij}).

In order to solve the optimization problem presented in Equation 2.5, it is necessary to find the distribution of local mechanical stimuli $\psi(\mathbf{x})$ within the bone. Since this stimulus is based on the local mechanical loading state, finite element (FE) analyses can be used to compute the distribution of stresses, strains or other derived quantities (e.g. strain energy density) for each load case L_i . The FE method is a general numerical method to find approximate discrete solutions for problems in engineering and physics and is described in detail elsewhere (e.g. see Oden [142] or Bathe [8]). In brief, the whole domain (here: the whole bone) is subdivided into a finite number of small elements to generate a so-called mesh and material properties are assigned to each element. Boundary conditions, i.e. constraints and forces, are then imposed onto the mesh and the local loading state can be computed within each element. Various strategies to model the geometry and material properties of bone have been investigated in detail in the past [24, 88] and allow to obtain accurate predictions of the load distributions.

Application at the continuum level

Fischer et al. [56] were the first to introduce optimization-based inverse remodelling and used 2D continuum-level FE models to obtain mechanical stimuli distributions required to solve the optimization problem presented in Equation 2.5. Continuum-level FE models use coarse meshes with elements that enclose a larger region of bone (element sizes in the millimetre range; see Figure 2.6) and use material models which account for the underlying bone structure in a simplified way. For instance, Fischer et al. defined the elastic moduli of each element depending on the local bone density. Using these continuum-level FE models, a discrete approximation for the volume integral of Equation 2.5 can be found:

$$\underset{\alpha_{ij},m_i}{\text{minimize}} \quad \sum_{\boldsymbol{x}\in\mathcal{X}} \left[\widetilde{\psi} - \left(\sum_{i=1}^n m_i \cdot f(\alpha_{i1}\boldsymbol{F}_{i1},\ldots,\alpha_{il}\boldsymbol{F}_{il},\boldsymbol{x})^k \right)^{1/k} \right]^2$$
(2.6)

In the above equation, \mathcal{X} is the discrete set of points x, defined either at the integration points [56] or nodes [57] of all elements. Element volumes are assumed to be equal and therefore considered irrelevant to the optimization problem.



Figure 2.6: Schematic comparison of continuum-level (left) and tissue-level (right) approaches to quantify the local mechanical loading. At the continuum level, the trabecular bone structure is only quantified by the local bone density ρ within a representative volume element and the mechanical stimulus of this element is denoted by ψ_c . At the tissue level, the trabecular bone architecture is fully resolved and the mechanical stimulus ψ can be directly quantified for the bone tissue.

Fischer et al. [56] defined the equilibrium stimulus $\tilde{\psi}$ in terms of effective stress [9]. This value is defined at the bone tissue level, i.e. within trabeculae or cortical bone (see Figure 2.6). In order to use the results of the continuum-level FE models, it is necessary to relate the continuum-level stimulus ψ_c to the tissue-level stimulus ψ . Based on the assumption that the local bone strength is proportional to the squared bone density (ρ), Fischer et al. [56] proposed the following relation between the continuum- and tissue-level stimulus:

$$\psi_{\rm c} = \psi \left(\frac{\rho}{\rho_{\rm max}}\right)^2 \Leftrightarrow \psi = \psi_{\rm c} \left(\frac{\rho_{\rm max}}{\rho}\right)^2$$
(2.7)

where ρ_{max} is the maximum bone density and defined based on values in literature. Combining Equations 2.6 and 2.7 and defining $f(\cdot)$ as the continuum-level effective stress $\hat{\sigma}_{c}(\cdot)$ leads to:

$$\underset{\alpha_{ij},m_i}{\text{minimize}} \quad \sum_{\boldsymbol{x}\in\mathcal{X}} \left[\tilde{\sigma} - \left(\sum_{i=1}^n m_i \cdot \hat{\sigma}_{c}(\alpha_{i1}\boldsymbol{F}_{i1},\ldots,\alpha_{il}\boldsymbol{F}_{il},\boldsymbol{x})^k \right)^{1/k} \left(\frac{\rho_{\max}}{\rho} \right)^2 \right]^2$$
(2.8)

In order to evaluate $\hat{\sigma}_{c}(\cdot)$, Fischer et al. [56] used linear elastic 2D continuum FE models with density based material properties. Since the model is linear, it is not necessary to solve the FE model for each evaluation of Equation 2.8. Instead, the effective stress for each load case *i* can be obtained by solving the model once for each unit load F_{ij} and subsequent scaling and superposition.

If only one unit load is acting during each load case, i.e. l = 1, Equation 2.8 can be rewritten compactly as:

$$\underset{\alpha_{i},m_{i}}{\text{minimize}} \quad \sum_{\boldsymbol{x}\in\mathcal{X}} \left[\widetilde{\sigma} - \left(\sum_{i=1}^{n} m_{i} \cdot (\alpha_{i} \cdot \hat{\sigma}_{c,i}(\boldsymbol{x}))^{k} \right)^{1/k} \left(\frac{\rho_{\max}}{\rho} \right)^{2} \right]^{2}$$
(2.9)

However, note that simultaneously acting forces (i.e. if l > 1) require the evaluation and superposition of the full stress tensor since in general [57, 59]:

$$\hat{\sigma}_{c}(\alpha_{i1}\boldsymbol{F}_{i1},\alpha_{i2}\boldsymbol{F}_{i2},\boldsymbol{x}) \neq \alpha_{i1} \cdot \hat{\sigma}_{c}(\boldsymbol{F}_{i1},\boldsymbol{x}) + \alpha_{i2} \cdot \hat{\sigma}_{c}(\boldsymbol{F}_{i2},\boldsymbol{x})$$
(2.10)

Overall, the continuum-level approach for inverse remodelling is computationally efficient and relies on a small number of parameters which are available in literature (e.g. from Carter et al. [29] and Beaupré et al. [9]). Fischer et al. verified the method using forward remodelling algorithms on generic shapes [56] and also found realistic results for whole proximal femora [57]. Using multiple forces applied to individual nodes of the mesh rather than fixed load distributions, it was even possible to reconstruct the bicentric load distribution typically observed on the head of the proximal femur [59]. Bona et al. [18, 19] extended the definition of the load cases and implemented a contact model to ensure more realistic bone loading and more direct functional interpretations. Bona et al. [17, 18] also applied this method to proximal femora of non-human species such as chimpanzees, gorilla, and grizzly, but interspecific comparisons were limited by the low sample size (only one sample of each species was used). To the best knowledge of

the author, no study has yet investigated the performance of the optimization-based inverse remodelling at the continuum-level using 3D FE models.

Application at the tissue level

Christen et al. [37] were the first to adapt the above presented methodology and successfully apply it to 3D FE models of bone biopsies [39], bone sections [38, 42], and even whole bones [41]. Christen et al. introduced the following main changes compared to the original algorithm of Fischer et al. [56]:

- (1) Micro-FE instead of continuum-level FE models were used
- (2) Local mechanical stimuli were expressed as mean instead of cumulative quantities
- (3) Strain energy density (SED) instead of effective stress was used to quantify the stimulus

In contrast to continuum-level models, micro-FE models utilize much finer meshes with element side lengths as small as 20-80 μ m [216]. The fine resolution ensures that all features of the bone, such as trabecular architecture or cortical thickness, are resolved in sufficient accuracy. This also eliminates the need for conversion between continuum- and tissue-level mechanical stimulus (Equation 2.7), since the local mechanical loading state is directly available at the tissue level.

Using the above listed changes, assuming that only sequential load cases are considered (i.e. l = 1), and setting k = 1 yields the following simple optimization problem based on Equation 2.9:

$$\underset{\alpha_{i},m_{i}}{\text{minimize}} \quad \sum_{\boldsymbol{x}\in\mathcal{X}} \left[\widetilde{U} - \left(\sum_{i=1}^{n} \frac{m_{i}}{m_{\text{tot}}} \cdot \alpha_{i}^{2} \cdot U(\boldsymbol{F}_{i}, \boldsymbol{x}) \right) \right]^{2}$$
(2.11)

In the above equation, $U(\cdot)$ is the tissue-level SED evaluated at the element centroids, \tilde{U} is the tissue-level equilibrium stimulus, $m_i/m_{\rm tot}$ is the relative number of load cycles of load case i, and α_i is the load magnitude scaling factor. α_i is squared since the SED scales quadratically with the imposed load magnitude. The optimization problem can be further simplified by introducing $s_i = m_i/m_{\rm tot} \cdot \alpha_i^2$ as a combined scaling factor:

minimize
$$\sum_{\boldsymbol{x}\in\mathcal{X}} \left[\widetilde{U} - \left(\sum_{i=1}^{n} s_i \cdot U(\boldsymbol{F}_i, \boldsymbol{x}) \right) \right]^2$$
 (2.12)

A solution to the above optimization problem can be obtained after solving micro-FE models and evaluating element specific SEDs once for each load case i. In these FE models, the bone material is be assumed to be homogeneous and linear elastic with a constant tissue elastic modulus and Poisson's ratio. The simplified optimization problem (Equation 2.12) can be solved to find the scaling factors s_i using highly efficient least-squares methods [113]. Since the algorithm cannot distinguish between frequently applied, low magnitude loading and infrequently applied, large magnitude loading, assumptions of either the number load cycles m_i or the load magnitude scaling factor α_i have to be made. Using these assumptions, the missing quantity can be computed from s_i as follows:

$$\alpha_i = \sqrt{\frac{m_{\text{tot}}}{m_i} \cdot s_i} \iff m_i = \frac{s_i}{\alpha_i^2} \cdot m_{\text{tot}}$$
(2.13)

The tissue-level approach of optimization-based inverse remodelling was first developed and validated using in vivo experiments conducted on mice vertebrae [37]. In these experiments, large uniaxial loading was imposed on the vertebral bones of one group, whereas no loading was applied to the bones of the control group. The inverse remodelling algorithm successfully identified the differences between loaded and unloaded groups and also correctly quantified the experimentally applied load magnitudes. Additionally, a verification of the algorithm was provided using forward remodelling simulations on bone biopsies (i.e. small bone cubes) [39]. More recently, the algorithm was tested by predicting section forces of human distal radius slices [42]. It was shown that the predicted results are reproducible, sensitive enough to differentiate between groups of low- and high-bone density, and robust with respect to the mesh resolution as long as the element size remains below 80 μ m. Only in one preliminary study Christen et al. attempted to predict actual joint loads of whole proximal femora [41]. Hip joint loads were predicted for both human and non-human mammals and showed that the algorithm might be sensitive enough to distinguish between bipedal and quadrupedal locomotion. However, these inferences were limited by the small sample size, again as small as a single specimen of each species.

2.1.2.3 Conclusions

A review of the literature showed that there are two different approaches to solve the inverse remodelling problem, namely the optimization-based and the mapping-based methods. The optimization-based method appeared to be more suitable to address the goals of this thesis as it is computationally more efficient if used for bones of multiple different shapes (here: bones of different species) and relies on a smaller number of parameters. Albeit the estimations of loading histories neglect many relevant factors of bone functional adaptation (e.g. loading rate, rest, and non-mechanical factors; see Section 2.1.1), the results of both continuum- and tissue-level inverse remodelling reported in the current literature are promising. Predictions of dominant hip joint loads using 2D continuum-level FE models were plausible, and applications

of 3D tissue-level FE models showed results in good agreement with in vivo data using simplified load cases (e.g. section forces). The performance of the inverse remodelling algorithm using more complex load cases (e.g. joint loads) and its potential to detect more subtle differences of bone loads engendered from habitual activities remains to be investigated.

2.2 Implementation and testing: Robustness and plausibility check

2.2.1 Introduction

In order to to investigate the possibility of predicting whole bones loads from bone architecture (subgoal 1 of this thesis, see Figure 2.1), an inverse remodelling algorithm as described in Section 2.1.2 needs to be implemented and tested prior to its application to metacarpal bones.

As described in the background section (Section 2.1.1), bone adapts to habitual external loading in a highly sensitive manner, which warrants functional interpretations of bone architecture. A review of inverse remodelling algorithms (Section 2.1.2) showed that optimization-based inverse remodelling provides an efficient and simple framework to estimate loading histories based on bone architecture. However, the review also revealed that the prediction of whole bone loading in 3D was so far limited to either simple load cases [37] or low sample sizes [41]. Investigations of parameter sensitivity were restricted to the mesh size dependency [42], while the influence of other parameters associated with high uncertainty such as bone material properties [132], remodelling equilibrium stimulus [140], or pressure distribution at the joint [18, 56, 59] has not yet been assessed. Finally, experimental validation has so far been limited to comparing the peak load magnitude of a single human proximal femur [41] to hip joint loads measured in vivo [12].

The goals of this study were to fill these gaps by (1) conducting a systematic investigation of the parameter sensitivity of the joint load predictions on one human proximal femur and (2) assessing the plausibility of the results by comparing the predicted joint load vectors (i.e. magnitude and direction) of ten proximal femora to hip joint loads measured in vivo. Specifically femoral bones and hip joint loads were chosen for this study since in vivo loading data are readily available in literature (e.g. from Bergmann et al. [14]; see also www.orthoload.com).

2.2.2 Materials and methods

2.2.2.1 Study outline

The study comprised two parts, a sensitivity study as well as a plausibility analysis (Figure 2.7). Predictions of the joint loading histories were performed following the algorithm of Christen et al. [37] using micro-FE models generated from high-resolution CT scans of human proximal femora. One proximal femur was used to investigate parameter sensitivity by predicting peak and mean joint load vectors and comparing them between a reference model and several parameter-varied models (Figure 2.7, left). The plausibility of the algorithm was assessed by comparing predicted peak joint load vectors and load direction ranges of ten femora with in vivo hip joint loads of ten subjects reported by Bergmann et al. [14] (Figure 2.7, right).



Figure 2.7: Graphical abstract of this study with two parts: (1) one specimen was selected and predicted peak and mean joint load vectors were compared between a reference model and parameter-varied models, and (2) plausibility was assessed by comparing peak joint load vectors and ranges predicted using the inverse remodelling algorithm with in vivo resultant hip joint forces reported by Bergmann et al. [14] (OrthoLoad data, www.orthoload.com).

2.2.2.2 Joint load prediction

Image processing

Ten human proximal femora (age: 81.9 ± 8.7 years; left/right: 7/3) were collected under permission of the german law "Gesetz über das Leichen-, Bestattungs- und Friedhofswesen des Landes Schleswig-Holstein - Abschnitt II, §9 (Leichenöffnung, anatomisch)" from 04.02.2005 at the Anatomy Institute of the Lübeck University. They were cut to approximately 160 mm length and scanned with an isotropic resolution of 30.3 μ m using a high resolution peripheral quantitative CT scanner (XtremeCT2, Scanco Medical AG, Brüttisellen, Switzerland; energy: 68 kVp; intensity: 1470 μ A). The 3D images were resampled by a factor of two (voxel size 60.6 μ m) to reduce computational effort without compromising the results of the load prediction [42]. A coordinate system was defined in each femur which was aimed to be consistent with the "implant coordinate system" used to measure joint loads with instrumented prostheses [14] (Figure 2.8). The origin of the coordinate system was located in the centre of the femoral head, defined as the centre of the best-fitting sphere. The vertical axis of this coordinate system was parallel to the shaft axis of the bone, which was defined by fitting a straight line to the shaft centroids of a 40 mm long section at the distal end of the bone. The anterior-posterior axis was defined as perpendicular to both the vertical and the neck axis. The neck axis was determined by the line connecting the femoral head centre and the midpoint of the femoral neck where the cross sectional area is smallest [209]. Finally, the medio-lateral axis was defined as perpendicular to both the vertical and the anterior-posterior axes.

The resampled CT scans of all femora were rotated into the new coordinate system and cropped by bounding boxes extending 1.5 times the femoral head radius in both lateral and distal directions. This size was chosen to reduce computational effort while still covering regions of dominant stresses and strains resulting from hip joint loading [47]. All images were filtered using a Gaussian filter (support: 2 voxels; $\sigma = 1.6$) to reduce image noise and segmented using a fixed threshold with a constant value for all specimens (greyvalue: 3000). The threshold was chosen manually after visual inspection of both the image histograms and segmentation results. Finally, a spherical layer of elastic material mimicking cartilage was added to all specimens to facilitate the load application on the FE models. The selected thickness of this layer (2.2 mm) was kept as small as possible but large enough to ensure that no bone material penetrated through its surface.

A representative specimen after image processing is displayed in Figure 2.8. All image processing steps were performed using medtool 4.0 (Dr. Pahr Ingenieurs e.U., Pfaffstätten, Austria) and additional custom Python scripts.



Figure 2.8: Definition of the specimen specific coordinate systems and bounding boxes in anterior (left) and superior (right) views. R is the specimen-specific femoral head radius, C_{Neck} is the midpoint of the femoral neck with smallest cross section, and C_{Head} is the centre of the femoral head.

FE modelling

To apply the inverse remodelling algorithm of Christen et al. [37], mechanical stimuli need to be evaluated from FE models representing different unit load cases. For this purpose, voxel-based FE models (element size 60.6 μ m) with four different sets of boundary conditions were generated (Figure 2.9). Nodes at the lateral and distal boundary were always fully constrained and distributed loads were applied for load cases L₁ to L₄ with resultant forces inclined by -20, 20, 60, and 100 °, respectively. The number of load cases was limited to four to avoid problems associated with overlapping load areas (for further explanation, see results and discussion section of the parameter sensitivity analysis in Sections 2.2.3.2 and 2.2.4) while still covering a meaningful range of force directions in the frontal plane. It was assumed that the load distribution is uniform and that all nodal force vectors act normal to the joint surface. The shape of the load area was defined by the intersection of the spherical joint surface and a cone with an opening angle of 40 °, resulting in an area of 224.24±23.44 mm² for all specimens. The resultant force magnitude of each load case was set to 1000 N.

Linear elastic, isotropic material was assumed for both the bone material and the cartilage layer. Material properties were defined following the study of Christen et al. [37] where load predictions were in good agreement with in vivo loads in whole mice vertebrae: Elastic moduli were set to 10 GPa for bone and 10 MPa for cartilage and the Poisson's ratios were set to 0.3.



Figure 2.9: Micro-FE models with different sets of boundary conditions representing the four unit load cases $(L_1 \text{ to } L_4)$ with resultant force vectors F_1 to F_4 used in the joint load prediction algorithm. All resultant force vectors were within a single plane (frontal plane). Coloured regions indicate the size of the load area and the direction of nodal force vectors. Open triangles indicate constrained surfaces.

The final micro-FE models had 473.0 ± 69.2 million degrees of freedom and were solved using the parallel octree solver ParOSol [60]. The typical computational time for each load case was 10 hours (wall-clock time) using 26 CPUs (Intel Xeon E5-2697 at 2.6 GHz).

Inverse remodelling algorithm

The joint load prediction was performed using the micro-FE-based inverse remodelling algorithm presented by Christen et al. [37] (see Figure 2.10 for a graphical overview). Although details were presented in Section 2.1.2, the algorithm will be briefly summarized again and the parameters used will be highlighted.

The underlying assumption of the algorithm is that the observed bone structure is the result of a simple remodelling law: Bone is either added or resorbed unless the local mechanical stimulus equals a certain remodelling equilibrium stimulus. Consequently, the most probable bone loading history is the one most closely leading to remodelling equilibrium within the whole bone.

The loading history is represented by a finite number of n unit load cases, which are assumed to act with a magnitude α_i for m_i load cycles within an observed timeframe. The local mechanical stimulus $U(\mathbf{x})$ at location \mathbf{x} within the bone is then computed by summarizing the SEDs $U_i(\mathbf{x})$ resulting from unit load cases 1 to n, weighed by their relative number of load cycles m_i/m_{tot} and magnitude α_i :

$$U(\boldsymbol{x}) = \sum_{i=1}^{n} \frac{m_i}{m_{\text{tot}}} \cdot \alpha_i^2 \cdot U_i(\boldsymbol{x})$$
(2.14)
Introducing the combined scaling factor $s_i = \alpha_i^2 \cdot m_i/m_{tot}$ allows to find the most probable loading history by solving a simple optimization problem which minimizes the difference between the local mechanical stimulus $U(\mathbf{x})$ and the remodelling equilibrium stimulus \tilde{U} at all locations \mathbf{x} within the bone:

minimize
$$\sum_{\boldsymbol{x}\in\mathcal{X}} \left[\widetilde{U} - \left(\sum_{i=1}^{n} s_i \cdot U_i(\boldsymbol{x}) \right) \right]^2$$
 (2.15)

Solving Equation 2.15 for the optimal scaling factors s_i and assuming a constant number of load cycles for all n unit load cases [37], the load magnitude α_i can be computed as follows:

$$\alpha_i = \sqrt{n \cdot s_i} \tag{2.16}$$

In this study, the optimization problem presented in Equation 2.15 was solved in Python using the non-negative least squares algorithm of SciPy [95]. The remodelling equilibrium stimulus \tilde{U} was set to 0.02 MPa as estimated by Mullender et al. [140] and used in previous studies [37, 41, 42]. Finally, joint load vectors were computed by multiplying the resultant force F_i of each unit load case i with the corresponding load magnitude scaling factor α_i (see Figure 2.10).



Figure 2.10: Graphical explanation of the inverse remodelling algorithm following Christen et al. [37] using one representative specimen of this study. SED distributions from four unit load cases L_1 to L_4 are combined and optimally scaled by factors α_1 to α_4 such that the difference to a remodelling equilibrium SED (typically 0.02 MPa) is minimized. White arrows indicate the scaled resultant force associated with each of the four unit load cases. The cartilage layer is not displayed. SED: strain energy density

The quality of the load prediction was quantified by comparing tissue loading homogeneity before and after optimization of the load scaling factors. Tissue loading inhomogeneity was quantified by the coefficient of variation (CoV) of the distribution of the mechanical stimuli U(x) [37] (see Equation 2.14). A Wilcoxon Signed-Rank Test was applied to verify whether the CoV was significantly reduced after optimization. This robust statistical test was chosen to reduce the effect of outliers.

2.2.2.3 Parameter sensitivity of the predictions

Parameter sensitivity of the joint load predictions was analysed by comparing the results of one specimen with a set of reference parameters (as described in Section 2.2.2.2) to those obtained after variation. In total, nine parameters with two variations each were investigated as listed in Table 2.1 and explained below. Variations of each parameter were tested separately, while keeping all other parameters constant (i.e. they were set to the reference value).

Image processing parameters

Previous studies have shown that image segmentation thresholds can affect morphometric measurements and mechanical properties evaluated with micro-CT and -FE methods [34, 76]. Thus, the influence of image segmentation was investigated by increasing ("variation 1") or reducing

Parameter	lcon	Reference	Variation 1	Variation 2
Image segmentation threshold		3000	3300	2700
Load area		215.1 mm^2	121.5 mm^2	54.2 mm^2
Nodal force distribution / alignment		Uniform / surface normal vectors	Uniform / parallel vectors	Ellipsoidal / parallel vectors
Bone elastic modulus		10 GPa	5 GPa	20 GPa
Cartilage elastic modulus		10 MPa	100 MPa	1000 MPa
Number of unit loads		4	7	13
Unit load location		0 °	-10 $^{\circ}$ rotation	$+10~^\circ$ rotation
Region of interest		Full model	5 mm reduction	10 mm reduction
Equilibrium stimulus		0.02 MPa	0.01 MPa	0.04 MPa

Table 2.1: Overview of the reference and varied parameters used in the parameter sensitivity analysis. The colours blue, green, and orange of the icons refer to the reference value, variation 1, and variation 2, respectively.

("variation 2") the threshold greyvalue separating bone from the background. The sensitivity of load predictions to image resolution was addressed in a previous study [42] and therefore is not tested here.

FE model parameters

Variations in the boundary conditions were investigated by changing the load area size as well as the distribution and alignment of nodal force vectors. In contrast to the reference configuration, nodal force vectors were considered to be parallel and uniformly distributed ("variation 1") or distributed following an ellipsoidal (Hertzian) pressure distribution ("variation 2")(Table 2.1). In all cases, the resultant force magnitude was set to 1000 N. Material properties of bone were varied to account for the large range of reported elastic moduli reported in literature ranging from 1 to 25 GPa [132, 240]. Additionally, the cartilage layer material was varied from soft ("variation 1") to very stiff ("variation 2") (Table 2.1).

Inverse remodelling algorithm parameters

The algorithm's robustness was investigated by increasing the number of unit loads, shifting the location where unit loads were applied, reducing the size of the region of interest (ROI) of the SEDs included in the optimization, and varying the remodelling equilibrium stimulus, as shown in Table 2.1. The number of unit loads was increased by generating and solving additional FE models with loading applied in regular intervals between -20 ° and 100 ° inclination. Unit load location was varied by solving additional FE models with unit load resultant forces rotated ± 10 ° around the anterior-posterior axis (for a definition of the anatomical axes see Figure 2.8 and 2.9). The ROI size was reduced by 5 and 10 mm at the lateral and distal boundary with respect to the original model dimensions. Finally, the remodelling equilibrium stimulus was varied from 0.01 to 0.04 MPa as the commonly used value of 0.02 MPa is known to be only a rough estimation [140].

Output variables

Peak and mean vectors of the joint load predictions were evaluated for the parameter sensitivity analysis. Mean vectors were defined as the sum of the scaled resultant force vectors of each load case divided by the number of load cases. Mean vectors were used as an output variable to quantify differences in the load predictions, irrespective of changes in the number and/or location of unit loads. Additionally, the optimally scaled resultant forces ($\alpha_i F_i$; see Figure 2.10) were compared qualitatively.

2.2.2.4 Plausibility of the predictions

The plausibility of the joint load prediction results was assessed by comparing load prediction results from all ten femora (with reference parameters as shown in Table 2.1) with the in vivo resultant hip joint forces previously presented by Bergmann et al. [14] (accessed from www.orthoload.com; dataset "Standard Loads Hip Joint"). Data selection and processing are desribed in the following sections.

OrthoLoad data selection and processing

In the study of Bergmann et al. [14], hip joint forces were reported for ten human subjects (age: 56.9 ± 5.5 years; weight: 88.7 ± 13.1 kg) during the most common activities of daily living [139]. Load data from the following activities were used for this study: walking at a self-determined speed, stair climb and descend without handrail, standing up, sitting down, and one legged stance. The measured forces were transformed from the "femur coordinate system" into the "implant coordinate system" [14] for comparison with the load predictions. Subject-specific peak loads were defined as the forces with largest magnitude throughout the full loading cycles of all activities. The range of force directions was evaluated by computing the maximum and minimum inclination angle with respect to the vertical axis in the frontal plane based on all resultant forces (considering full load cycles, all subjects, and all activities).

Output variables

Subject-specific in vivo peak loads were compared to the peak load vectors obtained from the load prediction. Peak load directions were quantitatively compared based on the angles of the force vectors with respect to the vertical axis in the frontal plane. Additionally, the range of force directions predicted by the FE models was compared to the full range of force directions measured in vivo.

2.2.3 Results

2.2.3.1 Joint load prediction results

Tissue loading inhomogeneity (CoV) was significantly reduced (p = 0.005) using the optimized load scaling factors α_i (Table 2.2). Furthermore, the CoV standard deviation was also considerably lower after optimization.

Specimen	α1 (-)	α_2 (-)	α ₃ (-)	α4 (-)	CoV_{init} (%)	CoV_{opt} (%)
1	1.25	3.32	1.39	0.65	203.83	137.55
2	1.02	2.47	0.12	0.97	403.04	146.89
3	0.97	3.92	0.22	0.08	1515.66	135.75
4	0.45	3.61	1.09	0.53	226.13	135.88
5	1.21	3.60	0.23	0.55	441.30	128.81
6	1.34	3.86	0.93	0.72	213.06	132.03
7	0.50	4.18	0.28	0.97	430.77	155.68
8	1.12	2.35	0.96	0.20	425.26	129.13
9	0.14	3.25	0.25	0.29	629.30	151.00
10	0.79	3.17	1.18	0.83	188.30	140.20
Mean	0.88	3.37	0.66	0.58	467.67	139.29
SD	0.40	0.60	0.49	0.31	394.86	9.17

Table 2.2: Load magnitude scaling factors α_i after optimization and the coefficient of variation (CoV) quantifying tissue loading inhomogeneity. The CoV was reduced significantly (p < 0.05) between uniformly (CoV_{init}) and optimally (CoV_{opt}) scaled unit loads. SD: standard deviation

2.2.3.2 Parameter sensitivity of the predictions

Overall, a single peak of the joint loads was predicted at roughly 20 $^{\circ}$ inclination with respect to the vertical axis of the femur and load magnitudes decreased towards the boundaries of the articular surface (Figure 2.11). This pattern was robust against variations of parameters except for changes in the number of unit loads. More than four unit loads caused fluctuations in the predictions without further considerably reducing the remaining tissue loading inhomogeneity (CoV=137.5 and 134.5 % for 4 and 13 unit loads, respectively).

The predicted peak joint load vector in the reference specimen was inclined by 20 $^{\circ}$ and had a magnitude of 3316 N. Directions of peak joint load vectors were robust against all parameter variations except for changes in the unit load location (range of differences: -10 to +10 $^{\circ}$). In contrast, the magnitudes of the predicted peak loads were more sensitive to variation in parameters, particularly changes to the load area size, segmentation threshold, bone elastic modulus, and equilibrium stimulus (range of differences: -971.2 to +1373.5 N). Changes to cartilage elasticity, number of unit loads, ROI size, unit load location, and load distribution had a lower effect on the predicted peak joint load magnitude (range of differences: -484.6 to 529.1 N).

The mean joint load vector in the reference specimen was inclined by 27.6 ° with a magnitude of 1373.3 N. Directions of mean joint load vectors were even less sensitive to parameter variations



Figure 2.11: Results of the parameter sensitivity study. Load predictions of one specimen with reference parameters (blue) were compared to the results after two parameter variations (green, orange). Squares and stars indicate peak and mean joint load vectors, respectively. The faint lines connect the predicted load magnitudes of each unit load case.

(range of differences: -6.5 to +6.6 °) than the direction of peak joint load. In contrast, magnitudes of mean forces were sensitive to changes in the parameters (range of differences: -404.7 to +568.9 N).

2.2.3.3 Plausibility of the predictions

Figure 2.12 shows the results of the load prediction for all ten femora (red) and the in vivo hip joint loads of ten subjects (green) from Bergmann et al. [14] in the frontal plane. The predicted peak joint loads of all femora were in good agreement with the subject-specific peak resultant hip joint forces measured in vivo. Predicted peak load directions of 20 ° were within one standard deviation of the in vivo data ($18.2\pm2.0^{\circ}$). However, predicted magnitudes of 3372.2 ± 597.9 N exceeded those measured in vivo (2707.6 ± 443.3 N).

The in vivo range of resultant force vectors was confined to inclinations of 3.7 to 66.6 $^\circ$ with respect to the vertical axis of the femur. In contrast, resultant forces predicted with the inverse remodelling algorithm ranged from -20 to 100 $^\circ$ (i.e. scaling factors of all load cases were non-zero).



Figure 2.12: Comparison of hip joint load predictions (red) with in vivo data (green) measured by instrumented prostheses (from Bergmann et al. [14]) in the frontal plane. SD: standard deviation

2.2.4 Discussion

The goal of this study was to investigate the parameter sensitivity and plausibility of joint load predictions obtained with an optimization-based inverse remodelling algorithm. A comparison with in vivo loading data of the hip joint showed that peak load predictions were plausible in terms of both load magnitude and direction. However, particularly the *magnitudes* of the load predictions have to be interpreted with caution considering their sensitivity to parameters associated with high uncertainty such as bone material properties and remodelling equilibrium stimulus.

The results of the parameter sensitivity analysis highlight many important factors to be considered when utilizing and interpreting load predictions using the inverse remodelling algorithm introduced by Christen et al. [37]. First, the number of applied unit load cases was found to strongly influence the general pattern of predicted load scaling factors without considerably affecting the remaining tissue loading inhomogeneity (see Figure 2.11, top right panel). This indicates the non-uniqueness of the solution when the loading areas of unit loads overlap and could also explain the large fluctuations of load scaling factors observed in earlier studies [41]. Second, the predicted load magnitudes were considerably affected by parameters with high uncertainty and/or variability such as bone material properties, remodelling equilibrium stimulus, and area of load application; leading to variations of more than 800 N of the predicted peak loads with the herein tested parameter range. The equilibrium stimulus in particular is still not accurately defined and might lie in a range as large as 0.001 to 0.068 MPa [132, 140]. This uncertainty dramatically affects the predicted load magnitudes, as just a variation of the equilibrium stimulus from 0.01 to 0.04 MPa in this study already elicited a 2000 N change in the predicted load magnitudes. Although the load magnitude might be biased by the selection of bone material properties and equilibrium stimulus, predicted *directions* of both peak and mean vectors were insensitive to variations in these parameters. Also, other potential sources of influence such as the cartilage elasticity, the ROI size, and load distribution were shown to have a limited effect on both the load directions and magnitudes. Overall, the results of this study suggest that the load predictions are potentially robust enough to compare dominant joint loads between different bones using the same set of parameters, and that predicted load directions are robust even if parameters vary. However, absolute values of load magnitudes should be interpreted with caution until validated parameters are available.

The comparison of joint load predictions of the full sample with the in vivo hip joint load data [14] showed that predicted peak loads were plausible both in terms of their direction and magnitude. However, large joint loads (> 500 N) were also predicted in directions outside the range of in vivo values. This might be explained by two factors: First, the joint load prediction

presumes that bone structure is solely the result of a mechanical stimulus. In reality, bone architecture is also influenced by other factors such as genetics [130], calcium homeostasis [25], and hormone levels [162] as explained in detail in Section 2.1.1. Second, the large range of joint loads might be an artefact resulting from the assumption of a simple uniform pressure distribution. The actual pressure distribution was reported to be horse-shoe-shaped due to joint incongruity [3, 222] and could trigger bone formation also in locations close to the boundary of the articular surface while the resultant force directions would still be in line with the in vivo loading data [18, 59].

Several limitations of this study remain to be mentioned. First, load predictions were performed on specimens obtained from elderly donors (age: 80.5 ± 7.6 years). Changes of bone structure and particularly bone density with age are well-documented [11, 133] and might influence the results. However, it was expected that the bones in this study sample were still adapted to loads from activities with moderate intensity such as level walking or stair climbing. Second, loading conditions were highly simplified. The assumption of circular load areas with static size and uniform load distributions are likely not perfectly physiological [18, 59, 222]. More complex shapes of the load areas and pressure distributions or even inclusion of articular contact [18] might improve the results but exceeded the scope of this study. Third, only four unit load cases were used to compare micro-FE based predictions to in vivo joint loads. The number of unit loads and size of the loading areas were chosen to allow identifying the plausibility of peak loads as accurate as possible without introducing load scaling fluctuations due to overlapping loading areas (as described above and shown in Figure 2.11). Additional load cases at the posterior and anterior side of the joint could have been added without overlap, but would have further increased the already large computational effort of approximately 40 hours wall-clock time for each specimen/parameter variation. Fourth, the in vivo data used in this study was collected in patients with instrumented prostheses. The hip replacement itself might lead to differences of the joint loads when compared to healthy subjects [191, 228]. Additionally, although an effort was made to mimic the "implant coordinate system" of Bergmann et al. [14] as good as possible based on the proximal femur geometry, deviations of the coordinate systems might exist and influence the results. Finally, the inverse remodelling algorithm of Christen et al. [37] is based on a highly simplified bone remodelling theory. Although there is evidence that bone formation and resorption are generally related to the magnitude of local mechanical loading [40], many other aspects relevant to bone remodelling as outlined in Section 2.1.1, such as the loading rate [224], rest periods [159], and the potential site dependency of the equilibrium remodelling stimulus [187] are not included in the inverse remodelling algorithm and their influence requires further investigation.

2.2.5 Conclusions

Overall, the results of this study suggest that joint load predictions obtained from inverse remodelling deliver plausible estimates of the most dominant loading experienced by a given bone structure. Load predictions are potentially robust enough to perform inter-subject or inter-species comparisons of joint loads, but absolute load magnitudes should be interpreted with caution considering both parameter sensitivity and many limitations inherent to the inverse remodelling algorithm.

2.2.6 Related publications and declaration of contributions

Section 2.2 is based on the publication "Plausibility and parameter sensitivity of joint load predictions at the proximal femur", *published* 2018 in the journal "Biomechanics and Modelling in Mechanobiology" and co-authored by Dieter H. Pahr (doi.org/10.1007/s10237-017-0996-1).

Author contributions: The first author and author of this thesis, *Alexander Synek*, designed the study and performed all parts described in the methods section except for the scanning of the specimens, which was kindly performed by Gianluca lori as acknowledged below. *Dieter H. Pahr*, the supervisor of this thesis, supervised the work and contributed to both study design and proofreading the manuscript.

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2.3 Application: Prediction of MCP joint loads

2.3.1 Introduction

In order to test whether activity-related differences can be predicted from bone architecture (subgoal 1 of this thesis, see Figure 2.1), the inverse remodelling algorithm presented in the previous section will be applied to metacarpal bones of humans and non-human primate species.

As shown in the previous section (Section 2.2), the inverse remodelling algorithm following Christen et al. [37] provides plausible estimates of joint loads which are likely sufficiently robust for interspecific comparisons as long as a consistent set of parameters is used. However, it was

also found that the directional accuracy of the joint load predictions, as defined by the number of unit loads, is strongly limited by fluctuations introduced by load cases with overlapping load areas (see Section 2.2.3.2 and specifically Figure 2.11). This limitation of accuracy might hamper the identification of activity-related differences from bone architecture. Previously presented studies using either the continuum- or tissue-level approach of inverse remodelling found qualitative differences in the predicted hip joint loads of varus and valgus patients [58] as well as mammalian species with distinct locomotor modes [18, 41] but were limited to sample sizes as small as a single specimen for each group. Given the coarse nature of the predictions and the lack of variability within the samples tested thus far, it is still unclear whether the inverse remodelling algorithm is sufficiently sensitive to detect activity-related differences of loading histories.

The goal of this study was to apply the inverse remodelling algorithm on a larger sample of metacarpal bones of humans and closely related primates (bonobo, chimpanzee, gorilla, orangutan) and investigate differences of bone loading related to distinct types of activities. More specifically, the MCP joint loading histories were predicted in order to find differences related to three distinct categories of primary hand use, namely: (1) manipulation/tool use, (2) climbing/suspension, and (3) knuckle-walking. Metacarpal bones were chosen due to previously reported evidence for hand use-related differences of bone architecture [7, 35, 201, 239]. In case differences can be detected, it was hypothesized that: (H1) predicted joint load directions correlate with the expected primary hand postures, and (H2) that predicted joint loads are larger when the hand is used for locomotion when compared to manipulation or tool use.

2.3.2 Materials and methods

2.3.2.1 Study outline

Third metacarpal bones of five primate species with different primary hand use were micro-CT scanned and the most probable MCP joint loading histories were computed using the micro-FE-based inverse remodelling algorithm previously presented by Christen et al. [37] and implemented as explained in Section 2.2 (Figure 2.13). The sample was divided into three groups based on the most frequent hand use behaviours: (1) manipulation and tool use (humans), (2) climbing and suspension (orangutans; see [27, 200]), and (3) knuckle-walking (bonobos, chimpanzees, gorillas; see [54, 207]). Primarily flexed MCP joint postures were assumed for species using their hands for grasping during manipulation/tool use or climbing/suspension [141, 167] and hyperextended joint postures were assumed for knuckle-walking species [94] (see Figure 2.13, second column). Details about the methodology are presented in the following sections.



Figure 2.13: Outline of the study. Metacarpal bones (dark grey in the second column) of five species with different primary hand use were micro-CT scanned and used to predict the MCP joint load history. The black arrows in the rightmost column represent the hypothesized dominant joint load, i.e. dorsal loading in knuckle-walking species, palmar loading in species using flexed hand postures, and overall larger loads in species using their hand for locomotion. CT: computed tomography; MCP: metacarpophalangeal

2.3.2.2 Study sample

Micro-CT scans of nine to ten third metacarpal bones of each species (see Table 2.3) were obtained using BIR ACTIS 225/300, or Diondo d3 scanners housed in the Department of Human Evolution, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany and the Cambridge Biotomography Centre, Cambridge, UK. Specimens were scanned with a voxel size of 24 to 47 μ m depending on the size of the specimen. The human sample comprised four individuals from Nubia Egypt (6-11th century), three individuals from Inden, Germany (19th century) and three individuals from Syracuse, Italy (20th century). All non-human apes were wild shot, apart from two captive orangutans and one captive bonobo. All specimens included in the study were free of noticeable pathologies.

The sample included both left and right specimens from both sexes (see Table 2.3). Since individual body masses were not available, sex- and species-specific mean values were used in

Species		Sample size	Side	Gender	Body mass (kg)
Group name	Taxon		(L/R)	(F/M/U)	(F/M/U)
Bonobo	Pan paniscus	10	4/6	4/6/0	33.2/45.0/39.1
Chimpanzee	Pan troglodytes	9	3/6	5/4/0	40.4/49.6/45.0
Gorilla	Gorilla gorilla	9	3/6	5/4/0	80.0/169.4/124.7
Orangutan	Pongo pygmaeus,	10	3/7	5/4/1	35.7/78.2/57.0
	Pongo abelii				
Human	Homo sapiens	10	0/10	2/7/1	54.4/62.2/58.3

this study [189]. In the two cases where sex was unknown, the average of the male and female body mass was used.

Table 2.3: Overview of the study sample. Third metacarpal bones of five different species were micro-CT scanned and sex- and species-specific average body mass values from Smith and Jungers [189] were used. The orangutan sample comprised both *Pongo pygmaeus* (n = 8) and *Pongo abelii* (n = 2). L/R: left/right; F/M/U: female/male/unknown; CT: computed tomography

2.3.2.3 Image processing

All micro-CT scans were downsampled to 60 μ m isotropic resolution in Avizo 6.3 (Visualization Sciences Group, SAS) to reduce computational effort without compromising the load prediction results [42]. The scans were filtered with a median filter (support: 2 voxels) and segmented using the Ray Casting Algorithm [178].

A custom Python script was then used to find the specimen specific MCP joint coordinate system in an automated fashion (see Figure 2.14). First, the images were further downsampled to 360 μ m resolution and voids inside the bone were filled using the "fill" algorithm of medtool 4.1 (Dr. Pahr Ingenieurs e.U., Pfaffstätten, Austria). The x-y plane was computed by finding the plane of the strongest radio-ulnar symmetry of the distal third of the bone using a planar reflective symmetry transform [149]. The centre of rotation (CoR) and radius of the metacarpal head ($R_{\rm H}$) were found by fitting a circle to the distal contour of the bone in the cross section coincident with the x-y plane. The points delimiting the distal contour in this cross section were identified semi-automatically using a custom algorithm which detects changes in the local curvature of the metacarpal head contour above a predefined threshold. Finally, the x- and y-axes of the MCP joint coordinate system were rotated around the z-axis to account for intra- and inter-species differences in bone curvature. In particular, a circular arc (radius $R_{\rm B}$ in Figure 2.14) was fitted to the central part (50 % of the bone length L) of the dorsal contour of the bone in the x-axis is tangent to the circle fitted to the dorsal contour of the bone.



Figure 2.14: A representative specimen after image processing and defining the MCP joint coordinate system. The MCP joint coordinate system was located at the centre of rotation of the metacarpal head and tilted to account for the dorsal bone curvature (radius $R_{\rm B}$). MCP: metacarpophalangeal; CoR: centre of rotation

After definition of the coordinate system, the segmented micro-CT scans (60 μ m resolution) were cropped to preserve only the distal third of the bone, which contains all or most of the relevant trabecular bone architecture (see Figure 2.13, fourth column, and Figure 2.14). Finally, a layer of material mimicking cartilage was added to facilitate load application to the FE models. The layer was defined by a sphere located at the CoR of the metacarpal head with a radius of 1.2 times the head radius $R_{\rm H}$ (see Figure 2.14) and cropped laterally and proximally to remove excess material. The radius of the cartilage sphere was chosen as small as possible but large enough to avoid bone material penetrating through the cartilage surface.

2.3.2.4 FE modelling

The processed micro-CT scans were converted into voxel-based micro-FE models with 60 μ m element side length using medtool 4.1. Six different load cases were defined for each model, representing joint loading in six postures ranging from -75 ° (extension) to +75 ° (flexion) (see Figure 2.15). The proximal end of the bone was fully constrained in all load cases and forces were applied at the joint surface. All resultant force vectors were within the x-y plane, pointed to the centre of rotation of the MCP joint, and had a magnitude of 100 N. The force was distributed uniformly on a spherical rectangle (40×30 °) and all nodal force vectors were acting in parallel to the resultant force vector. The load load area size was chosen such that it approximately represents the lower bound of the physiological MCP joint contact area of humans, which was reported to vary from 29.3±8.5 mm² to 40.2±3.1 mm² depending on joint

posture [198] and amounted to $25.9\pm4.6 \text{ mm}^2$ in the human FE models used in this study. The number of load cases was then chosen using intervals of load directions as small as possible but large enough to avoid overlapping load areas leading to problems in the inverse remodelling algorithm as described in Section 2.2.



Figure 2.15: FE models of a single specimen with six different load cases representing joint loading in postures ranging from highly extended (-75 $^{\circ}$; top left) to highly flexed (+75 $^{\circ}$; bottom right).

The material properties were defined following previous studies that compared load prediction results with in vivo measurements [37]: the elastic modulus of the bone and the cartilage layer were set to 10 GPa and 10 MPa, respectively, and Poisson's ratios were set to 0.3 for both materials.

The resulting 288 micro-FE models (48 specimens, six load cases each) with an average of 38.0 ± 19.7 million degrees of freedom were solved using the parallel octree solver ParOSol [60]. The typical computational time for each load case was 15 minutes (wall-clock time) using 24 CPUs (Intel Xeon E5-2697 at 2.6 GHz). SEDs were evaluated at the element centroids to obtain the load distribution within the bone.

2.3.2.5 Prediction of the joint loading history

The load history prediction was performed using the inverse remodelling algorithm of Christen et al. [37] as introduced in the Section 2.1.2 and implemented as described in the previous section (Section 2.2). Similar to the Section 2.2, the joint loading history was determined by solving the following optimization problem:

minimize
$$\sum_{s_i \in \mathcal{X}} \left[\widetilde{U} - \left(\sum_{i=1}^n s_i \cdot U_i(\boldsymbol{x}) \right) \right]^2$$
 (2.17)

using the non-negative least squares algorithm of SciPy [95] and computing the load magnitude scaling factors α_i from s_i by assuming a constant number of load cycles m_i for all n unit load cases:

$$\alpha_i = \sqrt{n \cdot s_i} \tag{2.18}$$

A graphical overview of the load prediction specifically for the metacarpal bones is provided in Figure 2.16. The remodelling equilibrium stimulus \tilde{U} was set to 0.02 MPa as estimated by Mullender et al. [140] and used in previous studies [37]. In contrast to the hip joint load prediction of proximal femora (Section 2.2), it was found that the large number of elements in the thick cortex of the diaphysis of the metacarpal bones would introduce a considerable dependency of the predictions on the model length. To eliminate this dependency and provide reproducible results, only SEDs of the trabecular region were used in the inverse remodelling algorithm (see Appendix A for a detailed justification). The selection of respective elements was performed using a trabecular bone mask generated using the "fill" algorithm of medtool 4.1.



Figure 2.16: Prediction of the loading history of a single specimen using six load cases representing joint postures ranging from -75 ° (extension) to +75 ° (flexion), with resultant forces F_1 to F_6 . The optimal loading history is computed by combining and optimally scaling the load cases such that the distribution of the mechanical stimulus U is as homogeneous as possible.

The results of the load history prediction were visualized by scaling the resultant force vector F_i of each load case i with the corresponding load magnitude scaling factor α_i (see Figure 2.16). Additionally, a mean joint load vector \bar{F} was computed to compactly represent the loading history and to facilitate inter-specimen comparisons:

$$\bar{\boldsymbol{F}} = 1/n \cdot \sum_{i=1}^{n} \alpha_i \boldsymbol{F}_i \tag{2.19}$$

The quality of the load prediction was assessed in terms of the remaining tissue loading inhomogeneity before and after optimizing the load scaling factors. The tissue loading inhomogeneity was quantified by the CoV of the mechanical stimulus U. A CoV value of 0 % would indicate perfectly homogeneous tissue loading (i.e., the whole bone is in a state of remodelling equilibrium).

2.3.2.6 Output variables and statistics

Differences in the predicted joint loading histories were assessed both qualitatively and quantitatively in terms of two factors: "hand use" (three levels: manipulation/tool use, climbing/suspension, knuckle-walking) and "species" (five levels: human, bonobo, chimpanzee, gorilla, orangutan).

Qualitative comparisons were performed visually using the optimally scaled resultant forces $(\alpha_i F_i)$ for each of the six load cases of each bone (see Figure 2.16). Quantitative comparisons were performed using the mean vector (\bar{F}) magnitude and direction of each specimen. The mean vector magnitudes were computed both in absolute numbers and relative to the speciesand sex-specific body mass (i.e., percentage of body weight).

Mean vector magnitudes and directions were statistically compared using one-way ANOVAs and Games-Howell post-hoc comparisons in SPSS 23 (IBM Corporation, Somers, NY, USA). The Games-Howell post-hoc test was chosen to account for unequal sample sizes. The factors "hand use" and "species" were analysed in separate analyses. The level of significance was set to 0.05.

2.3.3 Results

2.3.3.1 Quality of the joint load predictions

The remaining tissue loading inhomogeneity was successfully reduced in all groups after optimization of the load scaling factors when compared to the initial, uniform load scaling (see Table 2.4). Despite the reduction, the trabecular bone was still not loaded in a perfectly homogeneous way, with CoV values ranging from 96.7 to 107.5 %. However, the remaining tissue loading inhomogeneity after optimization was comparable across species indicating similar quality of the load history prediction.

Species	CoV_{init} (%)		CoV _{opt} (%)		
	Mean	SD	Mean	SD	
Bonobo	124.1	13.1	96.7	4.7	
Chimpanzee	123.8	12.7	107.5	12.0	
Gorilla	111.0	6.5	102.2	4.1	
Orangutan	192.5	106.0	104.8	12.1	
Human	142.7	39.7	102.9	11.4	
Mean	138.8	35.6	102.8	8.8	
SD	32.1	41.4	4.0	4.1	

Table 2.4: Remaining tissue loading inhomogeneity expressed in terms of the coefficient of variation (CoV) before (CoV_{init}) and after optimizing (CoV_{opt}) the load scaling factors. SD: standard deviation

2.3.3.2 Qualitative comparison of joint load predictions

Clear differences between species were observed in the overall magnitudes of the optimally scaled resultant forces ($\alpha_i F_i$), which were largest for the gorillas and smallest for the humans (Figure 2.17). Other than the load magnitude, the differences in the predicted loading histories were subtle. The peak load was associated with the 15 ° flexion load case in almost all specimens and the loading pattern was broadly similar across species. However, slight differences could be observed in terms of the force magnitude ratio of extremely flexed (+75 ° load case, factor α_6) and extended (-75 ° load case, factor α_1) postures. In particular, this ratio was larger in species primarily using their hand in flexed postures (human, orangutan; average ratio $\alpha_6/\alpha_1 = 1.88$) when compared to knuckle-walking species (bonobo, chimpanzee, gorilla; average ratio $\alpha_6/\alpha_1 = 0.89$).

2.3.3.3 Quantitative comparison of joint load predictions

Quantitative comparisons were performed based on the mean joint load vectors displayed in Figure 2.17. To facilitate inter-group comparisons, mean joint load vector directions were plotted against both the absolute and body weight-scaled magnitudes and the groups were indicated by error ellipses scaled to one standard deviation (see Figure 2.18). Despite the large variation within the groups and overall similarity of the predicted loading histories, these bivariate plots demonstrated differences related to primary hand use that will be highlighted in the following.

Knuckle-walking species (bonobo, chimpanzee, gorilla) were characterized by lower mean joint load angles (i.e., more extended MCP joint postures) when compared to species habitually using their hand with a flexed MCP joint for manipulation/tool use (human) or climbing/suspension



Figure 2.17: Predicted joint loading histories in terms of optimally scaled resultant forces $\alpha_i F_i$ (see Figure 2.16) for each specimen of each species (faint lines) and respective averages (solid lines with filled circles). Additionally, mean joint load vectors of each species are displayed as coloured arrows.

(orangutan). These differences were significant for the factor "hand use" and all pairwise comparisons of the factor "species" except between the orangutans and chimpanzees (see Table 2.5).

A tendency towards larger mean joint load magnitudes was observed in species using their hand for locomotion (bonobo, chimpanzee, gorilla, orangutan), particularly if the magnitude was scaled with respect to body weight (see Figure 2.18). The latter difference was significant for the factor "hand use" in all pairwise comparisons (see Table 2.5). However, not all pairwise differences of body weight-scaled load magnitudes were significant for the factor "species".

2.3.4 Discussion

The goal of this study was to investigate whether a previously presented micro-FE-based inverse remodelling algorithm is sensitive enough to detect differences of habitual hand use based



Figure 2.18: Bivariate plots of the mean joint load vector components (direction, magnitude). Individual specimens are plotted as empty circles and groups are indicated by error ellipses scaled to one standard deviation (SD). Magnitudes are displayed both as forces (left) and percentage of body weight (right). Positive and negative direction angles indicate flexion and extension, respectively (see also Figure 2.17). Shades of blue represent knuckle-walking species (bonobo, chimpanzee, gorilla), pink and green colours represent species using their hand for suspension (orangutan) and manipulation (human), respectively.

Factor	Group 1	Group 2	Magnitude		Direction
			Abs.	%BW	
Hand use	Knuckle-walking	Manipulation/tool use	0.001	0.000	0.000
		Climbing/suspension	0.064	0.251	0.005
	Manipulation/tool use	Climbing/suspension	0.306	0.039	0.988
Species	Human	Orangutan	0.564	0.098	1.000
		Gorilla	0.004	0.251	0.000
		Bonobo	0.023	0.000	0.001
		Chimpanzee	0.104	0.000	0.018
	Orangutan	Gorilla	0.028	0.287	0.006
		Bonobo	0.620	0.012	0.021
		Chimpanzee	0.955	0.233	0.052
	Gorilla	Bonobo	0.096	0.000	0.680
		Chimpanzee	0.045	0.000	0.852

Table 2.5: *p*-values of all pairwise comparisons of the mean joint load vector magnitudes and directions based on the factors "hand use" and "species". Mean joint load vector magnitudes were compared using both the absolute values (scaled forces, labelled "Abs.") and relative values (percentage of body weight, labelled "%BW"). Significant values (p < 0.05) are highlighted in bold.

on the joint loading histories predicted from metacarpal bone architecture. Two hypotheses were investigated for this purpose: first (H1), that the predicted joint load direction would correlate with the primary hand posture and second (H2), that the joint loads would be larger in species using their hand primarily for locomotion compared to those using it for manipulation. Although not as strongly as expected, both hypotheses were supported by this study: Mean joint load vector directions were in line with the primary hand postures during knuckle-walking locomotion (more extended MCP joint posture), climbing/suspension (flexed posture), and manipulation/tool use (flexed posture) and mean joint load vector magnitudes tended to be larger in species using their hands for locomotion.

The observed differences in the predicted loading histories are in agreement with previous studies comparing metacarpal bone architectures of various primate species [35, 201, 202, 239]. These studies showed that morphometric differences are small but measurable, particularly with new, holistic approaches to quantify bone architecture [201, 202]. For instance, knuckle-walking species were characterized by overall higher trabecular bone volume fraction and denser subchondral bone in the dorsal regions of the metacarpal head when compared to species using primarily flexed hand postures [35, 201]. The herein predicted larger dorsal mean joint loads for knucklewalking species are in line with these observations and further support the previously reported sensitivity of the inverse remodelling algorithm on morphometric parameters [42]. However, in contrast to morphometric parameters alone, the prediction of joint loading histories takes into account all features of the bone at once, including outer bone geometry, cortical thickness, and trabecular bone structure. Particularly the mean joint load vectors might, therefore, be a useful tool to find differences in bone architecture caused by varying activities. Moreover, mean joint load vectors are broadly robust against parameter variations (as shown in Section 2.2) and facilitate interpretation of the results as well as inter-specimen and inter-species comparison due to the low number of output variables (e.g. load magnitude and direction). In the present study, these advantages made it possible to identify small but clear differences in the loading histories consistent with expectations for species with distinct habitual manual activities.

Although the predicted mean joint load vector magnitudes and directions showed differences related to primary hand use, the extent of these differences was smaller than expected. In particular, the predicted patterns of the loading histories were broadly similar across species and peak values were consistently found for the +15 ° load case (see Figure 2.17). From a mechanical point of view, it appears reasonable that axial loads are upscaled in the optimization procedure since they cause considerably lower stresses/strains in the bone compared to loads perpendicular to the long bone axis (e.g., compare the SED distribution caused by F_4 and F_1 in Figure 2.16). This effect might overrule the comparatively subtle differences of trabecular

architecture documented across species [35, 201]. Another reason for the observed similarities across species might be that the bone architecture is influenced by other manual activities to a larger extent than anticipated. For instance, knuckle-walking is the primary locomotor mode of bonobos, chimpanzees, and gorillas, but all of the species also engage in climbing and suspension as well as object manipulation, in which the hand is using flexed MCP joint postures [48, 54, 90]. Furthermore, the actual loads acting at the MCP joint during locomotor and manipulative activities are not yet well investigated, particularly in non-human primates. While a correlation between joint load direction and posture appears reasonable due to articular contact, the magnitude of the joint load depends on multiple parameters including external loading, posture, and muscle activity [33, 155, 226]. The use of musucoskeletal models to estimate joint loads during different human and non-human primate activities (see Chapter 3) will enable a more robust interpretation of the inverse remodelling predictions.

There are several limitations of this study that should be mentioned. Firstly, the load cases used in this study were highly simplified. Actual joint load areas and load distributions are likely more complex and dependent on posture and load magnitude [198]. Including articular contact in the simulation would potentially lead to more realistic loading conditions [18] but is considered to be beyond the scope of this study. Instead, an effort was made to standardize the load cases as far as possible to achieve objective interspecific comparisons. Secondly, the inverse remodelling algorithm of Christen et al. [37] relies on a highly simplified remodelling theory and neglects many mechanical and non-mechanical factors relevant to bone functional adaptation (see Section 2.1.1). Particularly non-mechanical factors such as genetics [130] might play an important role for interspecific comparisons but are, currently, not accounted for in the inverse remodelling algorithm. For instance, Tsegai et al. [203] found consistently higher bone density in the whole skeleton of chimpanzees when compared to humans, which might explain the large predicted load magnitudes (relative to bodyweight) as shown in Figure 2.18. Moreover, the parameters of the inverse remodelling algorithm were chosen based on previous studies and still require validation. While the choice of parameters has a minor impact on the predicted load directions, load magnitudes might be influenced to a larger extent (see Section 2.2). Reported load magnitudes in this study should, therefore, mainly be considered as a measure of comparison across specimens rather than interpreted in terms of their absolute values. Finally, the study sample was limited to only five species and a single anatomical location. Including comparisons across more species and more anatomical locations (e.g. additional finger joints) could provide further insights into the relation of bone architecture and joint loading histories with respect to habitual activities.

2.3.5 Conclusions

Overall, this study suggests that the inverse remodelling algorithm is sensitive enough to detect activity-related differences in the predicted joint load histories despite its limited accuracy. However, the differences of predicted peak and mean joint loads were substantially smaller than expected. Musculoskeletal models could help to investigate whether these similarities are caused by truly similar joint loads engendered by habitual activities or caused by the many limitations inherent to the inverse remodelling algorithm.

2.3.6 Related publications and declaration of contributions

Section 2.3 is based on the publication "Inverse remodelling identifies habitual activities based on bone architecture", *submitted* 2018 to the journal "Biomechanics and Modelling in Mechanobiology" and co-authored by Christopher J. Dunmore, Tracy L. Kivell, Matthew M. Skinner, and Dieter H. Pahr.

Author contributions: The first author and author of this thesis, *Alexander Synek*, designed the study and performed all parts described in the methods section except for the acquisition and segmentation of the micro-CT scans (see Acknowledgements for more details). *Christopher J. Dunmore* organized the acquisition of the micro-CT scans and performed the image resampling, filtering and segmentation. *Tracy L. Kivell* and *Matthew M. Skinner* supported the micro-CT data acquisition and interpretation of the results. *Dieter H. Pahr*, the supervisor of this thesis, supervised the work and contributed to the study design. All co-authors supported this study by active discussions and proofreading the manuscript.

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Chapter 3

Musculoskeletal modelling

The goal of this chapter is to investigate the link between habitual activities and bone loading (Figure 3.1) in order to better interpret the results obtained with the inverse remodelling algorithm (Chapter 2, specifically Section 2.3). For this purpose, metacarpophalangeal (MCP) joint loads of humans and non-human primates during various activities (manipulation/tool use, climbing/suspension, knuckle-walking) were analysed using musculoskeletal finger models. To account for anatomical differences between humans and non-human primates, both a human and bonobo model were used. Section 3.1 provides the respective anatomical background and describes modelling approaches previously used in literature. Implementation and testing of the human and bonobo finger models are presented in Section 3.2. Finally, in Section 3.3, the finger models were used to compare MCP joint loads during tool use, climbing, suspension, and knuckle-walking.



Figure 3.1: Outline of this chapter in the context of the whole thesis as presented in Figure 1.1. MCP joint: Metacarpophalangeal joint

3.1 Background

3.1.1 Functional anatomy of the finger

The human hand is a highly versatile instrument which enables interaction with the environment both by perception and active manipulation [75]. Its ability to firmly grasp objects in various ways is considered to play a key role in human evolution [103] and inspired biomechanical research to enhance robotic grippers [74, 101]. These grasping abilities rely both on the anatomical structure as well as sophisticated neural control [199].

The goal of this section is to explain the anatomical structure of a single finger and how this structure relates to function, i.e. to finger movements and exertion of forces. Specifically, the kinematics will be described, followed by the actuators of the hand and fingers (i.e. their muscles) including their system of force transmission (i.e. tendons). Additional soft tissues relevant to finger function, particularly ligaments, will be described as well. All aspects are first presented in detail for the human finger due to the much larger body of available literature and briefly compared to bonobo finger anatomy in the final section. As this thesis focuses on reconstructing activities from third metacarpal bone loads, details will be provided particularly for the middle finger. Note that particularly the thumb anatomy differs from those of the remaining four fingers. In the following sections, the term "finger" refers to all fingers except for the thumb unless otherwise stated.

Further details on the functional anatomy of the human hand and fingers that go beyond the scope of this thesis are provided in books on hand biomechanics such as those of Brand and Hollister [20], Chao et al. [33] or Freivalds [63]. An overview of the primate hand anatomy and evolutionary aspects are presented in the comprehensive book of Kivell et al. [103].

3.1.1.1 Kinematics of the human finger

The kinematics of the finger are governed by three movable and one fixed bone segments, namely the distal phalanx, middle phalanx, proximal phalanx, and the metacarpal bone, interconnected by three joints: the distal interphalangeal joint (DIP joint), proximal interphalangeal joint (PIP joint), and the metacarpophalangeal joint (MCP joint) [63] (see Figure 3.2). The metacarpal bone itself is tightly connected to the carpus of the hand by carpometacarpal joints and also articulates with other metacarpals at the intermetacarpal joints. Since only limited motion is possible at these joints for digits two and three [63], they are often simplified [192] or neglected [22] in kinematic descriptions of the finger.



Figure 3.2: Bones (MC, PP, MP, DP) and joints (MCP, PIP, DIP) of the finger, highlighted for the third digit in dark grey. Digits are labelled from I to V starting from the thumb. Joint axes with respective motions are depicted on the right. MC: metacarpal; PP: proximal phalanx; MP: middle phalanx; DP: distal phalanx; MCP: metacarpophalangeal; PIP: proximal interphalangeal; DIP: distal interphalangeal

The finger joints enable flexion and extension at the DIP, PIP, and MCP joints, and ulnar/radial deviation at the MCP joint (see Figure 3.2) [20]. Consequently, the DIP and PIP joints are commonly described as hinge joints with one rotational degree of freedom (DoF), whereas the MCP joint is considered a condylar joint with two rotational DoF. Using two rather than three DoF to describe MCP joint motion is consistent with the observation that extensive ulnar and radial deviation is possible in neutral postures, but highly limited in flexed postures [20]. Moreover, this kinematic description was shown to be in line with biomechanical in vivo [192] and in vitro [233] studies.

The description of location and orientation of the joint axes is still a matter of debate, particularly at the MCP joint [22]. The complexity of these descriptions range from fixed, intersecting axes [233] to inclined [20] and moving axes [145, 223]. More recently, Stillfried and Van der Smagt [192] used an optimization approach to find the best possible kinematic description of the human hand in multiple postures. They concluded that using two orthogonal, intersecting and fixed axis to model the MCP joint and single fixed axes to model the DIP and PIP joints provides the best trade-off between complexity and accuracy of the kinematic description. Conveniently, determining the locations of these joint axes from anatomy, i.e. from the curvature of the articular surface proximal to the respective joint, was reported to deliver reasonably accurate estimates [22].

3.1.1.2 Muscles actuating the human finger

Muscles are biological actuators which can produce tensile forces by contraction and transmit these forces to bones through tendons [20]. The fingers are actuated by multiple muscles originating either in the palm (intrinsic muscles) or in the forearm (extrinsic muscles) [63]. As a result, the finger muscles are typically multiarticulate, i.e. they produce motion and torques at multiple joints [98, 115]. Finger muscles and their function will be described briefly in the following. All general descriptions are based on Brand and Hollister [20] if not stated differently.

The extrinsic muscles actuating the finger are the flexor digitorum profundus (FDP), the flexor digitorum superficialis (FDS) and the extensor digitorum communis (EDC) (see Figure 3.3, top row). The FDP muscle originates from the ulna and inserts into the base of the distal phalanx. It therefore contributes to flexion movements and torques around the DIP, PIP and MCP joints. The FDS originates from the humerus and radius and inserts into the base of the middle phalanx. As a result, flexion movements and torques are only produced at the MCP and PIP joints. Both the FDP and FDS tendons are tightly guided along the palmar side of the finger through several tendon sheaths and pulleys. FDP and FDS are considered the major contributors to forceful grasping, as shown in electromyographic (EMG) studies [129] and computational models [71, 176]. The EDC muscle originates from the humerus and inserts into a tendon network called the extensor mechanism (also called the extensor expansion or dorsal aponeurosis [124]) at the level of the MCP joint, which inserts into the base of the middle and distal phalanx (see also Figure 3.4). In general, the EDC contributes to extension movements and torques at all three joints of the finger [180] but may also function as an active antagonist during forceful grasping [134].

The intrinsic muscles actuating the finger are the lumbricals (LU), as well as dorsal and palmar interossei (DI and PI) muscles (see Figure 3.3, bottom row). Interosseous muscles originate from the metacarpal bones and insert into the extensor mechanism, sometimes also into the base of the proximal phalanx. Lumbrical muscles originate from the FDP tendon and insert into the extensor sheet. All intrinsic muscles function as flexors of the MCP joint and act mainly as extensors at the interphalangeal joints (DIP and PIP) through the extensor mechanism. Interossei muscles are also the main contributors to radial and ulnar deviation movements at the MCP joint. Given spatial constraints, intrinsic muscles are typically smaller and therefore weaker than extrinsic muscles. They are therefore considered essential for independent movements of the phalanges by balancing and fine tuning joint torques rather than directly contributing to grip strength [124, 129].



Figure 3.3: Extrinsic (top row) and intrinsic (bottom row) muscles actuating the finger. The third digit is highlighted in grey. EDC: extensor digitorum communis; FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis; DI: dorsal interossei; PI: palmar interossei; LU: lumbrical



Figure 3.4: Extensor mechanism of the finger in dorsal (top) and lateral (bottom) view. Interossei muscles are labelled in a generalized way as radial (RI) and ulnar interossei (UI). EDC: extensor digitorum communis; LU: lumbrical; TS: terminal slip; CS: central slip; RB: radial band; UB: ulnar band

The function of the intrinsic muscles and the EDC muscle is mainly governed by the structure of the extensor mechanism which distributes the forces of the attached muscles to the interphalangeal joints via various pathways (see Figure 3.4). A common description of this tendon network is the Winslow's rhombus [210, 237], stating that the extensor mechanism consists of a finite number of tendon segments; most importantly: the central slip, radial band, and ulnar band at the PIP joint and the terminal slip at the DIP joint. While the central and terminal slip mainly extend the DIP and PIP joints, the radial and ulnar band move palmary with PIP joint flexion and thus change their function from extensor to flexors [78]. In general, the tendon network of the extensor mechanism is thought to enable well coordinated movements of individual finger joints [109, 119] and to provide joint stability [237]. It is also considered to enable intrinsic muscles to fine balance torques at the DIP and PIP joints [124, 195] which might explain the significance of intrinsic muscles for forceful grasping [134] despite their limited force producing capabilities.

3.1.1.3 Ligaments of the human finger

In addition to bones, muscles, and tendons, ligaments also play an important role for the function of the finger. Although muscles are considered the primary stabilizers of finger joints, particularly collateral ligaments provide additional mechanical support [33]. While these ligaments are generally present in all of the three finger joints [117], their function is best studied at the MCP joint [15, 33, 138], which is also most relevant for this thesis. The collateral ligaments of the MCP joint originate proximally at the head of the metacarpal bone, dorsal with respect to the centre of rotation, and insert into the volar lip of the proximal phalanx base [33] (see Figure 3.5). Due to their alignment, they are slack when the joint is in neutral posture and become taut as the joint is flexed [15]. Also due to their alignment, collateral ligaments provide a joint-stabilizing force acting proximally and dorsally on the proximal phalanx, effectively counteracting subluxation through shear forces caused by flexor muscles [226].



Figure 3.5: Collateral ligaments (CL) of the finger (top) and specifically at the MCP joint in neutral and flexed posture (bottom). F_{lig} schematically indicates the direction of the ligament forces which comprise both a proximal and dorsal force component acting on the proximal phalanx (grey arrows) to counteract joint subluxation.

3.1.1.4 Comparison of human to bonobo anatomy

Owing to their close genetic relationship [153, 229], the general anatomical structure of human and bonobo hand and fingers are broadly similar [103]. In analogy to humans, the skeleton of bonobo digits comprises of three phalanges attached to metacarpal bones [97, 147]. The musculature of the third digit is also comparable, although the intrinsic muscle terminology differs and the homology of interossei muscles is still debated (see Lemelin and Diogo [120] for details). Biomechanically most relevant, both the human and bonobo third digit are actuated by a deep and superficial extrinsic flexor, an extrinsic extensor, a lumbrical, and two intrinsic muscles originating from the metacarpal bones.

Despite these similarities, some details of the anatomy of bonobos and African apes (bonobos, chimpanzees, gorillas) in general appear to be adapted to habitual activities such as knucklewalking [194]. Knuckle-walking in African apes is characterized by hyperextended MCP joints, a highly flexed PIP joint and large external loads in dorsal direction applied to the middle phalanx (see Figure 3.6) [207]; a load case which is highly unusual for the human finger. The relatively short phalanges of African apes when compared to more arboreal primates, for instance, were hypothesized to reduce bending stresses of the bones [147] and muscular effort [194] during knuckle-walking by reducing the lever arm of external forces. However, a direct comparison of bonobo to human finger segment length ratios shows that these differences are minor [147]. Another likely adaptation to knuckle-walking is the reduced extrinsic flexor tendon length [207] and a thick palmar plate at the volar side of the MCP joint [194]. The reduced length of the tendon might facilitate maintenance of the hyperextended MCP joint posture as the muscle is stretched and produces passive forces, and the thick palmar plate is considered to support this function by increasing the respective lever arm. Also, a transverse ridge at the dorsal side of the metacarpal head (see Figure 3.6) is considered to serve as a "bony stop" to prevent overextension and/or as a buttress for the proximal phalanx during knuckle-walking [158, 207]. However, the variable presence of this ridge at different digits and in knuckle-walking species in general, as well as its strong expression in metatarsals raised doubt about its functional significance [92, 122, 147].



Figure 3.6: Comparison of the human and bonobo finger anatomy. A typical knuckle-walking finger posture and schematic external loading (F_{ext}) is shown on the left and a comparison of typical finger segment lengths is provided on the right.

There are also some other anatomical differences between human and bonobo fingers which are not directly related to knuckle-walking. Most evidently, bonobo phalanges show a pronounced longitudinal curvature of the bones (see Figure 3.6) [194]. This curvature is considered as a reaction to bending stresses during powerful grasps of cylindrical substrates such as they occur during climbing and suspension [157]. Additionally, the bonobo metacarpals and phalanges are overall large when compared to humans both in absolute numbers [194] and relative to the length of the upper limb [147].

3.1.1.5 Conclusions

The human third digit is a musculoskeletal system consisting of three bones connected by three joints and actuated by six muscles. While the kinematics of the finger joints appear relatively simple, the mechanisms of finger actuation are complicated by the multiarticulate nature of the muscles and the tendon network formed by the extensor mechanism. A comparison of the bonobo and human anatomy showed that the general anatomical structures are broadly similar. However, some anatomical details, including bone lengths and shape, differ and might have biomechanical implications which remain to be investigated.

3.1.2 Literature review of musculoskeletal finger models

As mentioned in the introduction to this chapter, the goal of the musculoskeletal modelling part of this thesis is to predict MCP joint loads during different habitual activities. Even in static postures, joint loads are determined not exclusively by external forces, but depend to a large extent on muscle forces which must maintain torque balance at all joints. As a result, musculoskeletal models are required which take into account the posture, external forces as well as the anatomical structure, and allow to estimate joint loads as the sum of external and muscle forces [33, 72, 155].

Albeit previously presented models differ in several details, they share general modelling assumptions or modelling approaches of individual anatomical structures. Consequently, this section first describes general finger modelling considerations, followed by current modelling approaches of each biomechanically relevant anatomical structure. The basic scheme of computing joint loads with these models in static grasps and attempts of model validation are presented in the final subsections.

Again, this section focuses on aspects relevant to this thesis. Further details are provided in reviews such as those of Gustus et al. [75] and Fok and Chou [61]. A review of non-human primate finger models is not presented as no complete models are known to the author. However, the reader is referred to Schaffelhofer et al. [177] for the presentation of a macaque upper limb model to estimate tendon excursions or Chan and Moran [32], for a complete musculoskeletal macaque model of the upper limb excluding the fingers.

3.1.2.1 General finger model considerations

The first modelling consideration to be addressed is whether or not a single finger can be treated as an isolated mechanical system. In particular, the extrinsic muscles located in the forearm function not only as finger actuators, but also contribute to wrist joint stability and movement [123, 144]. Moreover, numerous studies showed that truly independent finger actions are hindered by so called enslaving effects caused by anatomical structure (e.g. multitendoned muscles or mechanical coupling between tendons) and limitations of neural control [125, 238]. Despite these considerations, most models presented in literature focus on a single or multiple fingers without taking into account mechanical coupling at the wrist or enslaving effects in favor of substantially lower modelling effort [115, 155, 176, 210]. For instance, including wrist joint balance requires that the model includes all instead of just one finger, and additionally all major muscles actuating the wrist joint [144].

Another general consideration is whether to use static or dynamic finger models. For obvious reasons, studies focusing on free movements of the finger used dynamic models which take into account the inertial properties of the individual finger segments [115, 175, 232]. Studies predicting muscle forces and joint loads during grasping mostly neglected inertial properties and assumed static conditions [72, 221, 226]. This assumption seems valid for two reasons: first, the joint postures are typically static during the grasp and second, inertial forces are likely small compared to substrate reaction forces due to small finger segment masses even if movements occur.

The final general assumption to be discussed is whether to use 2D or 3D models. Both model types were used (e.g. 2D: see [124, 226]; 3D: see [33, 210]) but no study comparing 2D to 3D models is known to the author of this thesis. Considering that the MCP joint range of motion in radial/ulnar deviation is relatively small (radial/ulnar deviation: -20 to +20 ° [135]; flexion/extension: approximately -45 to +90 ° [80]) and that finger loading occurs on the palmar side of the finger during typical manipulation tasks [33, 72], the 2D assumption appears like a reasonable simplification. A main aspect that is lost in 2D models and might influence joint loads is, however, the joint torque balance at the MCP joint around the radial/ulnar deviation axis. Most of the recent studies used 3D models, likely owing to the availability of 3D data for most modelling aspects such as kinematic description [4, 22] and tendon path points [4], as will be described in subsequent sections.

3.1.2.2 Modelling the kinematics of the finger

Almost all recently presented finger models use idealized joints to model the articulations of the finger [72, 210]. Only one study is known to the author where finger joint kinematics (carpometacarpal joint of the thumb) were modelled by articular contact and stabilization by ligaments and muscles [196].

In line with biomechanical investigations of finger kinematics presented in Section 3.1.1, the DIP and PIP joints are typically modelled as one DoF hinge joints with fixed centres of rotation [72, 210]. With few exceptions [16, 61, 155], MCP joints are mostly modelled as two DoF joints (flexion/extension, radial/ulnar deviation) with fixed, perpendicular and intersecting axes of rotation [71, 91, 210, 220]. As already described in Section 3.1.1, these common assumptions seem to represent the kinematics of fingers well and with a reasonable level of complexity [192]. Quantitative 3D data of finger segment lengths and axes locations required to implement finger kinematics are available in literature from Buchholz et al. [22] and An et al. [4] and were often used as the basis for musculoskeletal models [71, 210, 221].

3.1.2.3 Modelling finger actuation by muscles

The most common assumption to model actuation of the finger by muscles is to use a moment arm-based approach [71, 176, 210]. In this approach, muscles are considered to produce torques at each DoF corresponding to the tendon tension multiplied with the respective moment arm (see Figure 3.7). These torques result in motion of the finger and/or counteract torques engendered by external loading. Different approaches of modelling the muscle force generation as well as moment arm computation will be briefly explained in the following.



Figure 3.7: Schematic 2D representation of finger actuation in a moment arm-based model. Muscle i produces a certain tendon tension t_i within physiological lower and upper bounds $(t_{\min,i} \text{ and } t_{\max,i})$ which results in torques τ at each joint as governed by the respective moment arm r.

Muscle is a complex tissue which can exert both active forces by contraction and passive force as it is stretched. Various studies tried to explore its mechanical properties and the mechanism of muscle contraction and many biomechanical muscle models were developed (see Zajac [236] for a review). In brief, the total force generated by a muscle-tendon unit is governed by several constants (e.g. muscle architecture and elastic properties), but also variables such as the muscle activation level, current muscle length, and contraction velocity. However, muscle length and velocity were taken into account only in a few muscles as ideal actuators. As such, active forces are assumed to be independent of muscle length and velocity and only constrained by constant physiological lower and upper bounds, passive forces are neglected, and tendons are modelled as rigid [71, 210, 219]. Thus, the only parameters to be defined for each muscle are the lower and upper bounds of the active force. The lower bound is typically set to zero to ensure that muscles only exert tensile forces and the upper bound is defined by the maximum muscle stress σ_{max} and physiological cross sectional area (PCSA) of the respective muscle *i* [236]:

$$t_{\max,i} = \text{PCSA}_i \cdot \sigma_{\max} \tag{3.1}$$

Respective PCSA data of finger muscles to compute t_{max} are available from the literature (e.g. see [33, 93, 126]).

Finger actuation is usually modelled by computing the joint torques at each DoF from the tendon tension and a respective moment arm. Thus, moment arms are required for each tendon and each DoF of the model (see Figure 3.7). In general, these moment arms depend on joint posture [99] and can be derived either from experiments (e.g. tendon excursion experiments [5, 33]) or estimated by computational means. A common computational approach [71, 176, 226] is to model the tendon path with a finite number of so called via points (see Figure 3.7) and to estimate the moment arm from the line segment in proximity to the joint, e.g. using the generalized force method [186]. Quantitative data of these via points are available in literature, e.g. from An et al. [4] or Lee et al. [114]. The via point-based approach can be further improved with so called wrapping geometries [105] which avoid that tendons penetrate rigid bodies such as bones. Respective computational methods were previously developed [69] and are available in musculoskeletal software packages such as OpenSim [50].

An additional challenge in musculoskeletal finger models is the implementation of the extensor mechanism. As explained in Section 3.1.1, the extensor mechanism distributes the forces of intrinsic muscles and the EDC muscle across the interphalangeal joints along multiple pathways. Due to its functional significance, it was implemented in most of the models presented in literature [155, 210, 221]. In these studies, the implementation mostly followed the Winslow's rhombus description, i.e. reducing the complexity of the extensor mechanism into a tendon network with a finite number of rigid tendon segments (see Section 3.1.1 and Figure 3.4). The muscle force distribution at tendon bifurcations is then either set to fixed, empirically determined factors [155, 226] or computed in a posture dependent fashion [71, 219]. Other studies focused on investigating the extensor mechanism alone and modelled it as an elastic tendon network which can deform as external loads are applied [53, 85, 213].

3.1.2.4 Modelling the ligaments

Since the joints in musculoskeletal finger models are typically idealized (e.g. as hinge joints), ligament modelling is not essential to capture their general joint stabilizing effects. However, both the resistance to radial/ulnar deviation and their role in preventing proximal phalanx subluxation might warrant their implementation (as described in Section 3.1.1 and specifically Figure 3.5). For these reasons, radial and ulnar collateral ligaments of the MCP joint were included in multiple musculoskeletal finger models [71, 175, 226]. The ligaments were typically modelled as a single non-linear spring elements attached to either of the articulating bones. The coordinates of the attachments were taken from literature [33] and the spring law with respective parameters were estimated from whole joint stability analyses [138]. Although the accuracy of these parameters might be questioned, this modelling approach qualitatively captures the effect of increased ligament tightening in flexion to resist shear forces at the proximal phalanx. Weightman and Amis [226] pursued another modelling approach: they implemented MCP collateral ligaments indirectly by assuming that they do not contribute to joint torque, but only compensate excessive shear force components acting on the proximal phalanx.

3.1.2.5 Computation of muscle forces and joint loads

Using the above described model components (kinematic description, muscles, ligaments), it is possible to predict finger joint loads in static postures given a set of joint angles and external loading. This can be achieved in two main steps: (1) computation of muscle forces and (2) computation of joint loads as the sum of external and muscle forces. This process will be outlined briefly in the following and details specific to finger models will be highlighted.

In a static posture, the torques τ_{ext} engendered by external loading must be balanced by torques produced by muscles τ_{mus} at all DoF:

$$\tau_{\rm ext} + \tau_{\rm mus} = 0 \tag{3.2}$$

In the above equation, τ are $n \times 1$ vectors containing the torques at each of the n DoF of the model. τ_{ext} contains torques produced by external forces as well as passive forces e.g. from ligaments. In static conditions, the external forces F_{ext} can be mapped to joint torques [46, 210] using:

$$\boldsymbol{\tau}_{\text{ext}} = \sum_{j} \boldsymbol{J}_{\boldsymbol{p}_{j}}^{\text{T}} \boldsymbol{F}_{\text{ext},j}$$
(3.3)

where J_{p_j} is the $3 \times n$ Jacobian matrix which essentially contains the lever arms at each DoF for external force j applied at point p_j (see Figure 3.8, left). It can be computed using the partial derivatives of p_j with respect to each joint coordinate θ_i [184]:

$$\boldsymbol{J}_{\boldsymbol{p}_j} = \begin{bmatrix} \frac{\partial \boldsymbol{p}_j}{\partial \theta_1} & \dots & \frac{\partial \boldsymbol{p}_j}{\partial \theta_n} \end{bmatrix}$$
(3.4)


Figure 3.8: 2D sketch of a generic finger model, indicating torques τ resulting from application of an external force F_{ext} at point p expressed in a fixed global coordinate system located at the centre of the MCP joint (left). θ denote the joint coordinates. The external forces F_{ext} and muscle forces $t \cdot u$ relevant for the computation of joint loads F_{joint} are schematically shown on the right. u is the unit vector of the tendon segment in proximity to the joint governed by the tendon via points (red points).

The torque contributions of the muscles can be derived from:

$$\boldsymbol{\tau}_{\mathrm{mus}} = \boldsymbol{R}\boldsymbol{t} \tag{3.5}$$

where, t is the $m \times 1$ vector containing all muscle tensions and R is the $n \times m$ moment arm matrix containing moment arms of each muscle at each DoF (see Figure 3.7). In order to account for the extensor mechanism, the moment arms can be replaced by *effective* moment arms [116]. These effective moment arms are corrected for the fraction of force transmitted to a certain part of the extensor mechanism. For instance, if only 50 % of the muscle force is transmitted to a specific part of the extensor mechanism (e.g. the radial band), the respective moment arm is lowered by 50 % accordingly. The resulting matrix of effective moment arms will be called T in the following. Using Equation 3.5 and 3.3 and replacing R by T allows to rewrite the torque equilibrium equation (Equation 3.2):

$$\sum_{j} \boldsymbol{J}_{\boldsymbol{p}_{j}}^{\mathrm{T}} \boldsymbol{F}_{\mathrm{ext},j} + \boldsymbol{T}\boldsymbol{t} = \boldsymbol{0}$$
(3.6)

If the number of DoF (n) is equal to the number of muscles (m), the system is statically determinate and the muscle forces can be computed directly from Equation 3.6. However, since the number of muscles typically exceeds the number of DoF in the finger, additional assumptions have to be made. Some authors set individual tendon loads to zero, assuming that these muscles are inactive during the investigated task [124, 226]. For instance, the EDC

muscle was considered inactive during grasps in a study using a 2D model with three DoF and four muscles (three extrinsic muscles and one lumped intrinsic muscle), resulting in a statically determinate problem [124]. A more general method is to make assumptions about neural muscle activation strategies, e.g. minimization of muscle stresses or maximization of endurance. In general, this leads to an optimization problem of the form:

minimize
$$G(t)$$

subject to $\sum_{j} J_{p_{j}}^{T} F_{\text{ext},j} + Tt = 0,$ (3.7)
 $0 \le t \le t_{\text{max}}$

The constraints in the above optimization problem ensure that the solution satisfies the static equilibrium equations and that muscle tensions remain within physiological boundaries (i.e. only tensile forces, and forces lower than maximum isometric force). $G(\cdot)$ is the objective function and was defined in a variety of ways in previous musculoskeletal finger models. Most commonly it is assumed that the neural system aims to minimize the total muscle stress, such that:

$$G(t) = \sum_{i} \left(\frac{t_i}{\text{PCSA}_i}\right)^k$$
(3.8)

Exponent k in Equation 3.8 is a constant which was shown to control the degree of synergistic muscle activation [152, 156] and was set to different values ranging from two to four in previous musculoskeletal finger models [21, 72, 175, 219]. Particularly k = 2 showed good agreement with experimentally measured muscle activation patterns at the upper limb in static conditions [214].

Using the estimated muscle tensions t_i (e.g. by solving Equation 3.7), the force acting at a specific joint can be computed from the force equilibrium equations [71, 226]:

$$F_{\text{joint}} = -\left(\sum_{j} F_{\text{ext},j} + \sum_{i} t_{i} u_{i}\right)$$
 (3.9)

where $F_{\text{ext},j}$ are the externally applied forces and u_i is the unit vector indicating the direction of the tendon at the joint. Using a via point based model, u_i can be computed from the two via points in proximity to the joint as used for the moment arm computation (see Figure 3.8).

3.1.2.6 Validation of musculoskeletal finger models

The scheme of joint load computation presented above shows that many different aspects of the models can and should ideally be validated [82], including: (1) the computation of effective moment arms, i.e. matrix T, (2) the conversion of muscle force to external force, i.e. matrices T and J, (3) the computation of joint loads, which takes into account assumptions of tendon directions u_i , and (4) the muscle activation pattern predicted by solving the optimization problem presented in Equation 3.7.

However, studies attempting to validate musculoskeletal finger models are rare. Kociolek and Keir [105] compared the moment arm predictions of a via point-based model to experimental data and found a better agreement after implementing wrapping geometries and optimally adjusting their positions. Lee et al. [114] also reported that experimentally measured moment arms can be matched with via point-based models after optimizing the tendon path. The actual force transmission mechanism of the finger was validated by Qiu and Kamper [155] by comparing predicted to experimentally measured fingertip forces (i.e. F_{ext}) after applying a predefined load on each tendon (i.e. t_i). In terms of muscle activation patterns, Valero-Cuevas et al. [210] found a good agreement of the predictions of index finger muscle activity with EMG measurements during maximum isometric force generation at the fingertip. Good agreement between predicted muscle tensions and activity levels measured with EMG were also reported for the FDS muscle by Ikeda et al. [91] and Kurita et al. [106]. Although accurate predictions of muscle tensions can be considered as an indirect validation of joint loads, no study is known to the author that directly validated joint loads based on experimental data.

Overall, the above studies confirm that the general approach of using moment arm-based models and via points to describe the tendon paths delivers reasonable estimates of muscle tensions and respective activation patterns. However, the fact that model adjustments were needed in all of the above studies highlights the parameter sensitivity of the models and underlines the need for a careful choice of parameters.

3.1.2.7 Conclusions

The literature review showed that there is a vast body of literature on musculoskeletal models of the human, but not the non-human primate finger. Although almost all presented models differ slightly, they often share the same basic modelling approaches: Kinematics are usually described using three segments, three joints, and four rotational DoF and muscles are modelled as ideal actuators with tendon paths defined by multiple via points. The extensor mechanism and ligaments were implemented with varying degree of detail. Parameters for the human model, including kinematics, muscle geometry (PCSA), and tendon via points are available in literature, but adjustment to experimental data appears mandatory as indicated by previous validation studies. Moreover, there is currently no study which validated joint loads based on experimental data.

3.2 Implementation and testing: Comparison to in vitro experiments

3.2.1 Introduction

In order to investigate the link between habitual activities and bone loads at the third metacarpal of humans and non-human primates (subgoal 2 of this thesis, see Figure 3.1), musculoskeletal finger models need to be implemented and tested for their applicability.

As described in Section 3.1.2, various modelling aspects of musculoskeletal models of the human finger are well investigated and parameters are available in literature. In contrast, non-human primate hand or finger models are scarce, although comparative anatomy (Section 3.1.1) suggests that there are differences which might be biomechanically relevant [103, 194]. Moreover, efforts of model validation were limited to predicted moment arms [105, 114], fingertip forces [155], and muscle activation patterns [91, 210] and highlighted that model adjustments are essential to obtain realistic predictions. No study has yet tried to directly validate bone- or joint loads of the finger.

In order to fill these gaps, the goals of this study were to implement a human and bonobo musculoskeletal finger model and: (1) identify model parameters which minimize the error between predicted and in vitro measured fingertip forces and (2) to compare fingertip and metacarpal bone load predictions of the adjusted models to experimental measurements in different load cases for validation. Additionally, the human and bonobo model shall be compared with each other to investigate whether or not the use of a bonobo specific model is warranted.

3.2.2 Materials and methods

3.2.2.1 Study outline

Parameter identification was performed by adjusting the parameters of a human and bonobo third digit model to best match fingertip forces measured in vitro in four postures while loading each muscle/tendon individually (Figure 3.9, first row). In a second step, multiple tendons

were loaded simultaneously in the same four postures and the measured fingertip forces and metacarpal bone loading were compared to the model predictions (Figure 3.9, second row). Finally, differences between the human and bonobo models were evaluated in these combined tendon loading conditions.



Figure 3.9: Outline of the study. Parameters of a human and bonobo finger model were first identified by adjustment to in vitro experimental data (top row) and then validated in different load cases (bottom row). Additionally, human and bonobo models were compared to identify species-related differences. MC: metacarpal

3.2.2.2 In vitro experiments

The fingertip and metacarpal bone forces were assessed using a previously developed custom test setup [131] (see Figure 3.10). This setup permits the mounting of a dissected cadaveric finger both at the metacarpal bone and fingertip to ensure a fixed, static posture and to apply load by attaching weights to individual tendons. Fingertip forces and metacarpal bone forces are measured using a six-axes load cell (Nano 17-E, ATI Industrial Automation, Apex, NC, USA) which is positioned either at the proximal or distal bone clamp (labelled "Load cell location 1" and "Load cell location 2", respectively in Figure 3.10).

Study sample

The study sample comprised of three third digits of fresh frozen cadaveric human hand specimens (age: 89.7 ± 4.0 years; gender: 2 female, 1 male; side: left) and one third digit of a fresh frozen bonobo hand specimen (taxon: *Pan paniscus*; age: 8 years; gender: female; side: left).



Figure 3.10: Experimental test setup. The proximal and distal clamp fixate a dissected cadaveric finger in a static posture. Individual tendons can be loaded by applying weights to attached sutures. A load cell enables measuring both fingertip forces when positioned at "Load cell location 2" and net metacarpal bone loading when positioned at "Load cell location 1".

Human samples were obtained via the Human Body Donation Programme of the University of Leuven, Belgium and the bonobo sample was made available by the Antwerp Zoo by Centre for Research and Conservation, Royal Zoological Society Antwerp (KMDA/RZSA) as part of the Bonobo Morphology Initiative 2016.

Specimen preparation

The digits were disarticulated from the hands at the carpometacarpal joints and soft tissues were removed to identify the tendons of all intrinsic and extrinsic muscles as listed in Table 3.2. The soft tissues around the MCP joint were kept intact to the maximum extent possible to maintain physiological conditions. Sutures were applied to each tendon using the Clove-Hitch technique [2]. In cases where intrinsic muscle tendons clearly split into two parts inserting either at the extensor mechanism or proximal phalanx base, sutures were applied to each part of the tendon (see Table 3.2).

Experimental design

Each specimen was mounted to the test setup and placed in four postures to cover as much as possible of the range of motion (see Figure 3.10 and Table 3.1): (1) major flexion, (2) minor flexion, (3) hook grip, and (4) hyperextension. Respective joint angles were set using a goniometer. In each posture, the tendons were loaded in proportion to the maximum muscle force t_{max} , as estimated from the muscle specific PCSA and the maximum specific muscle tension of 45 N/cm² [84]. Human muscle PCSA data were taken from Chao et al. [33] and the bonobo muscle PCSAs were obtained from a dissection study on the contralateral arm of the bonobo (see Appendix B). The sutures were aligned in parallel to the long axis of the metacarpal bone (see Figure 3.10) to best approximate physiological loading conditions.

For parameter identification, the load cell was mounted at the fingertip clamp and forces were recorded while each individual tendon was loaded to 5 % of the maximum muscle force (see Table 3.2 for muscle-specific weights). In the combined tendon loading scenario, the fingertip forces and metacarpal bone loads were recorded while the flexor digitorum profundus (FDP) and flexor digitorum superficialis (FDS) muscle were loaded simultaneously at two different force levels, namely 5 % and 2 % of the maximum muscle force (see Table 3.2).

Posture	DIP flexion ($^{\circ}$)	PIP flexion ($^{\circ}$)	MCP flexion (°)
Major flexion*	40.0	50.0	60.0
Minor flexion	35.0	45.0	40.0
Hook grip	50.0	65.0	0.0
Hyperextension	45.0	50.0	-20.0

Table 3.1: Postures used in this study including joint angles. Ulnar/radial deviation was 0 $^{\circ}$ in all postures. * the major flexion posture was modified for the human fingers due to the specimen range of motion, such that DIP/PIP/MCP angles were 25 $^{\circ}/57 ^{\circ}/55 ^{\circ}$, respectively. DIP: distal interphalangeal; PIP: proximal interphalangeal; MCP: metacarpophalangeal

Data acquisition and processing

A compact data acquisition system (NI cDAQ-9174, National Instruments, Austin, TX, USA) and LabVIEW (National Instruments, Austin, TX, USA) were used to measure forces both in the loaded and unloaded finger. The fingertip and metacarpal bone forces were then computed as the difference of the measurements in the loaded and unloaded state.

After the experiments were conducted, the intended tendon load (governed by the attached weights) was compared to the true tendon loading computed based on static equilibrium equations using the fingertip force and metacarpal bone loading available from the combined tendon

Species	Muscle/tendon	PCSA (cm ²)	Mass (g)	
			5 % $t_{\rm max}$	2 % $t_{\rm max}$
Bonobo	FDS	3.5	800.0	300.0
	FDP	2.9	650.0	300.0
	EDC	1.1	250.0	-
	LU	0.2	40.0	-
	RI (EM)	0.8	200.0	-
	RI (PP)	1.5	350.0	-
	UI (EM)	0.8	200.0	-
	UI (PP)	0.9	200.0	-
Human	FDS	4.2	950.0	300.0
	FDP	4.1	950.0	300.0
	EDC	1.7	400.0	-
	LU	0.2	45.0	-
	RI (EM)	1.4	325.0	-
	RI (PP)	1.4	325.0	-
	UI (EM)	2.2	500.0	-
	UI (PP)	0.0	0.0	-

Table 3.2: Muscles and tendons loaded in the in vitro experiments. Intrinsics with split tendons inserting into either the extensor mechanism (EM) or the proximal phalanx base (PP) are labelled accordingly. Loads were applied in proportion to the PCSA as taken from Chao et al. [33] for the human fingers and own dissection data for the bonobo finger (see Appendix B). EDC: extensor digitorum communis; FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; PCSA: physiological cross sectional area.

loading scenarios. Deviations between intended and computed values were found and larger than expected. These deviations were attributed to friction at a pulley in the experimental setup which deflects the suture as required to apply the weights. In order to diminish the resulting error, a linear correction factor c was calculated:

$$c = \frac{1}{n} \sum_{i=1}^{n} \left(\frac{\|\boldsymbol{F}_{\text{tip},i} + \boldsymbol{F}_{\text{bone},i}\|}{m_i \cdot g} \right)$$
(3.10)

In the above equation, $m_i \cdot g$ is the weight attached to the tendons during load case *i* computed from mass m_i and the gravitational constant $g = 9.81 \text{ m/s}^2$, $F_{\text{tip},i}$ is the respective fingertip force, $F_{\text{bone},i}$ is the metacarpal bone loading, and $\|\cdot\|$ is the Euclidean norm. Including all four specimens, all four postures, and both load levels (i.e. n = 32) led to a correction factor of 0.835. This factor was used to correct all tendon tensions for both the combined and single tendon load cases.

3.2.2.3 Musculoskeletal finger models

Kinematics

Both the human and bonobo musculoskeletal models were generated based on the kinematic description and tendon via points provided by An et al. [4] and implemented using custom Python scripts. The kinematics comprise of three movable (proximal, middle, and distal phalanx) and one fixed (metacarpal) bone segments interconnected by three joints, namely the MCP, PIP and DIP joints. PIP and DIP joints were modelled as hinge joints with one DoF (flexion/extension) and the MCP joint as a condylar joint with two rotational DoF (flexion-extension and radial/ulnar deviation). All flexion/extension joint axes were fixed and parallel to each other and the two MCP joint axes were intersecting and perpendicular.



Figure 3.11: Topology of both the human and bonobo model, including the kinematic description with three joints (DIP/PIP/MCP) and the six muscles (FDP/FDS/EDC/RI/UI/LU). Dashed lines indicate the rotation axes of individual DoF of each joint. Black lines schematically indicate the tendons including the extensor mechanism, which was simplified to four tendon segments at the DIP and PIP joint, namely the terminal slip (TS), radial band (RB), ulnar band (UB), and central slip (CS). For the remaining abbreviations, the reader is referred to the main text or the list of abbreviations.

Muscles and tendons

Six muscles actuate the finger models (see Figure 3.11): the three extrinsic muscles FDP, FDS and extensor digitorum communis (EDC), and the three intrinsic muscles radial interosseus (RI), ulnar interosseus (UI) and lumbrical (LU). The extensor mechanism was included using the common Winslow's rhombus simplification [210, 237]. It consists of two slips and two bands, namely the central slip, terminal slip, ulnar band, and radial band (see Figure 3.11). The tendon paths were approximated by straight line segments using via points proximal and distal to each joint as described by An et al. [4]. These proximal and distal via points were assumed to be fixed with respect to the proximal and distal bone of the articulation, respectively.

Computation of fingertip forces

Following Valero-Cuevas et al. [210], static fingertip forces and moments $\boldsymbol{F}_{tip}^* = \left[\boldsymbol{F}_{tip}^T, M_z\right]^T$ (see Figure 3.12) were computed from the tendon tensions $\boldsymbol{t} = [t_{RI}, t_{LU}, t_{UI}, t_{FDP}, t_{FDS}, t_{EDC}]^T$ using the following linear relation:

$$\boldsymbol{F}_{\mathrm{tip}}^* = -\boldsymbol{J}^{-\mathrm{T}} \boldsymbol{T} \boldsymbol{t}$$
(3.11)

where J^{-T} is the 4×4 inverse transpose Jacobian matrix which converts joint torques into fingertip forces and torques and T is the 4×6 force transmission matrix which contains the effective moment arms of each muscle at each DoF as described in Section 3.1.2. The moment arms of each tendon segment were computed using the generalized force method [186] and the assumption of bowstringing between via point coordinates. Moment arms of tendon segment which would naturally wrap around the bone in a specific posture (e.g. the terminal slip in flexion, or flexor tendons in hyperextension) were computed using Landsmeer's model 1 [33], i.e. the moment arms were assumed to be constant for this tendon segment. Note that this assumption leads to similar results as using wrapping geometries (see Appendix C). All moment arm computations were verified using the musculoskeletal modelling software OpenSim [50] (see Appendix C).

Computation of metacarpal bone forces and MCP joint forces

Using the fingertip forces F_{tip} computed using Equation 3.11, the MCP joint loads F_{joint} can be calculated from the static equilibrium equation:

$$F_{\text{joint}} = -\left(F_{\text{tip}} + \sum_{i} t_{i} u_{i}\right)$$
 (3.12)

where t_i is the tension of muscle *i* and u_i is the unit vector pointing from the distal to the proximal via point of muscle *i* (see Figure 3.12, left). In case tendon segments would naturally wrap around the bone in a specific posture as described in the previous paragraph, direction u_i was considered constant with respect to the distal bone. Joint load computations were also verified by comparison to OpenSim (for details see Appendix C).

Assuming that the extrinsic flexor tendons run in parallel to the long axis of the metacarpal bone as in the experiment, the load acting on the metacarpal bone F_{bone} can be computed as:

$$\boldsymbol{F}_{\text{bone}} = \boldsymbol{F}_{\text{joint}} - \sum_{i} (t_i \boldsymbol{v}_i - t_i \boldsymbol{u}_i)$$
(3.13)

where v_i is the unit vector parallel to the long axis of the metacarpal bone, pointing in the proximal direction (see Figure 3.12, right). Note that compared to F_{joint} , F_{bone} takes into account pulley forces and forces from the tendon wrapping around the head of the metacarpal bone.



Figure 3.12: Overview of the computation of joint load F_{joint} (left) and the net metacarpal bone loading F_{bone} (right). Pulley forces F_{pulley} are added as a dashed vector in the graphical depiction of the equilibrium conditions to highlight the differences between F_{joint} and F_{bone} .

Initial model parameters

Initial parameters of the human model were taken from literature. Normalized bone segment lengths and tendon via points were taken directly from An et al. [4]. Force distributions due tendon bifurcations were initially set as follows: the fraction of force transmitted to the proximal phalanx and extensor mechanism was defined by the ratio of PCSA values of the muscles (e.g. 50:50 ratio for the RI muscle, see Table 3.2). The remaining transmission fractions were initially set to 50 % at each tendon bifurcation, e.g. 50 % of the RI muscle force transmitted to the extensor mechanism is transferred to the radial band, and the remaining 50 % is transferred to the central slip.

The initial bonobo model parameters were obtained from a dissection study on the contralateral arm of the bonobo specimen used in this study (see Appendix B for details). In brief, bone segment lengths were measured from a computed tomography (CT) scan using Blender (v2.64, Blender Foundation, Amsterdam, Netherlands) and custom Python scripts. Two via points for each tendon and each joint were then determined to obtain a description of the tendon paths consistent with that of An et al. [4] for the human finger model using the following method:

First, tendon paths were digitized at regular intervals relative to the closest bone using an electromagnetic motion tracking system (Patriot, Polhemus, Vermont, USA) and radio-opaque markers attached to each bone. Second, tendon path points were transformed into the CT coordinate system by registering the digitized bone marker locations to those identified in the CT scan. Third, one proximal and one distal point of each tendon relative to each joint which best represented an anatomical constraint (e.g. pulley of a flexor tendon) were chosen as the final via points. Initial force transmission fractions of the extensor mechanism of the bonobo were set in analogy to the human model.

3.2.2.4 Parameter identification

The goal of the parameter identification step was to minimize the difference between the predicted and experimentally measured fingertip forces resulting from single tendon loading in all four postures. Only via points and force transmission fractions within the extensor mechanism were included in the parameter identification since these parameters were assumed to be associated with the largest uncertainty. The model parameters x were then identified by solving the following optimization problem:

minimize
$$\sum_{i=1}^{n} (y_i - \hat{y}_i(\boldsymbol{x}))^2 + \sum_{j=1}^{m} w_j (x_j - x_{0,j})^2$$
 (3.14)

In the above equation, y is a one-dimensional vector containing the n components of the experimentally measured fingertip forces of all postures in the x-y plane, and \hat{y} contains respective model predictions. The second term in Equation 3.14 adds a penalty for large deviations of the model parameters x with respect to initial parameters x_0 and should avoid obtaining unphysiological models. The m model parameters contained in x comprise the x- and y-components of the tendon via points as well as the force transmission fractions of the extensor mechanism. w is a vector containing penalty weights which were manually set to 10 for all via point coordinates at the DIP and PIP joints, and to 1 at the MCP joint to qualitatively account for spatial constraints (i.e. more space is available at the MCP joint when compared to IP joints). Penalty weights of the extensor mechanism parameters were set to zero.

Since the FDS and FDP muscle parameters are independent of each other and of all other muscles attaching to the extensor mechanism, three separate optimizations were performed: (1) FDP muscle parameters (n=8 fingertip force components; m=12 via point parameters), (2) FDS muscle parameters (n=8; m=8), and (3) UI, RI, LU, EDC muscle parameters (n=32; m=32+4 via point plus extensor mechanism parameters). For the human model parameter

identification, the experimental fingertip forces y were averaged over all three specimens. The optimization was performed using a local optimizer (sequential least squares of SciPy [95]) to obtain the best set of parameters close to the initial, physiological parameters.

The remaining overall mismatch between predicted and measured fingertip forces was quantified by the root mean square error (RMSE) of the fingertip force components:

RMSE =
$$\sqrt{\frac{1}{n} \sum_{i=1}^{n} (y_i - \hat{y}_i(\boldsymbol{x}))^2}$$
 (3.15)

Additionally, the overall relative error $\mathsf{RMSE}_{\mathrm{rel}}$ was evaluated:

$$\text{RMSE}_{\text{rel}} = \frac{\text{RMSE}}{1/24 \cdot \sum_{k=1}^{24} \|\boldsymbol{F}_{\text{tip},k}\|}$$
(3.16)

where $F_{\text{tip},k}$ are the 24 fingertip force vectors of all six muscles and in all four postures. The mean magnitude of all fingertip forces was chosen as a reference value since it represents a PCSA-weighted mean of the fingertip forces generated by all muscles.

Finally, muscle-specific RMSE and $\rm RMSE_{rel}$ were evaluated in analogy to Equations 3.15 and 3.16, but considering only predicted and measured fingertip forces associated with the respective muscle.

3.2.2.5 Validation and comparison of models

The performance of the adjusted models was tested by comparing predictions of fingertip forces and net metacarpal bone forces to the experimental measurements during combined loading of the FDP and FDS tendons at two load levels. The differences were evaluated as the error of force vector magnitudes and directions in the x-y plane. Force magnitude errors were computed both in absolute values as well as relative to the experimental force magnitude.

In addition to the comparison between models and experiments, the MCP joint forces F_{joint} (see Equation 3.12) were compared qualitatively to the net metacarpal bone loads F_{bone} (see Equation 3.13) to judge the influence of tendon pulley or wrapping forces.

Finally, ratios of total muscle tension to predicted fingertip forces as well as metacarpal bone forces to fingertip force were evaluated and compared between human and bonobo models to investigate whether or not the implementation of a bonobo specific model is warranted.

3.2.3 Results

3.2.3.1 Parameter identification

Parameter identification led to physiologically plausible models both for the human and bonobo (see Figure 3.13; for the full set of optimized model parameters please refer to Appendix D). On average, the via points were shifted by 0.92 mm in the human model and 1.92 mm in the bonobo model, although individual points located at the MCP joint were shifted as much as 9.00 and 11.34 mm in the human and bonobo model, respectively. This shift reduced the overall RMSE (and RMSE_{rel}) of the fingertip forces from 0.53 N (52.10 %) to 0.11 N (10.73 %) in the human model and from 0.69 N (112.15 %) to 0.20 N (33.24 %) in the bonobo model.



Figure 3.13: Human and bonobo finger model before ("Init", top row) and after ("Opt", bottom row) optimization. White lines represent tendon paths, as defined by via points (white spheres). Black lines represent topological tendon connections due to the extensor mechanism.

Comparison of measured and predicted x- and y-components of the fingertip forces from all postures and muscles of the human finger shows that the remaining error (RMSE) of fingertip forces in the optimized model was similar for all muscles (Figure 3.14, left column), ranging from 0.08 N (FDP) to 0.15 N (FDS). Relative errors (RMSE_{rel}) were particularly large for muscles with small PCSA such as the LU (77.84 %) and low for muscle with large PCSA such as the FDP (3.55 %).

Absolute RMSE values of the fingertip forces of the bonobo finger model (see Figure 3.14, right) were again similar for all muscles, ranging from 0.14 N (LU) to 0.27 N (UI), but overall larger than in the human model. Relative errors (RMSE_{rel}) were again higher for muscles with smaller PCSA and ranged from 16.96 % (FDP) to 85.45 % (LU).



Figure 3.14: A comparison of measured fingertip force components in x- and y-direction (top/bottom row) to the human and bonobo model predictions for each muscle, both before ("init") and after parameter optimization ("opt"). Each muscle is represented by four points as fingertip force vectors were measured and predicted in four postures. EDC: extensor digitorum communis; FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical

3.2.3.2 Validation and comparison of models

Good agreement between experimental results and predicitions was observed in the combined extrinsic flexor tendon loading scenario at two load levels (Figure 3.15). Specifically, average directional and magnitude errors of the fingertip force vectors (human/bonobo) were 3.10 $^{\circ}$ / 5.76 $^{\circ}$ and 0.25 N (11.03 %) / 0.2 N (11.70 %).



Figure 3.15: A comparison of measured and predicted fingertip force vectors engendered by combined loading of the FDP and FDS muscles at two load levels in four postures. In the human data plots (left column), the coloured areas represent the experimental mean ± 1 standard deviation. In the bonobo data plots (right column), the coloured areas represent the measurement ± 10 % of the magnitude and ± 10 °. FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis

Similar to fingertip forces, metacarpal bone loads resulting from combined tendon loading were in good agreement with experimental results for both the human and bonobo finger model (Figure 3.16), with average errors (human/bonobo) of $3.32 \circ / 0.57 \circ$ and 0.16 N (2.34 %) / 0.26 N (4.10 %). Interestingly, the direction of the metacarpal bone force vector (F_{bone}) showed low variability with respect to posture and was negatively correlated with MCP joint angles, i.e. higher flexion at the MCP joint resulted in more palmarly oriented net force on the metacarpal bone (see Figure 3.16). In contrast, the directions of the actual joint loads F_{joint} (i.e. the bone loads without tendon wrapping/pulley forces) was positively correlated with MCP joint angle and were more variable with respect to finger postures when compared to the bone loads.



Figure 3.16: Net metacarpal bone force vectors (F_{bone}) predicted for combined loading of the FDP and FDS muscles at two load levels in four postures (solid lines) compared to experimental measurements (coloured areas). In the human data plots (top row), the coloured areas represent the experimental measurement ±1 standard deviation. In the bonobo data plots (bottom row), the coloured areas represent the measurement ±10 % of the magnitude and ±10 °. Additionally, the MCP joint load vectors (F_{joint}) are plotted with dashed lines for comparison. FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis

Finally, the ratios of tendon load to fingertip force, as well as bone load magnitude to fingertip force were compared between the optimized bonobo and human finger model in the combined tendon loading scenario. The average tendon load to fingertip force ratio was approximately 42 % higher in the bonobo (mean: 5.36; range: 5.06 to 5.66) when compared to the human (mean: 3.78; range: 3.54 to 4.10). The average ratio of bone load magnitudes to fingertip forces were approximately 55 % higher in the bonobo (mean: 4.44; range: 4.19 to 4.68) when compared to the human model (mean: 2.87; range: 2.55 to 3.15).

3.2.4 Discussion

The goals of this study were (1) to identify the parameters of both a human and bonobo finger model which minimize the error of predicted fingertip forces and (2) to compare the adjusted model predictions to experimental data in different load cases for validation. The parameter identification showed that even minor parameter changes led to a substantial reduction in the predictive error, although relative errors associated with intrinsic muscles remained comparatively large. The adjusted model predictions of fingertip forces and metacarpal bone loads during combined loading of extrinsic flexor muscles were in good agreement with experimental measurements, leading to average errors of force direction and magnitude below 6 $^{\circ}$ and 12 %, respectively.

To the best of the author's knowledge, this is the first study trying to identify optimal musculoskeletal finger model parameters using forces measured in vitro. Previous studies have already shown that the accuracy of moment arms of finger models can be considerably improved by adjusting via point locations [114] or by adding optimally positioned tendon wrapping geometries [105]. Qiu and Kamper [155] compared predicted to experimentally measured fingertip forces but needed to manually adapted proximal tendon via point locations at the MCP joint. In this study, it could be shown that a simple local optimization procedure allows to drastically reduce the predictive error while keeping model parameter changes to a minimum and thereby maintaining physiologically reasonable tendon paths. The large influence of even minor model parameter adjustments further highlights the parameter sensitivity of the models and warrants a careful validation procedure.

The fingertip forces resulting from intrinsic muscle (RI, UI, LU) loading generally led to larger relative errors when compared to extrinsic muscles. These errors might be caused by model simplifications but also by limitations of the experimental test setup. Although previous studies used a similar experimental design and specimen preparation procedure [5], it was discovered that the removal of soft tissue at the metacarpal level influenced the intrinsic muscle tendon path to a larger extent than expected, e.g. leading to excessive bowstringing. Experimental setups which keep more of the soft tissue intact were previously presented [155, 211], but applying load to intrinsic muscles remains challenging and was still not perfectly physiological in these studies. For instance, Valero-Cuevas et al. [211] applied the load of the dorsal interosseus muscle via nylon chords attached to a screw placed at the base of the proximal phalanx. Moreover, direct measurement of metacarpal bone loads is further complicated with these experimental setups. In contrast to the intrinsic muscles, the force transmission of extrinsic flexors, which are particularly important for forceful grasping [71, 129, 176], could be predicted with lower relative errors. Particularly the fingertip forces and metacarpal bone loads from the combined

tendon loading regime highlighted the models' good predictive abilities, with average errors of directions and magnitudes below 6 $^{\circ}$ and 12 %, respectively. These values are comparable to the validation results of Qiu and Kamper [155], who reported average errors of fingertip force direction and magnitude *beyond one standard deviation* ranging from 0 to 1.7 $^{\circ}$ and from 0 to 10 % for their model when compared to in vitro measurements.

The difference between the human and bonobo model was quantified by the ratios of muscle force to fingertip forces as well as metacarpal bone load magnitudes to fingertip forces; values that are often used to quantify the efficiency of force transmission. In the literature, ratios of extrinsic flexor (FDP/FDS) muscle force to fingertip force were reported to be highly variable and posture dependent, ranging from 0.71 to 7.92 [51, 107, 182]. Although both the human and bonobo model ratios fall within this range (average of 3.78 and 5.36, respectively) and the sample size used in this study is too small to draw direct conclusions, the larger muscular effort to counteract external load in the bonobo finger can be interpreted in terms of anatomical differences. Specifically, bonobo hand bones are longer but not necessarily wider at the epiphyses when compared to humans [194], which leads to large lever arms for externally applied loads relative to the moment arms of the muscles. Such differences cannot be captured with mere isotropic model scaling and justify the use of a species-specific set of model parameters.

Another interesting observation in this study was the direction of net metacarpal bone loading (F_{bone}) when compared to MCP joint loading (F_{joint}) . The metacarpal bone force direction varied little with posture, was mainly aligned with the long axis of the metacarpal bone, and was even slightly negatively correlated with MCP joint angle. This is in contrast to the MCP joint load directions predicted by the models presented here as well as in other studies [226], which showed large variability and a positive correlation with the MCP joint angle. These results indicate that pulley forces play a larger role in the metacarpal bone loading than initially expected. Although individual studies claimed that modelling the tendon-pulley interaction is important to obtain realistic dynamic finger movements [115], their effect on metacarpal bone loading was not investigated so far and surprising in its magnitude.

Several limitations of this study remain to be mentioned. An obvious and substantial limitation is the low sample size, which was mainly caused by the rarity of fresh frozen ape specimens. Still, the idea of using a simple local optimization approach to improve the accuracy of the model could be tested and general biomechanical differences of the human and bonobo finger could be discussed. Another limitation is the coarse approximation of physiological intrinsic muscle/tendon paths due to dissection of soft tissues at the metacarpal level in the experiments. Other experimental designs [155, 211] may have kept more of the soft tissue intact but would have complicated intrinsic muscle loading and the measurement of metacarpal bone forces. Also, the parameter identification was limited to forces in the sagittal (x-y) plane and included only parameters of the tendon paths and extensor mechanism. Other parameters, such as location and orientation of joint axes might also influence the force transmission [212] and their inclusion might help to further improve the accuracy of the predictions.

3.2.5 Conclusions

This study presents the first attempt to implement both a human and bonobo finger, and to optimize the models using fingertip forces measured in vitro. Although experiments and models could be further improved, good agreement between predicted and measured fingertip forces as well as metacarpal bone loads were found upon extrinsic flexor tendon loading. Since extrinsic flexor muscles are most relevant for forceful grasping, these results suggest that the models are likely accurate enough for comparisons of joint loads engendered by human and non-human primate activities where differences are expected to be large (e.g. tool use and suspension). Albeit compromised by sample size, the observed differences between human and bonobo model were in line with general biomechanical considerations and indicate that the use of a species-specific set of parameters is warranted in comparative studies.

3.2.6 Related publications and declaration of contributions

Section 3.2 is based on the manuscript "Musculoskeletal models of a bonobo and human finger: Parameter identification and comparison to in vitro experiments" *in preparation* with co-authors Szu-Ching Lu, Tracy L. Kivell, Evie Vereecke, and Dieter H. Pahr.

Author contributions. The first author and author of this thesis, *Alexander Synek*, designed the study, performed all computations as described in the methods section and supported the experimental design and data collection. *Szu-Ching Lu* designed the experimental test setup, performed the specimen preparation and experiments, and provided all necessary experimental data. *Tracy L. Kivell* supervised Szu-Ching Lu and contributed to the experimental design and interpretation of the results. *Evie Vereecke* performed the specimen dissection and supported the data collection. *Dieter H. Pahr* supervised the work of Alexander Synek and supported the interpretation of the results.

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3.3 Application: Prediction of MCP joint loads

3.3.1 Introduction

In the previous section, musculoskeletal finger models of a human and bonobo digit were implemented and adjusted to best match in vitro experimental data. These models shall now be used to establish a link between habitual manual activities of humans and non-human primates to characteristic MCP joint loads (subgoal 2 of this thesis, see Figure 3.1) and thereby improve the interpretation of the joint load predictions of the inverse remodelling algorithm presented in Section 2.3.

As explained in Section 2.3, it was assumed that MCP joint load directions roughly coincide with habitual joint postures (e.g. flexed joint postures induce dorsally oriented joint loads) and that joint load magnitudes are directly related to external loads acting on the finger (e.g. larger external loading causes larger joint loading). These are common assumptions also used in anthropological studies investigating differences of bone architecture [35, 201]. However, these qualitative assumptions neglect the influence of the muscle forces, which, as shown in the previous section, might outweigh external loads by a factor of up to seven [51, 107, 182]. Musculoskeletal models can be used to obtain estimates of joint loads for a given posture and external finger loading which do account for muscle forces. Such models were previously used to predict finger joint loads during generic grasps such as pinch or power grasp [72, 221, 226] or activities such as tool use [164]. However, most of these studies focused on investigating joint load magnitudes rather than joint load directions, even though joint load directions are equally, if not more, important for functional inferences (e.g. to distinguish knuckle-walking from tool use activities). Moreover, finger joint loads engendered by primate locomotor activities such as climbing, suspension, and knuckle-walking have not yet been investigated at all. This is likely because experiments with non-human primates are much more challenging when compared to experiments with human subjects; including organizational, ethical, but also methodological issues.

This study represents a first attempt to face these challenges and investigate fundamental differences of MCP joint loads during various activities of humans and non-human primates using the musculoskeletal models presented in Section 3.2 and a collection of in vivo measurements of finger posture and external loading. The primary objectives were (1) to investigate differences of joint loads during tool use and suspension of humans, and (2) to investigate differences of joint loads during different types of locomotion (vertical climbing, suspension, knuckle-walking) of bonobos. The secondary objective was to test whether joint posture and total external

finger loads are good proxies for MCP joint loading, i.e. whether joint load directions are well represented by MCP joint angles and whether joint load magnitudes can be directly related to external finger loading.

3.3.2 Materials and methods

3.3.2.1 Study outline

In vivo data of bonobo locomotion and human suspension were directly obtained from previous experiments of project partners [127, 174] and human tool use experiments were repeated following a previously presented protocol [230] (see Figure 3.17). Additional evaluations were performed to obtain finger posture and external loading of the third digit at the time of peak loading. These data were applied to musculoskeletal models of a human and bonobo finger (see Section 3.2) to estimate MCP joint load vectors (i.e. load magnitude and direction) during each activity. Differences of joint loads were then evaluated between human suspension and tool use activities (objective 1 of this study), as well as between different locomotor modes (vertical climbing, suspensory locomotion, knuckle-walking) of the bonobos (objective 2 of this study). Additionally, the MCP joint postures and external finger loading evaluated from the experiments were compared to MCP joint load directions and magnitudes predicted by the models to accomplish the secondary objective.



Figure 3.17: Study outline. External loading and finger posture were experimentally captured in various in vivo experiments of humans and bonobos, used as an input for musculoskeletal finger models, and the predicted joint loads were compared among activities. MCP: metacarpophalangeal

3.3.2.2 In vivo Experiments

Human tool use

Tool use experiments were conducted following the protocol previously presented by Williams-Hatala et al. [230] to quantify finger loading, but extended for this study to simultaneously capture finger kinematics. The data collection was approved by the School of Sport and Exercise Sciences Research Ethics and Advisory Group (Prop 54_2017_18). Three subjects (age: 27-42 years; 1 female, 2 male) were recruited to perform activities with different tools, including cracking almonds, hazelnuts, and bones with hammer stones, cutting meat with stone flakes and hand axes of two different sizes each, and knapping with hammer stones (see Williams-Hatala et al. [230] for details). The study aimed to collect at least five to ten successful trials in each activity.

The kinematics of the third digit were captured by applying 4 mm diameter retroreflective markers at the dorsum of the hand and fingers (see Figure 3.18) and tracking their movement using a Qualisys motion capture system with 11 cameras (Qualisys AB, Goteburg, Sweden; sampling rate: > 100 Hz). The joint flexion angles of the DIP and PIP joints were then computed as the angles enclosed by vectors connecting the markers at the articulating finger segments (e.g. m1-m2 vs. m3-m4 to obtain the DIP flexion angle, see Figure 3.18). The MCP joint flexion/extension and radial/ulnar deviation were quantified following Su et al. [193] using Eulerian angles where the three markers at the dorsum of the hand (markers m7 to m9) define the base coordinate system.



Figure 3.18: Pressure sensors and marker locations for the tool use experiments. The schematic figure on the right shows the finger joints and labels of finger markers (m1 to m9). MCP: metacarpophalangeal; PIP: proximal interphalangeal; DIP: distal interphalageal

Finger loading was quantified using $17 \times 17 \text{ mm}^2$ pressure sensors (Novel Pliance S2134 manual pressure system, novel GmBh, Germany; sampling rate: > 100 Hz) attached to the palmar surface of each finger segment (i.e. three sensors for the third digit; see also Figure 3.18). Normal forces acting on each finger segment were then computed by multiplying the recorded pressure with the true sensor cell area which was slightly smaller than its external dimensions $(15.94 \times 15.94 = 254 \text{ mm}^2)$. Peak loading was defined as the point in time when the sum of all measured forces was maximal.

Human suspension

Experimental data on human suspension were previously acquired and presented in the thesis of Lockwood [127]. The data collection was granted from the Faculty of Social Sciences Research Ethics Advisory Group for Human Participants (reference number 0331617). In brief, six subjects (age: 24-41 years; 3 female, 3 male) were recruited to engage both in static and dynamic single-handed suspension on horizontally aligned poles of three different diameters (45, 80, and 105 mm). The study aimed to collect at least three successful trials for each subject, activity, and diameter.

Finger kinematics were captured using the same motion capture setup, marker configuration, and processing methods as described for the tool use experiments described above. Finger loading was quantified using a pressure mat consisting of 16×32 sensor cells with 10×10 mm² sensor size (S2119 pressure mat, Novel GmbH, Munich, Germany, 35 Hz sampling rate) wrapped around the pole. The location of the pressure mat was digitized using additional retroreflective markers attached to the pressure mat, which enabled projecting each finger marker into the pressure mat coordinate system and to identify marker specific pressures (see Lockwood [127] for details and Figure 3.19 for clarification). The data was evaluated at the point in time when the largest pressures were detected at the third digit.

Whereas Lockwood [127] only computed peak pressures at individual sensor cells, further processing was required for this study to obtain finger loads for each finger segment. This was performed in an automated fashion using custom Python scripts (see Figure 3.19): First, the long axis of the digit in the pressure mat coordinate system was approximated by a straight line fitted to the finger marker locations in a least squares sense. Second, the joint centre locations were defined as the mean of the finger markers proximal and distal to the respective joint, projected onto the digit axis. Finally, the pressure mat data was resampled (factor: 5) and finger segment loads were defined as the cumulative force within 16 mm wide rectangles aligned with the digit axis. 16 mm width was chosen as this value is consistent with the true side length of the pressure sensors used in the tool use experiments.



Figure 3.19: Identification of finger marker locations and finger segment force evaluation in the human suspension experiments. Finger markers were projected into the pressure mat coordinate system, the digit axis was approximated by a least squares fit to markers m1 to m7, joint centres (MCP/PIP/DIP) were identified, and the finger segment loading for the proximal (PP, cyan), middle (MP, magenta), and distal (DP, purple) phalanx was estimated as the cumulative force within the indicated, 16 mm wide rectangular areas. MCP: metacarpophalangeal; PIP: proximal interphalangeal; DIP: distal interphalageal

Bonobo locomotion

The experimental bonobo locomotion data was previously collected and presented by Samuel et al. [174] with ethical approval granted by the Centre for Research and Conservation in Antwerp, Belgium. In brief, hand pressures and qualitative kinematics during vertical climbing, suspension and arboreal knuckle-walking were collected from eight adult captive bonobos (taxon: *Pan paniscus*; gender: 4 female, 4 male) using an instrumented pole (120 mm diameter) placed in an indoor enclosure at the Planckendael Zoo (Royal Zoological Society of Antwerp, Belgium). Since no contact with the bonobos was allowed, trials were only recorded when the individuals voluntarily moved along the pole. The pole was positioned vertically to collect data during vertical climbing locomotion and horziontally to collect data during suspension and knuckle-walking.

In order to capture finger kinematics, three cameras (GigE ac640-120gm, Basler AG, Ahrensburg, Germany; sampling rate: 120 Hz) were positioned around the pole (see Figure 3.20) and used to film the hands in contact with the substrate. Pressure data were measured in analogy to the human suspension experiments, i.e. using a Novel pressure mat (S2119 pressure mat, Novel GmbH, Munich, Germany; sampling rate: 35 Hz) wrapped around the pole.

In addition to the evaluations presented by Samuel et al. [174], quantitative finger kinematics and finger segment loading were required for this study. Kinematics were evaluated at moment of peak pressure using still images of the three cameras and the video digitization software DLTdv3 [81]. In order to increase the sample size, kinematics of digits two and four were also included. Since the obstructed view did not allow an estimation of the MCP joint angle during suspension, these missing angles were estimated using a multiple linear regression model of the human suspension data using DIP and PIP joint angle as well as the ratio of digit length to pole diameter as predictors ($R^2 = 0.46$, RMSE = 8.2°). Finger segment forces were estimated manually based on the pressure mat data and still images of the cameras, as quantitative data was insufficient for an automated evaluation as described for the human suspension experiments.



Figure 3.20: Sample images of the cameras capturing the bonobo finger kinematics during knucklewalking, suspension and vertical climbing. Just one out of three camera angles is shown for each activity.

Due to several challenges faced during the collection of the bonobo locomotion data (e.g. overall low number of available trials and difficulties in the digitization of finger postures due to obstructed views), the number of trials where finger loading and all joint angles could be evaluated simultaneously was too low to perform quantitative comparisons. As a result, another strategy was pursued: First, each of the six minimally required input quantities for the musculoskeletal models (three flexion joint angles, three finger segment loads) was statistically modelled by fitting probability distributions to the experimental measurements. Second, individual trials were generated by randomly combining joint postures and finger segment loads drawn from the fitted probability distributions. This method allowed obtaining rough estimates of the finger posture and loading which represent the upper bound of the variability since correlations are not considered. Details of this method are presented briefly in the following.

Experimentally obtained sample sizes for each activity and each of the six input quantities ranged from n=4 to n=23, except for the DIP and PIP joint angles of knuckle-walking where only a single measurement was available. Joint angles were assumed to follow normal distributions and the finger segment loads were assumed to follow gamma distributions as they were estimated from non-negative pressure measurements [86, 111]. 100 trials were then randomly drawn from these probability distributions using the Latin hypercube method [137]. Using 100 trials ensured that the deviation between the probability distribution parameters of the randomly drawn and the experimental sample of each quantity were acceptable (< 5 %). Since DIP and PIP angles during knuckle-walking could only be evaluated in one trial, the measured value was assumed to represent the mean and the standard deviation was set to the mean standard deviation of all measured joint angles (5.60 °).

3.3.2.3 Musculoskeletal models

Model description

Musculoskeletal models of the third digit of a human and bonobo (as described in Section 3.2 and shown in Figure 3.21, left) were used to predict joint loads taking into account both external forces and estimates of muscles forces. In brief, both models comprise of three movable segments (distal phalanx, middle phalanx, proximal phalanx) interconnected by three joints (DIP, PIP, MCP) with a total of four rotational DoF (flexion/extension at the DIP and PIP joint; flexion/extension and ulnar/radial deviation at MCP joint). The fingers are actuated by six muscles, namely the flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), extensor digitorum communis (EDC), radial interosseus (RI), ulnar interosseus (UI), and the lumbrical (LU).



Figure 3.21: Outline of the musculoskeletal model topology including three movable bone segments (PP/MP/DP), one fixed segment (MC), three joints (MCP, PIP, DIP), and six muscles (FDP/FDS/EDC/RI/UI/LU). Joint angles θ and external loading $F_{\rm ext}$ are indicated schematically in the right figure. For an explanation of the abbreviations, the reader is referred to the main text or the list of abbreviations.

Tendon paths were modelled with a via point-based approach and used to compute posture dependent moment arms of each muscle at each DoF. Bowstringing between via points was assumed for all tendons unless the tendon would naturally wrap around the bone (e.g. flexors in hyperextension), in which case Landsmeer's model 1 [33] was used. The extensor mechanism was modelled using Winslow's rhombus, which simplifies the extensor mechanism to a finite set of tendon segments, namely the radial terminal slip (TS), central slip (CS), radial band (RB), and ulnar band (UB) (see Figure 3.21, left). The model parameters for both the human and bonobo model including finger segment lengths, via point locations, and force distribution parameters within the extensor mechanism were directly taken from the parameter identification study (see Section 3.2 and Appendix D).

Computation of muscle forces

Muscle forces counterbalance external loads and, thereby, contribute largely to joint loads. The estimation of muscle forces in this study followed the general scheme as presented in Section 3.1.2 and will be explained briefly in the following. Assuming a static finger posture, the muscle tensions $\boldsymbol{t} = [t_{\rm RI}, t_{\rm LU}, t_{\rm UI}, t_{\rm FDP}, t_{\rm FDS}, t_{\rm EDC}]^{\rm T}$ must fulfil the following torque equilibrium equation:

$$\sum_{j} \boldsymbol{J}_{\boldsymbol{p}_{j}}^{\mathrm{T}} \boldsymbol{F}_{\mathrm{ext},j} + \boldsymbol{T}\boldsymbol{t} = \boldsymbol{0}$$
(3.17)

In the above equation, $J_{p_j}^{T}$ is the 4×3 transpose Jacobian matrix transforming external loads $F_{\text{ext},j}$ applied at location p_j into torques around all four DoF. T is the 4×6 force transmission matrix which contains effective moment arms of all muscles and, therefore, maps the 6×1 muscle tension vector t to joint torques. Effective moment arms account both for the moment arm of individual tendon segments at a specific DoF, but also for the force distribution dictated by the extensor mechanism (see Sections 3.1 and 3.2 for details). External forces acting on each of the three digit segments (see Figure 3.21) were defined using the force magnitude measured in the in vivo experiments as explained above. All forces were assumed to act at the centre of the respective bone segment and perpendicular to the long bone axis [71, 72].

Since the number of muscles exceeds the number of DoF, additional assumptions have to be made in order to compute muscle forces. Here, it was assumed that the neural system aims to minimize muscle stress [175, 219] and estimates of the muscle forces were obtained by solving the following optimization problem:

$$\begin{array}{ll} \underset{t}{\text{minimize}} & \sum_{i} \left(\frac{t_{i}}{\text{PCSA}_{i}} \right)^{2} \\ \text{subject to} & \sum_{j} J_{p_{j}}^{\text{T}} F_{\text{ext},j} + Tt = \mathbf{0}, \\ & \mathbf{0} \leq t \leq t_{\text{max}} \end{array}$$
(3.18)

In Equation 3.18, $PCSA_i$ is the physiological cross sectional area of muscle *i* and t_{max} contains the maximum isometric muscle forces. Any feasible solution of Equation 3.18 satisfies the torque equilibrium equations (Equation 3.17) within the physiological constraints for the muscle tensions. t_{max} was computed using the PCSA of each muscle, the maximum specific muscle stress σ_{max} , and a correction factor *s* following Goislard De Monsabert et al. [71]:

$$t_{\max,i} = s \cdot \mathrm{PCSA}_i \cdot \sigma_{\max} \tag{3.19}$$

 $\sigma_{\rm max}$ was set to 35.4 N/cm² [210, 236] and *s* was introduced to compensate the low PCSA values reported in cadaveric studies which are usually obtained from elderly donors [71]. For the human model, the PCSA data were taken from Chao et al. [33] and the correction factor was set to s=3 as this value was found to maximize the number of solvable trials. No correction was imposed for the bonobo model (i.e. s=1) since the PCSA data was obtained from a young individual (see Section 3.2 and Appendix B).

Computation of MCP joint loads

The joint load computations also followed the general scheme presented in Sections 3.1.2 and 3.2. In brief, the external forces $F_{\text{ext},j}$ and the estimated muscle tensions t_i of each of the six muscles were used to compute the MCP joint loads based on the static force equilibrium equation:

$$F_{\text{joint}} = -\left(\sum_{j} F_{\text{ext},j} + \sum_{i} t_{i} u_{i}\right)$$
 (3.20)

In the above equation, u_i is the unit vector pointing from the distal to the proximal via point of muscle *i* (see also Section 3.2 and specifically Figure 3.12). In case tendon segments would naturally wrap around the bone in a specific posture, direction u_i was considered constant with respect to the distal bone to mimic the effect of tendon wrapping geometries (see also Appendix C). The computations of muscle forces and joint loads were verified using a simplified finger model in OpenSim (see Appendix C).

Compensation of model simplifications using reserve actuators

In order to expand the set of feasible solutions and to compensate for missing modelling details (e.g. joint capsule, ligaments, or contact between finger segments), reserve actuators were implemented following the suggestions of Hicks et al. [82]. These reserve actuators generate torques at each DoF, i.e. they contribute to joint torque equilibrium, but do not contribute to joint loads. They were implemented in this study as muscles with unit length moment arms and unconstrained tendon tensions in the optimization problem of Equation 3.19 and their "PCSA" was used to control their contribution to joint torques. Specifically, the PCSA of each reserve actuator acts as a weight in the cost function of Equation 3.19 and leads to large contributions.

to joint torques if set to high values, and low contributions if set to small values. For all DoF and activities except PIP joint flexion/extension during knuckle-walking, the reserve actuator PCSAs were set to 0.0001 cm² and the simulation was considered successful only if the reserve actuator joint torque remained below 10 % of the torque engendered by external loads at the respective DoF. During knuckle-walking, PIP joint flexion/extension torques were assumed to be the result of contact between finger segments rather than muscle force (see Figure 3.20), such that the reserve actuator PCSA was set to 1 and the 10 % torque contribution limit was suspended.

3.3.2.4 Investigating activity-related differences of joint loads

Joint loads were investigated based on their magnitude ($F_{\text{joint}} = ||F_{\text{joint}}||$) and load direction relative to the long axis of the metacarpal bone (denoted by angle φ in the following) in the sagittal plane (see also symbolic insets in Figure 3.23, left column). Activity-related differences of MCP joint load magnitudes and directions were quantified using Cliff's delta [44]. Cliff's delta (d) is a robust measure for effect size, i.e. it allows to judge the relevance of sample differences taking into account the sample distribution. d ranges from from -1 to 1 and can be used to categorize effects into negligible (|d| < 0.147), small (|d| < 0.330), medium (|d| < 0.474), and large ($|d| \ge 0.474$) [165]. For the human data, the hypothesis of |d| = 0 (i.e. no effect) was additionally tested and respective *p*-values were computed following Hogarty and Kromrey [83]. Hypothesis testing was not performed for the bonobo data, as the chosen size of the randomly generated samples would strongly affect the test results.

3.3.2.5 Investigating the relation of joint posture and external loading to predicted joint loads

As mentioned in the introduction, joint posture and total external finger loads are frequently used as proxies for joint load direction and magnitude, respectively [35, 201]. In order to test these assumptions, activity-related differences were also evaluated for MCP joint flexion/extension angles ($\theta_{MCP,FE}$) and total external finger load $F_{ext,tot} = \sum_{j} ||F_{ext,j}||$. The extent of the differences were again quantified using Cliff's delta as explained above. The relation between measured total external finger loading and predicted joint load magnitudes was further investigated by computing activity-specific ratios $F_{joint}/F_{ext,tot}$. Finally, measured MCP joint angles $\theta_{MCP,FE}$ and predicted joint load directions φ were compared with robust linear regression models established using the "statsmodels" package of Python [183].

3.3.3 Results

3.3.3.1 Tool use and suspension of humans

Experimentally measured finger posture and external loading

Evaluation of posture and external loading data obtained from all 173 trials (suspension: 72 trials; tooluse: 101 trials) from the in vivo experiments showed that individual joint angles were broadly similar, whereas both the load magnitude and load distribution among finger segments was clearly different (Figure 3.22). In particular, overall finger loads were larger during suspension and proximal finger segments (proximal and medial phalanx) were subject to more loading when compared to tool use.



Figure 3.22: Boxplots of the experimentally measured finger posture (θ , left panel) and external loading (F_{ext} , right panel) during tool use and suspension. The insets on the very right show the average posture and loading during tool use and suspension, respectively. See also Figure 3.21 for a graphical representation of the variables.

Activity-related differences of predicted MCP joint loads

Predictions of joint loads were successful for 159 out of the 173 experimental trials (91.9 %), i.e. solutions were found without violating the limits of the reserve actuators. Predicted joint load magnitudes (Figure 3.23, top left panel) were substantially larger during suspension when compared to tool use (|d| = 1.00, p < 0.001). The effect of activity on the MCP joint load direction (Figure 3.23, bottom left panel) was negligible with |d| = 0.05 (p = 0.571).



Figure 3.23: Boxplots of the predicted MCP joint load magnitudes and directions (left column) and the experimentally measured total external finger loads and MCP joint angles (centre column). Black squares indicate the mean. The rightmost column shows the ratios of MCP joint loads to total external finger loading (top) as well as the robust regression of MCP joint load directions vs. MCP joint angles (bottom). MCP: metacarpophalangeal

Comparison of MCP joint posture and total external loading to MCP joint loads

The activity-related differences of MCP joint posture and total external loading were consistent with the differences observed in the predicted MCP joint loads. Specifically, total external finger loading was substantially larger during suspension when compared to tool use (Figure 3.23, top centre panel), with an effect size of |d| = 1.00 (p < 0.001), and the difference of MCP joint angles between suspension and tool use was negligible (|d| = 0.10, p = 0.289) (Figure 3.23, bottom centre panel).

The ratios of joint load to total external loading (Figure 3.23, top right panel) were more variable and larger during tool use, with a small but significant effect (|d| = 0.27, p = 0.002). Joint load directions were highly correlated to MCP joint angles (Figure 3.23, bottom right panel) for both activities (suspension: $R^2 = 0.93$; tool use: $R^2 = 0.74$). However, joint load directions were consistently smaller than MCP joint angles, i.e. joint loads were more aligned with the long axis of the metacarpal bone than the joint posture would suggest.

3.3.3.2 Knuckle-walking, climbing, and suspensory locomotion of bonobos

Measured finger posture and external loading

Evaluation of the stochastically sampled finger postures and loading of the bonobos during knuckle-walking, climbing, and suspensory locomotion (100 trials in each group) showed that joint angles were broadly similar during suspension and climbing, although the finger was overall less flexed during climbing (Figure 3.24, left panel). As expected, the finger posture during knuckle-walking was clearly different from climbing and suspension, with a strongly hyperextended MCP joint and highly flexed PIP joint. Joint loading patterns were different between all three locomotor modes (Figure 3.24, right panel). In particular, finger segment loads were large and only acting at the middle phalanx during knuckle-walking, evenly distributed among finger segments during suspension, and concentrated distally during climbing.



Figure 3.24: Boxplots of the experimentally measured finger posture (θ , left panel) and external loading (F_{ext} , right panel) during different locomotor modes. The insets at the bottom show the average posture and loading during knuckle-walking, suspension, and climbing. Note that due to missing data, radial/ulnar deviation at the MCP joint was set to zero for all activities. See also Figure 3.21 for a graphical depiction of the variables.

Activity-related differences of predicted MCP joint loads

294 of 300 trials (98.0 %) could be simulated successfully within the boundaries of the reserve actuator limitations. Interestingly, predicted joint load magnitudes were broadly similar between all locomotor activities (Figure 3.25, top left panel), with negligible effect sizes |d| ranging from 0.07 to 0.12 for all pairwise comparisons. MCP joint load directions were strongly affected by activity, with |d| ranging from 0.93 to 1.00 (Figure 3.25, bottom left panel).



Figure 3.25: Boxplots of the predicted MCP joint load magnitudes and directions (left column) and the experimentally measured total external finger loads and MCP joint angles (centre column). Black squares indicate the mean. The rightmost column shows the ratio of MCP joint loads to total external finger loading (top) as well as the robust regression of MCP joint load directions vs. MCP joint angles (bottom). MCP: metacarpophalangeal

Comparison of MCP joint posture and total external loading to MCP joint loads

In contrast to predicted MCP joint load magnitudes, total external finger loading was moderately to strongly affected by activity (see Figure 3.25, top centre panel), with |d| ranging from 0.44 to 0.75. Differences of the MCP joint angles (see Figure 3.25, bottom centre panel) were

consistent with the differences in MCP joint load directions, i.e. a strong effect of activity was found in all pairwise comparisons (|d| ranging from 0.97 to 1.00).

The ratios of MCP joint load magnitudes to total external loading (Figure 3.25, top right panel) were strongly affected by activity (|d| ranging from 0.82 to 1.00), with particularly low ratios during knuckle-walking and high ratios during climbing activities. Similar to human tool use and suspension activities, MCP joint load directions were generally correlated to MCP joint angles (Figure 3.25, lower right panel) with a goodness of fit (R^2) from 0.38 (suspension) to 0.91 (knuckle-walking). In activities using flexed postures (climbing/suspension), MCP joint load directions were again consistently smaller than MCP joint angles, whereas almost a 1:1 relation was found for knuckle-walking. As a result, the differences between knuckle-walking and activities with flexed finger postures (climbing/suspension) were large in terms of MCP joint angles (average difference: 83.21 °) but considerably smaller in terms of MCP joint load directions (average difference: 56.29 °) (see Figure 3.25, bottom left and centre panel).

3.3.4 Discussion

The goals of this study were to investigate fundamental differences of MCP joint loading between (1) tool use and suspension activities and (2) various primate locomotor modes, and to test whether joint posture and external finger loading can be used as proxies for joint load direction and magnitude. A comparison of tool use and suspension activities showed that differences of peak MCP joint loads are evident in terms of load magnitudes but not load directions. These results were in line with experimental observations of larger external loads during suspension and highly similar MCP joint postures. However, MCP joint load vectors were more aligned with the long axis of the metacarpal bone than the joint posture would suggest. Interestingly, different locomotor activities engendered clearly different external finger loading but broadly similar MCP joint load magnitudes. Differences of joint load directions during these locomotor modes were evident but smaller than the MCP joint angles would suggest.

Although differences of MCP joint loads during tool use and suspension were generally clear and in line with observations of external finger loading and posture, there were two interesting observations that are potentially relevant for functional interpretations of bone loading and, ultimately, bone architecture. First, the MCP joint load angles did not show a 1:1 relation to MCP joint angles. Instead, the MCP joint load direction were roughly 20-30 ° lower than the MCP joint angles, indicating that large shear forces must act at the proximal phalanx base. These shear forces were previously reported to be the effect of the extrinsic flexor muscle forces in flexed postures and counteracted to a large extent by the congruent shape of the joint surfaces, which enable deviations of joint load direction and joint angle of at least 20 ° [223]. Collateral ligaments may also counteract shear forces [33, 138, 226] but could not be implemented in the finger models due to a lack of available data particularly for the bonobos. Thus, the quantitative difference between MCP joint angle and joint load direction reported here must be considered as an upper bound. The second interesting effect observed when comparing tool use to suspension simulation results was that the ratio of joint load to external load was highly variable and larger during tool use (tool use: 4.56 ± 3.15 ; suspension: 2.75 ± 0.73) due to different patterns of external finger loading. This is in line with a previous study comparing pinch and power grasp [72] where even larger differences of joint load to external load ratios (pinch grip: ~9; power grasp: ~3) were reported. Taken together, these results suggest that the true difference of peak joint load magnitudes between tool use and suspensory locomotion might be more similar than expected from external finger loading.

The comparison of peak MCP joint loads during knuckle-walking, suspension, and climbing of bonobos showed that load magnitudes were remarkably similar (effect size |d| below 0.12). This is in contrast to previous studies which hypothesized that joint load magnitudes engendered by knuckle-walking are likely higher due to the magnitude and orientation of external loads which would directly compress the metacarpal bone [201]. In this study, it was found that joint loads during knuckle-walking are diminished by relatively low ratios of joint loading to external loading. From a biomechanical point of view, these low ratios can be explained by the lower lever arm of external forces with respect to the MCP joint (see Figure 3.24), which results in a lower joint torque demand and, finally, lower muscle activity. Although this consideration seems intuitive even without musculoskeletal models, this study allowed quantifying this effect taking into account realistic postures and loading scenarios. A possible limitation of the models is that quasistatic conditions were assumed although finger muscles might also contribute to propulsion at the finger or wrist joints. However, EMG studies on African apes showed that the activity of digital flexors is limited during knuckle-walking [194, 206] and nearly constant during suspension [194], which makes their contribution to propulsion unlikely and supports the use of quasistatic models. In contrast to joint load magnitudes, joint load directions clearly distinguished knucklewalking from the other locomotor activities. Although the difference of joint load directions between these activities was smaller than expected from joint posture (average difference of MCP joint load directions: 56.29 °; MCP joint angles: 89.21 °), the effect of the type of activity was still large (effect size |d| above 0.93).

Several limitations of this study remain to be mentioned. The strongest limitation is certainly related to the experimental data used as an input to the musculoskeletal models. While the above mentioned, general observations are still considered valid as they are in line with literature and basic biomechanical considerations, more detailed interpretations are restricted by
the low sample size of the bonobo experiments and limitations inherent to all experimental setups. For instance, measuring only pressures during the experiments allowed to estimate forces perpendicular to the finger segment or substrate, but other force components could not be assessed. Particularly during tool use (and pinch grip in general), forces may also act in the proximal and lateral directions [164, 185]. Lateral force components might also play a role during vertical climbing where friction between the hand and substrate is required to counteract gravitational forces and to enable upwards propulsion [108, 151]. Another strong limitation is that the bonobo data needed to be randomly sampled. However, non-human primate data is extremely challenging to collect and using the randomized approach allowed to obtain at least rough quantitative estimates for joint loads including their variability. In addition to limitations of the in vivo experiments, several aspects of the model needed to be simplified. Aside from general model simplifications described in Sections 3.1 and 3.2, a major modelling limitation in this study is the assumption that the full extension torque at the PIP joint during knuckle-walking is maintained by contact of the proximal and middle phalanx. Although visual observation (see Figure 3.20) qualitatively confirmed these assumptions, muscle forces might still contribute to joint torque and ultimately increase MCP joint loading. Also the finger loading conditions were highly simplified. Due to a lack of pressure data in sufficient resolution, the whole resultant force was applied at a single point located at the centre of each bone segment. Finally, this study was limited to only two species, the third digit, and a small set of activities. Although bonobos are generally considered good models for comparative studies with humans due to their close genetic relationship [153] and the third digit has been shown to be particularly relevant for locomotion [174, 201], the extent of the herein described effects have yet to be investigated for different species, digits, and activities.

3.3.5 Conclusions

Despite limitations of the experimental data set used, this study provides more detailed biomechanical insights into MCP joint loads during primate locomotion and tool use. Both MCP joint load directions and magnitudes were found to differ less between tool use and locomotor activities than external loading and finger posture would suggest. Thus, this study generally highlights limitations of hypothesized joint loading based on observations of posture and external loading, and emphasizes the importance of musculoskeletal models to assess true activity-related differences of joint loads; which are of particular relevance for functional interpretations of bone architecture.

3.3.6 Related publications and declaration of contributions

This section is based on the manuscript "Comparison of metacarpophalangeal joint loads during tool use and locomotion of humans and bonobos" *in preparation* with co-authors Szu-Ching Lu, Tracy L. Kivell, and Dieter H. Pahr.

Author contributions. The first author and author of this thesis, *Alexander Synek*, designed the study, performed all computational parts as described in the methods section as well as the evaluation of the human suspension pressure data and generation of the stochastic sample of the bonobo data. *Szu-Ching Lu* supported the acquisition of the human suspension and tool use experimental data and performed the respective data evaluation. Additionally, she evaluated the bonobo kinematics. *Tracy L. Kivell* supervised Szu-Ching Lu, supported the experimental data acquisition and conducted the manual pressure data evaluation of the bonobo experiments. *Dieter H. Pahr* supervised the work of Alexander Synek and supported the interpretation of the results.

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Chapter 4

Synthesis and outlook

The primary goal of this thesis was to investigate the feasibility of predicting different types of habitual activities from bone architecture (Figure 4.1). Bone loading was considered as the intermediate quantity which should be predicted from bone architecture (subgoal 1) and enable to establish a link to habitual activities (subgoal 2). In this chapter, the main results of both the inverse remodelling (Chapter 2) and musculoskeletal modelling (Chapter 3) methods will be briefly summarized and then synthesized to discuss the feasibility of predicting habitual activities from bone architecture based on the test case of using metacarpophalangeal (MCP) joint loads predicted from metacarpal bones to identify habitual hand use. Questions to be addressed in future studies are presented in Section 4.2, followed by a general conclusion of this thesis in Section 4.3.



Figure 4.1: Outline of this chapter in the context of the whole thesis as presented in Figure 1.1. MCP joint: Metacarpophalangeal joint

4.1 Synthesis

4.1.1 Predicting bone loads from bone architecture (subgoal 1): Main results

In Section 2.2 it was shown that hip joint loads predicted using an optimization-based inverse remodelling algorithm are plausible when compared to in vivo measurements of instrumented prostheses. However, a parameter sensitivity analysis revealed that predicted joint load magnitudes were generally sensitive to parameters with large uncertainty such as the elastic modulus of bone or the size of the load area and have to be interpreted with caution. Predicted Joint load directions were more robust but limited in accuracy due to restrictions to load cases with non-overlapping load areas.

Despite these limitations, Section 2.3 showed that the inverse remodelling algorithm is sensitive enough to detect activity-related differences of joint loads. Based on the herein used test case of predicting MCP joint loads from primate metacarpal bones, differences related to habitual hand use (knuckle-walking, climbing/suspension, manipulation/tool use) could be found both in terms of load directions and load magnitudes. However, the predicted differences were smaller than expected from habitual joint posture and external finger loading. It remained unclear whether the surprisingly small extent of differences was caused by limitations of the inverse remodelling algorithm or truly smaller differences of joint loading experienced by the bone during the investigated habitual activities.

4.1.2 Linking bone loads to habitual activities (subgoal 2): Main results

In Section 3.2, a human and a bonobo finger model were implemented and the model predictions showed a good agreement with in vitro experimental measurements after the tendon via points of the models were adjusted. A comparison of the human and bonobo finger model revealed quantitative differences in the muscle force transmission (i.e. ratios of muscle force to external force), which suggests the use of distinct sets of model parameters in interspecific comparisons. Additionally, forces caused by the tendon-bone interaction (tendon pulley and contact forces) were found to influence the net metacarpal bone loading to a larger extent than expected, leading to broadly similar load directions irrespective of the MCP joint posture.

In Section 3.3, a comparison of MCP joint loads during different human and non-human primate activities (knuckle-walking, climbing/suspension, manipulation/tool use) predicted using the muscluloskeletal models showed that the differences in joint loading are evident but smaller than expected from external finger loading and posture. Specifically, differences in external finger loading patterns tended to reduce the gap of joint load magnitudes caused by tool use and suspension activities and, more surprisingly, joint load magnitudes engendered by different locomotor modes of bonobos (knuckle-walking, climbing, suspension) were broadly similar. Additionally, MCP joint load vectors were found to be more aligned with the long axis of the metacarpal bone than the MCP joint angle would suggest.

4.1.3 Predicting habitual activities from bone architecture: Feasible or not?

Overall, the above results suggest that predicting habitual activities from bone architecture is feasible but only if the differences of bone loading are sufficiently large, e.g. if joint load directions differ clearly (knuckle-walking vs. tool use/manipulation/climbing/suspension activities). When differences of bone loading are minor, e.g. if they differ in load magnitude but not load direction (tool use/manipulation vs. suspension/climbing), limitations of the inverse remodelling algorithm become more influential and hamper a reliable reconstruction of habitual activities. These findings will be discussed in the following.

Differences related to habitual activities with clearly distinct habitual joint postures (knucklewalking vs. tool use/manipulation/climbing/suspension activities) could be identified in the inverse remodelling algorithm predictions (see Section 2.3) and the observed differences were qualitatively in line with the estimations obtained with the muscluloskeletal models (see Section 3.3). Although differences could be detected with the inverse remodelling algorithm, they were more subtle than initially expected. The musculoskeletal models provide multiple possible explanations for this observation: First, the difference of MCP joint load directions engendered by activities with flexed and extended postures was lower than the MCP joint angle would suggest (see Section 3.3). Second, it was shown that the tendon-bone interaction forces play a larger role for net metacarpal bone loading than expected (see Setion 3.2). In particular, net forces were aligned with the long axis of the metacarpal bone irrespective of joint posture such that almost no bending of the bone occurred. This is in contrast to the assumed loading conditions in the inverse remodelling study of Section 2.3, where strong bending was induced by loads representing highly flexed or extended postures. Thus, these large flexion/extension load cases might have been downscaled by the algorithm due to oversimplified load case modelling. A third explanation for the small extent of differences detected with the inverse remodelling algorithm is the highly similar joint load magnitude of all locomotor modes of the bonobos (Section 3.3). Considering that the extent of bone adaptation is strongly related to load magnitude, but even a few load cycles suffice to elicit the maximum osteogenic response (see Section 2.1.1), the metacarpal bones of knuckle-walking species might be similarly well adapted to both infrequent grasping activities and frequent knuckle-walking activities.

Differences between activities with distinct joint load magnitude but similar habitual joint postures (tool use/manipulation vs. suspension/climbing) could also be identified using the inverse remodelling algorithm (see Section 2.3), but these differences were barely significant and much more subtle than the musculoskeletal models would suggest (see Section 3.3). One explanation for this result might be that the true differences of joint load magnitudes between tool use/manipulation and suspension/climbing activities are diminished due to different finger loading patterns as shown and discussed in Section 3.3. However, a more likely source of the surprisingly low differences in predicted joint load magnitudes are limitations inherent to the inverse remodelling algorithm. These include the parameter sensitivity of joint load magnitude predictions (see Section 2.2), but also the many simplifications of the underlying remodelling theory such as negligence of numerous factors influencing bone adaptation other than load magnitude (e.g. loading rate and rest periods, see Section 2.1.1). Additionally, non-mechanical factors such as genetics are not included in the algorithm and might hamper interspecific comparisons in particular. For instance, it was previously shown that systemic differences of bone architecture exist between humans and chimpanzees, with an overall higher bone volume fraction in chimpanzees (see Tsegai et al. [203] and Section 2.1.1). This might in part explain why MCP peak joint loads predicted with the inverse remodelling algorithm are roughly in line with the musculoskeletal model predictions for the human (musculoskeletal modelling: 402.5 ± 93.5 N; inverse remodelling: 469.2 ± 178.9 N; see Sections 3.3 and 2.3) but not for the bonobo (musculoskeletal modelling: 75.2±35.5 N; inverse remodelling: 796.2±182.6 N; see Sections 3.3 and 2.3). Thus, interspecific differences of predicted joint load magnitudes might reflect not only distinct habitual activities but also systemic/genetic factors and need to be interpreted with caution.

4.2 Outlook

The above synthesis showed that there are two main aspects that need to be improved to obtain more robust and accurate predictions of activities from bone architecture: (1) enhancement of the inverse remodelling algorithm to improve predictions of load magnitudes and directions, and (2) more realistic modelling of the bone loading scenario.

4.2.1 Improvement of inverse remodelling algorithm accuracy

A major limitation of the herein used inverse remodelling algorithm initially presented by Christen et al. [37] is that it is based on a highly simplified remodelling theory. If used with a fixed number of load cycles (as done in this thesis and all other studies using inverse remodelling

approaches), it essentially only captures the effect of load magnitude on the bone architecture. Many other parameters of the loading regime were shown to influence bone remodelling (e.g. loading rate, resting periods, load cycle number; see Section 2.1.1), but their inclusion in the inverse remodelling algorithm would potentially lead to ambiguous rather than more accurate results. Instead, a thorough identification of a low number of the most influential parameters (e.g. including a parameter quantifying systemic effects) based on in vivo experiments could enhance the accuracy at least for specific applications (e.g. to distinguish joint loads of different mammalian species; or the prediction of subject specific hip joint loads). While this approach could improve load magnitude predictions, the directional accuracy of peak load predictions remains limited due to restrictions to load cases with non-overlapping load areas and this limitation can hardly be overcome. Using multiple load predictions with slight perturbations in the point of force application (see Section 2.2 and specifically Figure 2.11, lower left panel) might improve the accuracy of predicted peak load directions, but this approach remains to be investigated in future studies.

4.2.2 Improvement of load case modelling

The second major improvement to be introduced is the physiological modelling of bone loading conditions in the inverse remodelling algorithm. In this thesis, load cases were defined in a simple but reproducible way to enable unbiased interspecific comparisons. However, the musculoskeletal models showed that the used assumptions were not perfectly physiological particularly for load predictions of the MCP joint. A potential remedy is the implementation of actual joint contact as well as different soft tissues including tendons, pulleys, the joint capsule, and ligaments. While these improvements can hardly be implemented with the herein used micro-finite element (micro-FE) models, the inverse remodelling algorithm could be adapted to continuum-level FE models which facilitates modelling of more complex load cases. As described in Section 2.1.2, Fischer et al. [56] already used such continuum-level models, but their studies were limited to 2D models and no study is known to the author investigating an application of this approach in 3D. One reason for the lack of 3D load predictions with continuum-level FE models might be that using only bone density dependent material properties is insufficient to predict bone loads with adequate accuracy. This problem could be overcome using recently presented enhanced 3D continuum-level FE models, which take into account separation of cortical and trabecular bone and use material models that rely not only on bone density but also the local trabecular structure [146, 217].

4.3 Conclusions

The goal of this thesis was to investigate the feasibility of predicting habitual activities from bone architecture using an inverse remodelling algorithm to predict bone loading and musculoskeletal models for functional interpretations. The results suggest that reconstructing activities from bone architecture is generally feasible but only if the differences of bone loading are sufficiently large (e.g. MCP joint loads engendered during tool use activities vs. knuckle-walking). The fact that actual bone loads might deviate from expectations based on observations of external loading and posture warrants the use of musculoskeletal models for accurate functional interpretations. In order to obtain more sensitive and accurate load predictions and, ultimately, a more direct link between bone architecture and habitual activities, numerous challenges remain to be overcome. These include unresolved questions of the remodelling and inverse remodelling problem, but also improved modelling of the complex loading conditions experienced by the bone.

Appendix A

Inverse remodelling: Influence of ROI size

During the application of the inverse remodelling algorithm (see Chapter 2, specifically Section 2.3), a considerable dependency of the predicted metacarpophalangeal (MCP) joint loading histories on the chosen model length was discovered if the strain energy densities (SEDs) of the full bone were used. In Section 2.3, using only the trabecular bone region was claimed to eliminate this dependency on model length. The goal of this appendix is to demonstrate the advantage of using only trabecular bone in the algorithm when compared to using both cortical and trabecular bone regions.

The load prediction of all 48 metacarpal bones was preformed using the micro-FE-based inverse remodelling algorithm as described in detail in Section 2.3. The load prediction was conducted for the metacarpal bones using the full bone region (trabecular + cortical bone), as well as the isolated trabecular bone region for differently sized regions of interest (ROIs). The ROI sizes were varied from 33 % to 8 % of the total bone length in 5 % steps (Figure A.1).



Figure A.1: Selection of ROI sizes in this sub-study, displayed on a representative specimen. The red area indicates the trabecular bone region, the variable L is the total bone length. ROI: region of interest

The load magnitude scaling factors α_1 to α_6 were computed for each ROI size and bone region (full bone/trabecular bone) to investigate their influence on the load predictions. Respective methods are presented in detail in Section 2.3 (see specifically Figure 2.16 for a description of the variables).

If the full bone was considered, the ROI size influenced the load scaling factors α_1 to α_6 predicted by the inverse remodelling algorithm to a large extent (Figure A.2). If only trabecular bone was considered, the influence of the ROI size was comparatively small in the range from 18 % to 33 % of the bone length. Reducing the ROI size to below 18 % influenced the results obtained both with full and isolated trabecular bone regions. This threshold at an ROI size of roughly 18 % well corresponds to the transition from low to high trabecular bone density towards the metacarpal head (see Figure A.1). Figure A.2 also shows that the predicted load scaling factors were quite similar between the full or trabecular bone region for ROI sizes of 18 % or smaller.



Figure A.2: Results of the sub-study investigating the ROI size dependency of the load history prediction. The six plots represent the overall mean (n = 48) load scaling factors α_1 to α_6 as predicted by the inverse remodelling algorithm (see Section 2.3 and specifically Figure 2.16 for a description of the variables).

In conclusion, these results show that using the trabecular bone region avoids the necessity of defining the most appropriate ROI size for interspecific comparisons while still delivering comparable results to predictions using the full bone region in the metacarpal head area.

Appendix B

Bonobo dissection and model parameter acquisition

As mentioned in Section 3.2, initial parameters for the bonobo finger model were needed in analogy to those of the human finger model available from literature (specifically from An et al. [4]). This comprises the following data:

- (1) Finger segment lengths for the kinematic description
- (2) Via point coordinates of each muscle/tendon at each joint
- (3) Physiological cross sectional areas (PCSA) of each muscle

The respective parameters were obtained from a dissection study performed at the Jan Palfijn Anatomy Lab of the KU Leuven and coordinated by Evie Vereecke. A bonobo specimen (8 years old; female; right arm) was made available by the Antwerp Zoo by Centre for Research and Conservation, Royal Zoological Society Antwerp (KMDA/RZSA) as part of the Bonobo Morphology Initiative 2016. The author of this thesis assisted during the dissection and reconstructed the model parameters as described in the following.

Kinematic description

Following An et al. [4], the finger was modelled by three bony segments (distal, middle, and proximal phalanx) interconnected by three joints, namely the distal interphalangeal (DIP) joint, proximal interphalangeal (PIP) joint, and the metacarpophalangeal (MCP) joint. An et al. [4] defined the kinematics and muscle via points using coordinate systems located proximal and distal to each joint (O_1 to O_6) (Figure B.1). O_2 , O_4 , and O_6 represent the centres of the DIP, PIP, and MCP joint, respectively, and O_1 , O_3 , and O_5 are located at the base of each bone. O_0 was added to represent the tip of the finger.

Coordinate systems O_0 to O_6 were identified using a computed tomography (CT) scan of the bonobo specimen (Discovery CT750, GE Healthcare, USA; voxel size: $0.56 \times 0.56 \times 0.5 \text{ mm}^3$). The CT image was segmented using the "fill" algorithm of medtool 4.1 (Dr. Pahr Ingenieurs e.U., Pfafstätten, Austria) and smooth triangulated surface meshes were generated using the



Figure B.1: Schematics of the kinematic description following An et al. [4] defined by the locations of the coordinate systems O_0 to O_6 . DIP: distal interphalangeal; PIP: proximal interphalangeal; MCP: metacarpophalangeal; DP: distal phalanx; MP: middle phalanx; PP: proximal phalanx; MC: metacarpal

model maker of 3DSlicer v4.1.0 [55]. Undesired connections between the surfaces of adjacent bones were manually deleted using Blender (v2.64, Blender Foundation, Amsterdam, Netherlands) and the bones were remeshed with the "remesh modifier" of Blender to ensure all holes of the mesh were closed. The average edge length of the final triangulated meshes of all bones was 0.47 mm.

The joint axes were defined based on the following method (Figure B.2): First, a principal component analysis (PCA) was performed on the vertices of the bone surface mesh to find their longitudinal axes. Second, a plane was defined using the eigenvectors obtained from the PCA which represent the flexion/extension plane or sagittal plane (see Figure B.2). Third, a cylinder geometry was manually fitted to the distal articular curvature of the bone. Fourth, the intersection between the long axis of this cylinder and the flexion/extension plane was computed to find the approximate joint centre of rotation. Steps three and four were repeated five times to investigate their repeatability and led to acceptably low standard deviations below 0.11 mm for each coordinate of the centre of rotation. Finally, the flexion/extension axis was defined by the normal vector of the flexion/extension plane and located at the joint centre of rotation.

The above procedure was directly applied to find the flexion/extension axis of the MCP joint using custom Python scripts in Blender. For the interphalangeal joints (PIP, DIP), the normal vectors of the flexion/extension planes of the phalanges were averaged to define a "phalangeal" flexion/extension plane (see Figure B.2). Thus, approximate positions of the joint centres for MCP, PIP, and DIP could be found (i.e. points O_2 , O_4 , and O_6). The "fingertip" (point O_0 in Figure B.2) was manually selected as the most distal point of the distal phalanx, i.e. the point on the bone surface furthest from O_2 .

Points at the base of each each bone (i.e. points O_1 , O_3 , and O_5) were defined using the following method: First, the line connecting two adjacent joint centres was found (e.g. dashed line between O_0 and O_2 in Figure B.2). Second, the intersection between this line with the respective bone geometry (e.g. distal phalanx bone geometry between points O_0 and O_2) was computed and the most proximal intersection point was selected. By definition, this point also lies on the phalangeal flexion/extension plane. Repeating the above procedure for every bone



Figure B.2: Reconstruction of the kinematic model parameters based on the triangulated surfaces extracted from computed tomography (CT) scans of the bonobo specimen. MC: metacarpal

allowed to find points O_1 , O_3 , and O_5 . All computations were performed using custom Python scripts in Blender.

Finally, two local coordinate systems were defined for each joint (see Figure B.2): The proximal coordinate system is located at the joint centre and the distal coordinate system is located at the base of the bone distal to the joint. The z-axes of those coordinate systems were defined to be perpendicular to the corresponding flexion/extension plane. The x-axes were defined to be aligned with the connection line between the origin of the coordinate system O_i and point O_{i+1} . The locations of all coordinate systems of the third digit are displayed in Table B.1. Values are presented both in absolute numbers and normalized to segment O_2O_3 following An et al. [4].

Segment	O_0O_1	O_1O_2	O_2O_3	O_3O_4	O_4O_5	O_5O_6
Length (mm)	17.54	3.30	33.91	5.09	49.08	10.00
Normalized Length (-)	0.517	0.097	1.000	0.150	1.447	0.295

Table B.1: Segment lengths defining the kinematics of the third digit of the bonobo, both in absolute values and normalized to O_2O_3 . See Figure B.1 and B.2 for a graphical representation of points O_0 to O_6 .

Muscle/tendon via points

Following the definition of An et al. [4], each muscle/tendon path needs to be defined by two via points located proximally and distally with respect to each joint and expressed in proximal and distal coordinate system, respectively. In analogy to the human model, tendons of six muscles of the third digit were included in the bonobo model: flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), extensor digitorum communis (EDC), lumbrical (LU), radial interosseus (RI), and ulnar interosseus (UI). Additionally, the via points of the extensor mechanism parts, namley radial band, ulnar band, central slip, and terminal slip were required.

The via points were recorded from the bonobo specimen using an electromagnetic six degrees of freedom (DoF) motion tracking system (Patriot, Polhemus, Vermont, USA). First, tendon path points were collected by digitizing points along the tendon at regular intervals (see Figure B.3). In order to obtain tendon path points for all muscles in common coordinate frames, the points were recorded relative to landmarks placed on each bone. These landmarks were defined by four radio-opaque markers (garnet stones attached with bee's wax, see Figure B.3, left) placed on each bone. Thus, the digitized landmarks could be registered to the landmarks identified in the CT scan (Figure B.3, right) and all tendon path points could be transformed into common, bone specific coordinate frames. The landmark registration was performed using the method of Veldpaus et al. [218] implemented with custom Python scripts.





Figure B.3: Via point digitization and location of radio-opaque markers during dissection (left) and as identified in the computed tomography scan (right). DP: distal phalanx; MP: middle phalanx; PP: proximal phalanx; MC: metacarpal

Finally, one proximal and one distal point of each tendon relative to each joint which best represented an anatomical constraint (e.g. pulley of a flexor tendon) were chosen and their positions were evaluated in the respective coordinate systems. The resulting via point locations are displayed in Table B.2 and Figure B.4.



Figure B.4: 3D visualization of the tendon via points digitzed during the dissection and registered to the computed tomography (CT) scan. FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis

Joint	Tendon	Distal Point			Proximal Point		
		Х	Y	Z	Х	Y	Z
DIP	TS	-0.177	0.085	-0.025	-0.024	0.052	-0.035
	FDP	-0.056	-0.057	0.037	0.229	-0.084	0.033
PIP	FDP	-0.304	-0.122	0.091	0.101	-0.244	0.109
	RB	-0.063	0.116	0.139	0.217	0.259	0.082
	UB	-0.099	0.071	-0.223	0.253	0.205	-0.214
	FDS	-0.348	-0.185	-0.057	0.105	-0.224	-0.020
	CS	-0.129	0.142	-0.020	-0.022	0.198	-0.047
MCP	FDP	-0.192	-0.273	0.030	0.051	-0.346	-0.075
	FDS	-0.277	-0.224	0.040	-0.036	-0.437	-0.074
	RI	-0.219	-0.053	0.237	0.165	-0.208	0.164
	LU	-0.160	-0.186	0.170	0.068	-0.455	0.042
	UI	-0.155	-0.079	-0.244	0.086	-0.354	-0.207
	EDC	0.022	0.357	-0.010	0.059	0.318	0.048

Table B.2: Proximal and distal tendon via points at each joint, expressed in proximal and distal coordinate systems, respectively. All values were normalized to segment length O_2O_3 as provided in Table B.1. FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis; TS: terminal slip; CS: central slip; RB: radial band; UB: ulnar band

Muscle PCSAs

The physiological cross sectional area (PCSA) of each muscle was computed following the definition of Sacks and Roy [173] based on the muscle volume $V_{\rm m}$, the average muscle fibre length $l_{\rm m}$, and the pennation angle ϕ :

$$PCSA = \frac{V_{\rm m}}{l_{\rm m}} \cdot \cos\phi \tag{B.1}$$

 $V_{\rm m}$, $l_{\rm m}$, and ϕ were measured following a previously presented protocol [215]. In brief, $V_{\rm m}$ was assessed by submersion of the muscle belly in a physiological saline solution, $l_{\rm m}$ was measured using a digital caliper, and ϕ was determined from digital photographs using the software Fiji [181]. $l_{\rm m}$ and ϕ were measured at three or more sites of the muscle belly and subsequently averaged. If multiple tendons were attached to a muscle belly, the muscle belly volume was divided by the number of tendons attached. Final muscle volumes, averaged fibre lengths, averaged pennation angles, and PCSA values are shown in Table B.3.

Muscle	Volume (cm ³)	Fibre length (cm)	φ (°)	PCSA (cm ²)
EDC	7.50	6.41	11.00	1.1
FDS	22.50	5.83	23.77	3.5
FDP	28.33	8.97	24.27	2.9
LU*	n/a	n/a	n/a	0.2
RI (EM)**	2.50	2.73	24.70	0.8
RI (PP)**	2.50	1.53	24.57	1.5
UI (EM)**	1.75	1.99	23.57	0.8
UI (PP)**	1.75	1.78	22.20	0.9

Table B.3: PCSA data for all muscles of the bonobo specimen. *LU data was not available from the investigated bonobo specimen. Instead, it was averaged from three other specimens previously dissected. **RI and UI consist of two muscle bellies with two tendons, attaching either to the extensor mechanism (EM) or directly to the proximal phalanx (PP). FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis

Appendix C Musculoskeletal finger model verification with OpenSim

In order to ensure that the musculoskeletal finger models as presented in Sections 3.2 and 3.3 were implemented correctly, their predictions were verified using the frequently used open source musculoskeletal modelling software OpenSim [50]. In OpenSim, moment arm-based models (as described in Section 3.1.2) can be easily implemented and computations of moment arms, muscle forces, and joint loads can be performed. However, tendon bifurcations, such as they occur in the extensor mechanism of the finger, cannot be accounted for. Given the functional significance of the extensor mechanism (see Section 3.1), a custom model implementation in Python was preferred over an OpenSim model.

In this appendix, a simple finger model including six muscles but no extensor mechanism was implemented in both OpenSim 3.2 and Python (see Figure C.1). All model parameters (bone segment lengths, tendon via points, physiological cross sectional areas) were similar. In the OpenSim model, cylindrical wrapping geometries were added for all tendon segments except the intrinsic muscles (radial and ulnar interosseus, lumbricals) at the metacarpophalangeal (MCP) joint and the radial and ulnar band at the proximal interphalangeal (PIP) joint (see Figure C.1, left). The radii of the wrapping geometries were set to the moment arms of the respective tendon segments in neutral posture. In the Python implementation, wrapping geometries were not directly modelled. Instead, it was assumed that moment arms remain constant if the tendon would naturally wrap around the bone, e.g. an extensor tendon in flexion (see Figure C.1, right). Otherwise, bowstringing conditions were assumed, e.g. a flexor tendon in flexion (also shown in Figure C.1, right). All computations of the Python model followed the descriptions provided in Sections 3.1.2, 3.2, and 3.3.



Figure C.1: Simplified finger model with wrapping geometries implemented in OpenSim (left) and schematics of simulating tendon wrapping and bowstringing conditions in the Python model (right). r_{bow} and r_{wrap} are the moment arms of two representative tendon segments in bowstringing and wrapping conditions, respectively, and are shown in two different joint postures. u_{bow} and u_{wrap} are the unit vectors dictating muscle force direction which are necessary for the joint load computation (see Section 3.1.2 for details of the joint load computations).

Moment arms

Moment arms of each muscle/tendon at each degree of freedom (DoF) were compared within a predefined range of motion (interphalangeal and MCP joint flexion/extension: -20 to +80 °; MCP joint radial/ulnar deviation: -20 to +20 °). As shown in Figure C.2, the results of the Python implementation were in good agreement with the computations of OpenSim except for a slight mismatch of the extensor digitorum communis (EDC) moment arm for radial/ulnar deviation. The mean absolute error ranged from 0 to 0.03 mm for all but the EDC muscle moment arm in radial/ulnar deviation, which was 0.16 mm.

Joint torques, muscle forces, and joint loads

The computation of joint torques from external finger loading, muscle forces, and joint loads were verified with OpenSim using five different test cases (Figure C.3, left column). Test case one was a random posture with loads applied at each finger segment with random magnitude and random orientation. Test cases two to five represented the postures described in Section 3.2, with loads applied at the centre of the distal phalanx and oriented perpendicular to the long bone axis.

The results of the Python model were generally in line with OpenSim, although a slight mismatch of muscle force estimations could be observed (Figure C.3). The error is likely caused by the simplifying assumptions of the wrapping geometries. As expected, this error also propagated to the joint load predictions, where the error of individual force components ranged from 0 to 0.18 N (0.05 N on average). Relative to the joint load magnitude computed by OpenSim, this means that the error of the force components was within a range of 0 to 2.09 % (0.61 % on average). This relative error was considered acceptable to justify the simplified tendon wrapping assumptions of the Python implementation as a good trade off between accuracy and modelling effort.



Figure C.2: Comparison of moment arms predicted by OpenSim and the custom Python implementation over a large range of motion at all degrees of freedom. θ are the joint coordinates and shown in more detail in Figure 3.21 of Section 3.3. FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis; DIP: distal interphalangeal; PIP: proximal interphalangeal; MCP: metacarpophalangeal



Figure C.3: Joint torques resulting from external finger loading at all degrees of freedom (τ_{DIP} , τ_{PIP} , $\tau_{\text{MCP,FE}}$, $\tau_{\text{MCP,RU}}$), muscle forces (t_{RI} , t_{LU} , t_{UI} , t_{FDP} , t_{FDS} , t_{EDC}), and MCP joint load components (F_x , F_y , F_z) predicted by the OpenSim model and custom Python implementation in five test cases as shown in the leftmost column. FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis; DIP: distal interphalangeal; PIP: proximal interphalangeal; MCP: metacarpophalangeal

Appendix D Final parameters of the musculoskeletal finger models

This appendix contains the complete and final set of parameters for the musculoskeletal models of a human and bonobo finger as identified in Section 3.2 and used in Section 3.3.

Segment lengths

The finger segment lengths describing the kinematics of the finger (see Figure B.1) were directly taken from An et al. [4] for the human model and from the dissection study (see Appendix B) for the bonobo model. The segment lengths, normalized to O_2O_3 , are shown in Table D.1.

For the human, O_2O_3 was set to 23.63 mm as measured and averaged from computed tomography scans of the three cadaveric fingers used in Section 3.2. Similarly, O_0O_1 of the human finger was estimated based on these three specimens. For the bonobo finger, O_2O_3 was set to 33.91 mm as measured in the dissection study (see Table B.1 of Appendix B).

Segment	O_0O_1	O_1O_2	O_2O_3	O_3O_4	O_4O_5	O_5O_6
Human	0.710	0.170	1.000	0.220	1.620	0.370
Bonobo	0.517	0.097	1.000	0.150	1.447	0.295

Table D.1: Human and bonobo segment lengths, normalized to O_2O_3 . See Figure B.1 of Appendix B for a graphical representation of segment lengths O_0O_1 to O_5O_6 . The human data was taken from An et al. [4] except for O_0O_1 , which was estimated from computed tomography scans of the three cadaveric specimen used in Section 3.2. The bonobo data was directly measured from computed tomography scans as described in Appendix B.

Muscle/tendon via points

Muscle/tendon via points were identified as described in Section 3.2 to best match experimentally measured fingertip forces. The final values after optimization for the human and bonobo finger model are presented in Tables D.2 and D.3, respectively. See An et al. [4] for the initial values of the human finger model and Appendix B for the initial values of the bonobo finger model.

Joint	Tendon	Distal Point			Pro	oximal P	oint
		Х	Y	Z	Х	Y	Z
DIP	TS	-0.050	0.154	-0.022	0.000	0.158	-0.015
	FDP	0.035	-0.128	0.032	0.293	-0.278	0.033
PIP	FDP	-0.286	-0.287	-0.004	0.416	-0.291	-0.004
	RB	-0.180	0.170	0.227	0.102	0.092	0.242
	UB	-0.180	0.161	-0.247	0.102	0.079	-0.279
	FDS	-0.264	-0.163	0.001	0.332	-0.133	-0.016
	CS	-0.030	0.247	-0.024	0.000	0.231	-0.019
MCP	FDP	-0.232	-0.314	0.023	0.385	-0.518	0.012
	FDS	-0.324	-0.294	0.039	0.487	-0.561	0.019
	RI	-0.312	0.070	0.331	0.269	-0.184	0.471
	LU	-0.370	-0.116	0.328	0.411	-0.598	0.422
	UI	-0.368	0.044	-0.357	0.388	-0.240	-0.358
	EDC	-0.069	0.266	-0.018	0.055	0.409	-0.039

Table D.2: Final muscle/tendon via points of the human model, normalized to segment length O_2O_3 and expressed in the proximal and distal coordinate system of each joint (see also An et al. [4]). FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis; TS: terminal slip; CS: central slip; RB: radial band; UB: ulnar band

Extensor mechanism parameters

The extensor mechanism parameters were partly fixed and partly identified by the optimization procedure presented in Section 3.2. Since radial interosseus (RI) and ulnar interosseus (UI) muscles might insert both in the extensor mechanism and proximal phalanx, the parameters included (1) the fraction of force transmitted to the extensor mechanism $e_{\rm EM}$ (value assumed as fixed based on the PCSA values), and (2) the fraction of force transmitted to the central slip $e_{\rm CS}$ and terminal slip $e_{\rm TS} = 1 - e_{\rm CS}$. Lumbrical (LU) and extensor digitorum communis (EDC) muscle parameters were limited to the force transmission fractions $e_{\rm CS}$ and $e_{\rm TS}$ since they insert exclusively into the extensor mechanism. All force transmission fractions after optimization are presented in Table D.4.

Joint	Tendon	Distal Point			Pro	Proximal Point		
		Х	Υ	Z	Х	Y	Z	
DIP	TS	-0.177	0.084	-0.025	-0.023	0.058	-0.035	
	FDP	-0.031	-0.053	0.037	0.228	-0.087	0.033	
PIP	FDP	-0.281	-0.085	0.091	0.169	-0.272	0.109	
	RB	-0.073	0.105	0.139	0.227	0.254	0.082	
	UB	-0.102	0.075	-0.223	0.254	0.208	-0.214	
	FDS	-0.344	-0.144	-0.057	0.149	-0.133	-0.020	
	CS	-0.129	0.142	-0.020	-0.022	0.202	-0.047	
MCP	FDP	-0.304	-0.136	0.030	0.344	-0.428	-0.075	
	FDS	-0.362	0.009	0.040	0.306	-0.512	-0.074	
	RI	-0.208	0.028	0.237	0.210	-0.019	0.164	
	LU	-0.165	-0.148	0.170	0.107	-0.449	0.042	
	UI	-0.181	0.178	-0.244	0.378	-0.181	-0.207	
	EDC	0.014	0.285	-0.010	0.123	0.283	0.048	

Table D.3: Final muscle/tendon via points of the bonobo model, normalized to segment length O_2O_3 and expressed in the proximal and distal coordinate system of each joint (see also Appendix B). FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis; TS: terminal slip; CS: central slip; RB: radial band; UB: ulnar band

Muscle	Human				Bonobo		
	e_{EM}	$e_{\rm CS}$	$e_{\rm TS}$	$e_{\rm EM}$	$e_{\rm CS}$	$e_{\rm TS}$	
RI	0.500	0.363	0.637	0.353	0.002	0.998	
LU	-	0.379	0.621	-	0.456	0.544	
UI	1.000	0.381	0.619	0.472	0.350	0.650	
EDC	-	0.495	0.505	-	0.255	0.745	

Table D.4: Force transmission fractions at tendon bifurcations of the extensor mechanism for all intrinsic muscles (RI, UI, LU) and the EDC muscle. RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; EDC: extensor digitorum communis; TS: terminal slip; CS: central slip

Muscle PCSA

Physiological cross sectional areas (PCSA) of the finger muscles were not part of the parameter identification procedure and already presented in Table 3.2 of Section 3.2. They are reported again in Table D.5 to provide a complete parameter description of the finger models in this chapter.

Muscle/tendon	Bonobo	Human
	$PCSA\ (cm^2)$	$PCSA\ (cm^2)$
FDS	3.5	4.2
FDP	2.9	4.1
EDC	1.1	1.7
LU	0.2	0.2
RI (EM)	0.8	1.4
RI (PP)	1.5	1.4
UI (EM)	0.8	2.2
UI (PP)	0.9	0.0

Table D.5: PCSAs of the muscles of both the human and bonobo finger. Intrinsics with split tendons inserting into either the extensor mechanism (EM) or the proximal phalanx base (PP) are labelled accordingly. Human finger PCSA values were taken from Chao et al. [33] and bonobo finger PCSA values were taken from own dissection data (see Appendix B). EDC: extensor digitorum communis; FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis; RI: radial interosseus; UI: ulnar interosseus; LU: lumbrical; PCSA: physiological cross sectional area

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Alexander Synek

Curriculum Vitae

Personal data

Date of birth	11.09.1988	Email:	alexander.synek@hotmail.com
Nationality	Austria	Phone:	+43 680 2339765
Address	Schönbrunnerschlossstraße 31A/21, Vienna, Austria		

Education and training

Euucation ai	ia training	
2015 - present	 Doctoral program in engineering sciences Vienna University of Technology, Austria Thesis: "Predicting habitual activities from bone architecture using a biomechanical approach" 	
June 2015	Bone cell & tissue biomechanics summer school International Centre for Mechanical Sciences, Italy	
2011 - 2015	 Master program biomedical engineering Vienna University of Technology, Austria Graduation with distinction Thesis: "A specimen specific finite element validation study of distal radius fracture osteosynthesis" 	
2009 - 2011	 Master program mechatronics and robotics University of Applied Sciences Technikum Wien, Austria Graduation with distinction Thesis: "Simulation of a human finger joint with sliding surfaces" 	
2006 - 2009	Bachelor program mechatronics and robotics University of Applied Sciences Technikum Wien, Austria	

Graduation with distinction

Work experience

Dec. 2014 - present	 Project assistant Institute of Lightweight Design and Structural Biomechanics, Vienna University of Technology, Austria Processing of high resolution 3D images and conducting micro-finite element analyses Generation and validation of musculoskeletal models Assisting in project management and teaching activities 		
Feb Sept. 2014	Research assistant Laboratory for Biomechanics and Experimental Orthopaedics, Ludwig Maximilians University Munich, Germany Preparation and mechanical testing of human bones with implants Processing of computed tomography scans and finite element model validation		
Feb Aug. 2011	 Student employee Bionics Group, German Aerospace Center, Germany Acquisition and processing of magnetic resonance images Musculoskeletal modelling of a human finger joint 		
Languages			
German: Native	English: Fluent Spanish: Basic skills		
IT Skills			

3D image processing:	ParaView, 3DSlicer, Medtool	Programming:	Python, Matlab, C++ (basics)
3D modelling:	Solidworks, Blender	Office:	MS Office, Latex
Numerics:	Abaqus, Simpack , OpenSim	OS :	Windows, Linux

Peer reviewed journal articles

- <u>A.Synek</u>, D. H. Pahr: "Plausibility and parameter sensitivity of micro-finite element based joint load prediction at the proximal femur"; Biomechanics and Modelling in Mecahnobiology, 17 (2018), p. 843–852.
- S.F. Baumbach, J. Binder, <u>A. Syne</u>k, F.G. Mück, Y. Chevalier, E. Euler, G. Langs, L. Fischer: "Analysis of the Three-Dimensional Anatomical Variance of the Distal Radius Using 3D Shape Models"; BMC Medical Imaging, 17 (2017), 23.
- E. Benca, A.G. Reisinger, J. Patsch, L. Hirtler, <u>A. Synek</u>, S. Stenicka, R. Windhager, W. Mayr, D. H. Pahr: "Effect of Simulated Metastatic Lesions on the Biomechanical Behavior on the Proximal Femur"; Journal of Orthopaedic Research, 35 (2017), 11; p. 2407 - 2414.
- <u>A. Synek</u>, D. H. Pahr: "The Effect of the Extensor Mechanism on Maximum Isometric Fingertip Forces: A Numerical Study on the Index Finger"; Journal of Biomechanics, 49 (2016), 14; p. 3423-3429.
- <u>A. Synek</u>, L. Borgmann, H. Traxler, W. Huf, E. Euler, Y. Chevalier, S.F. Baumbach: "Using Self-Drilling Screws in Volar Plate Osteosynthesis for Distal Radius Fractures: a feasibility studyOutcome of In Vitro Experiments"; BMC Musculoskeletal Disorders, 17 (2016), 120.
- <u>A. Synek</u>, Y. Chevalier, C. Schröder, D. H. Pahr, S.F. Baumbach: "Biomechanical Testing of Distal Radius Fracture Treatments: Boundary Conditions Significantly Affect the Outcome of In Vitro Experiments"; Journal of Applied Biomechanics, 32 (2016), 2; p. 210-214.
- S.F. Baumbach, <u>A. Synek</u>, H. Traxler, W. Mutschler, D. H. Pahr, Y. Chevalier:
 "The Influence of Distal Screw Length on the Primary Stability of Volar Plate Osteosynthesis A Biomechanical Study"; Journal of Orthopaedic Surgery and Research, 10 (2015), 139; 8 p.
- <u>A. Synek</u>, Y. Chevalier, S.F. Baumbach, D. H. Pahr: "The Influence of Bone Density and Anisotropy in Finite Element Models of Distal Radius Fracture Osteosynthesis: Evaluations and Comparison to Experiments"; Journal of Biomechanics, 48 (2015), 15; p. 4116-4123.

Peer reviewed conference papers

<u>A. Synek</u>, M. Settles, G. Stillfried: "Multi-body simulation of a human thumb joint by sliding surfaces"; 4th IEEE RAS & EMBS International Conference on Biomedical Robotics and Biomechatronics (2012), p. 379-384.

Conference talks

- <u>A. Synek</u>, D. H. Pahr: "Parameter Sensitivity and Plausibility of Micro FE Based Joint Load Prediction at the Proximal Femur"; 23rd Congress of the European Society of Biomechanics, Sevilla; 02.07.2017 05.07.2017.
- <u>A. Synek</u>, D. H. Pahr: "The Effect of the Extensor Mechanism for the Force Producing Capabilities of a Human Finger"; 22nd Congress of the European Society of Biomechanics (ESB 2016), Lyon; 10.07.2016 13.07.2016.
- <u>A. Synek</u>, S. Baumbach, D. H. Pahr: "CT-Based Finite Element Models of Locking Plate Fracture Fixations for the Prediction of Stiffness and Screw Loads"; 21st Congress of the European Society of Biomechanics, Prague; 05.07.2015 08.07.2015.
- <u>A. Synek</u>, Y. Chevalier, J. Binder, S.F. Baumbach, D. H. Pahr: "The Influence of Bone Density and Orientation on Stiffness Predictions of Distal Radius Fracture Osteosynthesis Using the Finite Element Method"; V. Münchner Symposion für Experimentelle Orthopädie, Unfallchirurgie und Muskuloskelettale Forschung, München; 06.03.2015 - 07.03.2015

Conference poster presentations

- <u>A. Synek</u>, Y. Chevalier, J. Binder, D. H. Pahr, S.F. Baumbach: "Validierung von Finite Elemente Modellen distaler Radiusfraktur-Osteosynthese: Relevanz der lokalen Knochendichte und -orientierung"; Deutscher Kongress für Orthopädie und Unfallchirurgie, Berlin; 20.10.2015 - 23.10.2015.
- <u>A. Synek</u>, Y. Chevalier, Y. Schröder, D. H. Pahr, S.F. Baumbach: "Einfluss der Randbedingungen in biomechanischen Experimenten distaler Radiusfrakturen: Eine biomechanische Studie"; 55. Kongress der Deutschen Gesellschaft für Handchirurgie, Baden-Baden; 09.10.2014 11.10.2014.

- Travel award of the European Society of Biomechanics, 2015
- Scholarship for academic excellence of the Technical University of Vienna, 2012/2013
- Scholarship for academic excellence of the University of Applied Sciences Technikum Wien, 2010/2011
- Scholarship for academic excellence of the University of Applied Sciences Technikum Wien, 2009/2010

References

Dr. Dieter H. Pahr	Dr. med. Sebastian Baumbach
Associate professor	Trauma surgeon
TUW, Vienna, Austria	LMU, Munich, Germany
pahr@ilsb.tuwien.ac.at	sebastian.baumbach@med.uni-muenchen.de

Dr. Yan Chevalier Head of biomechanics lab LMU, Munich, Germany yan.chevalier@med.uni-muenchen.de