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Fakultät für Sport- und Gesundheitswissenschaften

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# Biomechanical assessment of stretch-induced performance enhancement in submaximal voluntary human leg muscle contraction

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To my family, whose love and support was an essential part for finishing this thesis.

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## Zusammenfassung

Die vorliegende Arbeit beschäftigt sich mit der Frage, inwiefern eine aktive, exzentrische Muskelaktion eine im direkten Anschluss folgende isometrische Muskelaktion beeinflusst. Der Name des untersuchten Muskelphänomens lautet residual force enhancement (RFE). Dieses ist einerseits gekennzeichnet durch erhöhte Kräfte während einer isometrischen Kontraktion nach einer aktiven Dehnung, verglichen mit einer reinen isometrischen Muskelaktion bei gleicher Muskellänge und Muskelaktivierungslevel. Andererseits kommt es nach der einer aktiven Dehnung folgenden isometrischen Kontraktion zu einer reduzierten Muskelaktivität, wiederum verglichen mit einer rein isometrischen Kontraktion. Voraussetzung hierbei ist sowohl eine identische Muskellänge als auch das gleiche Kraftlevel.

RFE wurde bereits in einer großen Bandbreite von Studien untersucht, beginnend beim Halb-Sarkomer bis hin zu mehrgelenkigen Muskelaktionen. In dieser Arbeit ist der Fokus zum einen auf den Bereich der mehrgelenkigen Muskelaktionen und somit auf alltagsnahe menschliche Bewegungen gerichtet. Zum anderen wird die Auswirkung von RFE auf eine mögliche Ökonomisierung bzw. Optimierung der Muskelkontraktion betrachtet. Ziel dieser Arbeit, welche sich aus vier Publikationen zusammensetzt, ist es vorhandene Wissensdefizite herauszustellen und wissenschaftlich zu bearbeiten.

Die ersten beiden Publikationen beschäftigen sich mit der Relevanz des residual force enhancement hinsichtlich alltagsnaher Bewegungen. Hierfür wurde das Phänomen während mehrgelenkiger Beinstreckungen auf einer isokinetischen Kraftmaschine untersucht. Die erste Studie zeigte hierbei das Vorhandensein von RFE unter submaximalen Kontraktionsbedingungen auf. Es konnten signifikante Unterschiede im Bereich der resultierenden Kraft, sowie den berechneten Gelenksmomenten gezeigt werden. Für das Treffen einer Aussage hinsichtlich alltäglicher Relevanz, sind jedoch neben einem submaximalen Aktivierungslevel auch die Gelenkwinkelpositionen entscheidend. Während täglichen Bewegungen wie dem Gehen erfolgt nur ein leichtes Beugen der beteiligten Gelenke. Folglich arbeitet die Oberschenkel- und Wadenmuskulatur im Bereich des aufsteigenden Astes der Drehmoment-Längen-Relation. Daher schloss das zweite Paper neben einer submaximalen Kontraktionshöhe auch alltagsnahe Gelenkwinkelpositionen mit ein. Diese Arbeit zeigte wiederum das vorhanden sein von RFE auf, wenn auch nicht für alle der

teilnehmenden Probanden. Des Weiteren konnte gezeigt werden, dass erhöhte Kräfte während der Dehnung eine Voraussetzung für das untersuchte Muskelphänomen darstellen.

Publikation drei und vier zielten auf den Nachweis einer verbesserten neuromuskulären Effizienz, ausgelöst durch eine aktive Dehnung, ab. Die dritte Arbeit verwendete diesbezüglich eine ermüdende Intervention an der Beinstreckermuskulatur. Die Kontraktionsdauer betrug 60 s bei einer Intensität von 60% der maximal willentlichen Kontraktionshöhe. Für die untersuchte Oberschenkelmuskulatur konnte eine Reduktion der muskulären Nettoaktivität in der isometrischen Muskelaktion nach aktiver Dehnung, verglichen mit einer rein isometrischen Muskelaktion, nachgewiesen werden. Jedoch konnte kein Nachweis gefunden werden, welcher auf eine erhöhte Leistungsfähigkeit hinsichtlich erhobener Ermüdungsparameter hinweist. Im Gegensatz zu einer indirekten Messung möglicher Ökonomisierungseffekte, ausgelöst durch eine aktive Dehnung, war es Ziel der vierten Studie einen direkten Nachweis zu erbringen. Hierfür wurde mittels der Nahinfrarotspektroskopie der Sauerstoffverbrauch des gastrocnemius medialis unter Anwendung eines arteriellen Verschlusses erhoben. Trotz einer geringeren muskulären Aktivierungshöhe, konnte der Nachweis eines verringerten Sauerstoffverbrauchs in der isometrischen Phase nach einer aktiven Dehnung, verglichen mit einer rein isometrischen Muskelaktion, nicht erbracht werden.

Zusammenfassend konnte mit der Arbeit gezeigt werden, dass residual force enhancement in alltagsnahen Laborbedingungen, unter Berücksichtigung von Gelenkwinkelposition sowie der Kontraktionshöhe, vorhanden ist. Für die Annahme einer erhöhten neuromuskulären Effizienz konnte nur indirekt ein Nachweis durch eine reduzierte Muskelaktivität nach aktiver Dehnung erbracht werden. Beweise bezüglich einer erhöhten Leistungsfähigkeit definiert durch Ermüdungsparameter oder erniedrigtem muskulärem Sauerstoffverbrauch konnten nicht aufgezeigt werden.

## Abstract

History dependence of muscle action describes among other things the effect of stretching on force production regarding a following muscle action. The following work is about how an active eccentric muscle action influences the following isometric contraction, regarding force production and muscle activation of a voluntary activated human muscle compared to a pure isometric contraction. The underlying phenomenon is called residual force enhancement (RFE), which means: After an active stretch the isometric force a muscle can exert is enhanced, compared to a pure isometric contraction with the same muscle length and the same muscle activation. By maintaining the same amount of force, RFE is characterized by a muscle activation reduction (AR) in the isometric phase after an active stretch, compared to a pure isometric contraction at the same muscle length.

Residual force enhancement has been investigated over a broad range of different conditions, but especially when it comes to its relevance regarding daily human movement, e.g. multi-joint movements, there is still a lack of scientific knowledge. Another missing link is, the effect of RFE on the neuromuscular efficiency of a muscle resulting in a higher muscle economisation. To gain new insights regarding the muscle phenomenon residual force enhancement, four studies were carried out.

Study one and two investigated RFE in the context of multi-joint leg extension and hence its relevance regarding human movement. The first paper could show that RFE is present in submaximal, voluntary multi-joint leg extension contractions concerning measured forces, calculated ankle and knee torques. Regarding daily human movement paper one disregarded the fact that, e.g. during walking the joints are only slightly flexed. Therefore, the quadriceps femoris and the triceps surae are acting on the ascending limb of their torque-length relationship. Hence, the second study aimed to mimic joint angle configurations of daily locomotion during submaximal contractions. The work could show that in a setup comparable to human movement RFE is present for at least 8 out of 13 subjects. Additionally, the study showed the necessity of enhanced forces during stretch for the appearance of residual force enhancement.

Study three and four focused on beneficial effects regarding enhanced neuromuscular efficiency triggered by an active stretch. In the third study, subjects had to perform 60s lasting leg extensions maintaining a force level of 60% maximum voluntary contraction

(MVC). Activation reduction occurred in the net-EMG of the quadriceps femoris, but the study failed to show any beneficial effects associated with RFE in terms of reduced performance fatigability. Study four focused on providing a direct evidence for the beneficial effects of the investigated muscle phenomenon. Contrary to using indirect measurement tools like the interpolated twitch technique used in paper 3, the forth study directly measured the oxygen consumption of the investigated muscle. Therefore, a near-infrared spectroscopy device was used in combination with arterial occlusion on the gastrocnemius medialis. Like the third study, paper four again showed activation reduction of the investigated muscle group but did not find beneficial effects of an active stretch regarding the following isometric contraction, compared with a pure isometric contraction regarding muscle oxygen consumption.

Overall, the thesis showed the existence of residual force enhancement in experimental setups comparable to daily human movement concerning joint angle configurations and activation level. In contrast, a beneficial effect regarding an enhanced neuromuscular efficiency could only be shown indirectly through reduced muscle activation. Nevertheless, it could not be proven that reduced performance fatigability or reduced oxygen consumption are connected with the muscle phenomenon of residual force enhancement.

## List of scientific papers

I. Seiberl, W., **Paternoster, F.**, Achatz, F., Schwirtz, A. & Hahn, D. (2013). On the relevance of residual force enhancement for everyday human movement. Journal of Biomechanics, 46(12), 1996 – 2001.
Impact Factor: 2.496

II. **Paternoster, F.K.**, Seiberl, W. Hahn, D., & Schwirtz, A. (2016). Residual force enhancement during multi-joint leg extensions at joint- angle configurations close to natural human motion. Journal of Biomechanics, 49(5), 773 – 779.
Impact Factor: 2.664

III. Seiberl, W. Hahn, D. & **Paternoster, F.K.** (2016). Reduced activation in isometric muscle action after lengthening contractions is not accompanied by reduced performance fatigability. Scientific Reports, 6, 39052.
Impact Factor: 4.259

IV. **Paternoster, F.K.,** Hahn, D., Stöcker, F., Schwirtz, A., Seiberl, W. (2017). Oxygen consumption of gastrocnemius medialis muscle during submaximal voluntary isometric contraction with and without preceding stretch. Scientific Reports, 7, 4674.
Impact Factor: 4.259

# 1 Introduction

The following thesis on history-dependent properties of skeletal muscles refers to a phenomenon of muscle contraction called residual force enhancement. In the first subsection (1.1), a brief introduction is given regarding basic knowledge about the investigated muscle feature mostly established in *in vitro* research. On this basis the following subsection (1.2) introduces research from *in vivo* studies, as this is the basis of the present work. The section 1.3 will present the research questions and in the last subchapter of the introduction (1.4), the methods are presented which were used in this thesis.

## 1.1 Residual force enhancement

If an external force is applied to an active muscle and the muscle-force is lower than the external force the muscle lengthens during force production, also known as “eccentric muscle action”, in this thesis also named “active stretch”. In contrast, “isometric muscle action” means that the external force and the active muscle force are in equilibrium or the active muscle force acts against an insurmountable resistance. Hence, the muscle length stays the same throughout the contraction. The eccentric and isometric muscle action are the protagonists of the following manuscript.
Commonly, the force a muscle can achieve during an isometric muscle contraction is related to the number of attached cross-bridges, based on the so-called cross-bridge theory (Huxley, 1957), whereby the number of bindings depends on the overlap of actin and myosin (Gordon, Huxley, & Julian F.J., 1966) (Figure 1).

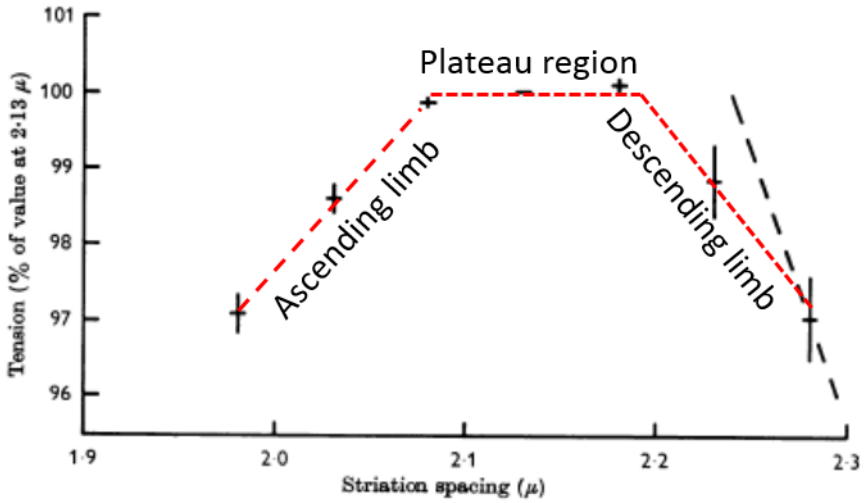


*Figure 1: Modified from Gordon et al. (1966). The figure shows data from isolated frog muscle fibres. The x-axis represents the length of the fibre and the y-axis the related tension in percent of the peak tension at 2.13 µ. From ~ 1.98 µ to 2.1 µ, there is an increase in the percentage of force (ascending limb), from 2.1 µ to 2.2 µ the percentage of force stays nearly the same (plateau region). From 2.2 µ to 2.3 µ, the percentage of force decreases (descending limb).*

Figure 1 shows the so-called force-length relationship (f-l-r). As a function of the actin-myosin overlap zone, the plateau region of the f-l-r is found where the muscle has the highest number of possible cross-bridge connections resulting in the highest amount of force. To the left side of the plateau region is the ascending limb. With increasing muscle-length there is also an increase in the number of attached cross-bridges and hence an increase in force. On the right side of the plateau region there is the descending limb. With increasing muscle-length the number of cross-bridges decreases and thus the force decreases.

Five years preceding the cross-bridge theory of Huxley (1957), Abbott and Aubert (1952) showed in a series of experiments that an active stretch changes the muscular properties of the following isometric phase, which means there is a history-dependent effect triggered by the active eccentric contraction on the following isometric contraction. Despite having the same muscular length (hence the identical number of attached cross-bridges) and the same level of activation, Abbott and Aubert (1952) figured out that the isometric force of a muscle after an active stretch exceeds the isometric force of a contraction with no preceding active stretch. This phenomenon of muscle contraction, named residual force enhancement (RFE), is the main topic of the following thesis (Figure 2).

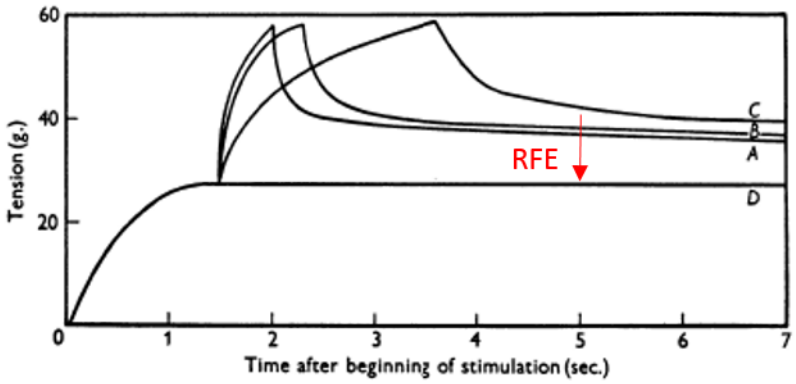


*Figure 2: Modified from Abbott and Aubert (1952). Note: D represents the isometric reference contraction without an active stretch, whereas A, B and C included an active stretch (with different stretch velocities). After the peak tension in A, B and C there is a decrease in the tension followed by a steady state phase. The difference between this steady state phase and the isometric tension of D is called residual force enhancement (RFE). The red arrow show exemplary RFE for the different conditions.*

Trying to explain these results by using the cross-bridge theory (Huxley, 1957) including the f-l-r of a muscle (Gordon et al., 1966), it can be ascertained that the theory cannot provide a valid explanation of the results from Abbott and Aubert (1952).
Since the first occurrence RFE was consistently observed in experimental studies on different structural levels of the muscle, ranging from half-sarcomere/ sarcomere level (Rassier & Pavlov, 2012) to whole muscle preparation (Herzog & Leonard, 2000). During this continuing research several basic principles of RFE could be identified:

Residual force enhancement

- increases with increasing amplitudes of stretch, but only during *in vitro* research (Abbott & Aubert, 1952; Edman, Elzinga, & Noble, 1978)
- is independent regarding the velocity of stretch (Edman et al., 1978; Sugi & Tsuchiya, 1988)
- is long lasting and can be eliminated by deactivating the muscle and occurs on the entire force-length relationship (f-l-r) of a muscle (Abbott & Aubert, 1952; Herzog, Schacher, & Leonard, 2003).

Albeit continuing research the mechanism(s) underlying RFE are still not set in stone. The following theories are currently being discussed:

*Sarcomere length non-uniformity theory (Edman, 2012)*

When sarcomeres on the descending limb are stretched, some sarcomeres are elongated beyond actin-myosin overlap (popped sarcomeres), whereas the others stay at shorter length allowing them the production of higher forces. The force difference between the popped and the shorter sarcomeres is counterbalanced by passive structures. Hence, according to the f-l-r the short sarcomeres can produce more force compared to a muscle activated and held at the final length (Figure 3). As RFE was shown to be present on the entire f-l-r, the sarcomere length non-uniformity theory cannot alone explain enhanced forces.

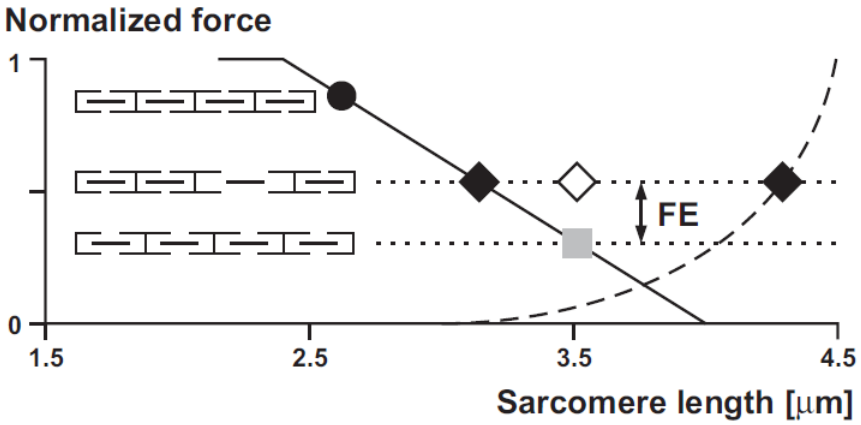


*Figure 3: Illustration from Herzog (2014) shows the sarcomere length non-uniformity theory. From a starting position (black circle), an active stretch occurs reaching the same sarcomere length as a pure isometric contraction (grey square). The white diamond, representing the average sarcomere length after an active stretch, consists of sarcomeres stretched beyond actin-myosin filament overlap held by passive forces (right black diamond). In addition, the left black diamond represents sarcomeres, which are shorter than the average sarcomere length and hence can produce according to the force-length relationship more active force. Therefore, the sarcomere length non-uniformity theory is based on the interplay of overstretched and shortened sarcomeres resulting in higher overall forces compared to a pure isometric contraction despite having the same average sarcomere length.*

*The spring-like molecule titin (Herzog, Schappacher, DuVall, Leonard, & Herzog, 2016)*

According to this theory the molecule titin binds calcium at specific sites and attaches to actin during an active stretch, resulting in a shorter titin length. In addition $Ca^{2+}$ also increases the stiffness of titin. The shorter titin in combination with an increased stiffness lead to enhanced forces of titin during an active stretch (Figure 4). Finally this results in enhanced forces in the isometric phase after active stretch compared to a pure isometric contraction.

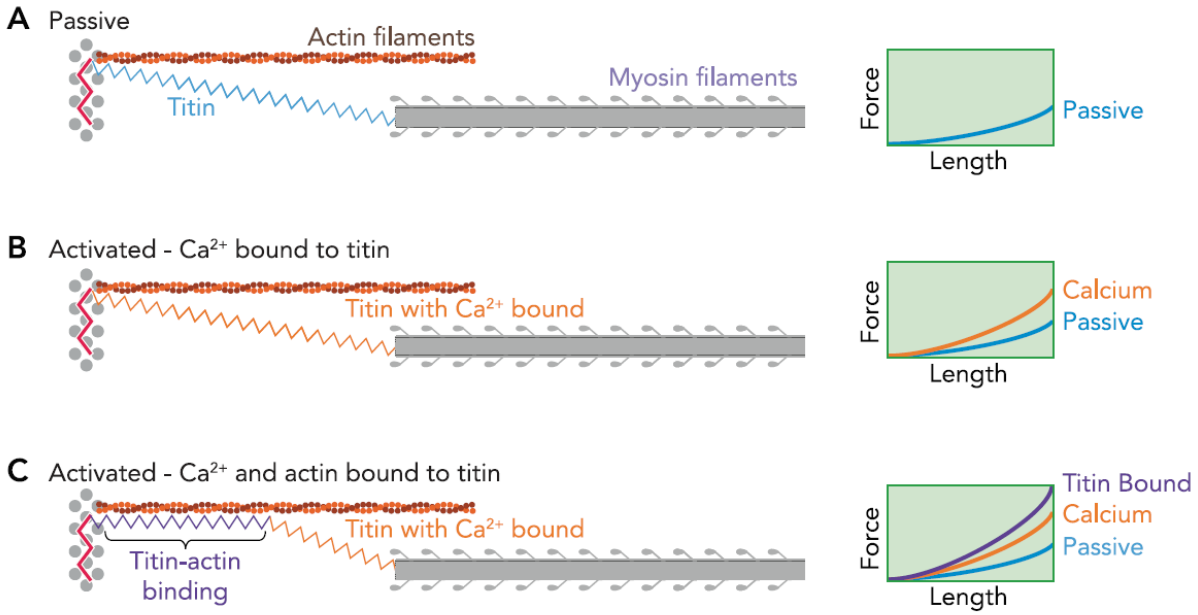


*Figure 4: Illustration taken from Herzog et al. (2016). The force-length diagrams on the right side representing the force caused by an elongation of Titin. A: By doing a passive stretch there is neither an actin-titin interaction nor an increased stiffness of titin, resulting in pure passive forces (blue line). B: An active stretch (using $Ca^{2+}$) in conjunction with an inhibition of actin-titin interaction, results in higher passive force due to the stiffness increase of Titin as $Ca^{2+}$ binds at specific segments of the protein (yellow line). C: A normal eccentric contraction results in an actin-titin interaction that shortens Titin. In concert with an enhanced stiffness of Titin like in B, the resultant force is higher compared to B and A (purple line). Hence, enhanced forces in the isometric phase after an active stretch compared to a pure isometric contraction are a combination of shortened and stiffer Titin.*

*The increase in the average force per cross-bridge (Leonard, DuVall, & Herzog, 2010)*

This theory deals with the assumption when triggered by an active stretch, beside a substantial increase of the number of attached cross bridges, the stiffness of each cross bridge increases, too. The authors themselves “rendering this idea unlikely” (Leonard et al., 2010, C1400), but it is not yet rejected (Seiberl, Power, & Hahn, 2015).

*The attachment of a second motor domain of myosin head (Brunello et al., 2007)*

During an isometric contraction, myosin is attached to actin by a single motor domain even though every myosin has two motor domains. According to the authors a large stretch is accompanied by a rapid attachment of the second motor domain of some myosin molecules with respect to the braking action of a muscle (Figure 5).

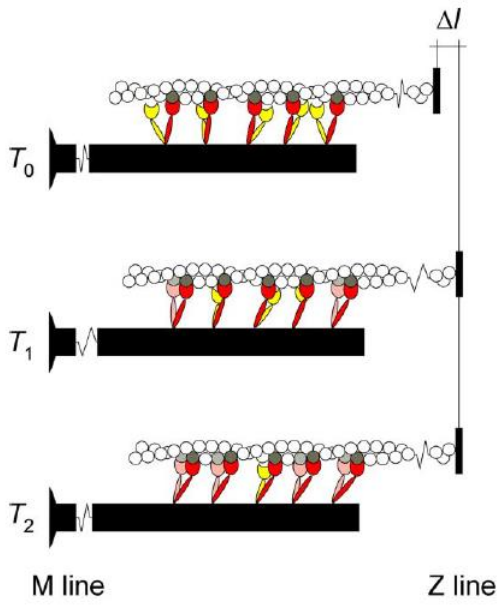


*Figure 5: Modified from Brunello et al. (2007). Figure shows the interaction of myosin and actin at three different time points ($T_0$ – $T_2$).$T_0$ shows myosin heads attached to actin (red) and partner heads not attached to actin (yellow) during an isometric contraction. During $T_1$, some of the partner heads (pink) have attached to the adjacent monomer (light grey). $T_1$ represents the time-point of the peak force during the active stretch. The attachment of partner heads (pink) continues at $T_2$, representing the isometric phase after active stretch. Hence, enhanced forces in the isometric phase after active stretch compared to pure isometric contractions can be explained by additional myosin-heads connected to actin in the isometric phase after an active stretch.*

As these theories derive from studies on a microscopic muscle level, an identification of the mechanism underlying RFE is beyond methods and scope of this work. Therefore only a brief overview was provided. For more detailed information the reader is forwarded to excellent reviews focusing on the mechanisms (Campbell & Campbell, 2011; Edman, 2012; Herzog, 2014; Herzog et al., 2016; Rassier, 2012).

A first definition of RFE is as follows:

*(1) Using the same level of muscle activation and muscle length, the isometric force after an active stretch is enhanced compared to an isometric contraction without a preceding stretch.*

## 1.2 Residual force enhancement *in vivo*

The first *in vivo* work on residual force enhancement was done by Cook and McDonagh (1995). For their experiments they used the first dorsal interosseous muscle in combination with electrical stimulation. They found an enhanced force after active stretch of 30% compared to a pure isometric contraction. Hence, RFE is not only present during *in vitro* work, but also in human muscles. A limiting factor in this study

is that the authors used electrical stimulation. The goal of studies using electrical stimulation was the assignment of *in vitro* results onto human muscles (Lee & Herzog, 2002; Ruiter, Didden, W. J. M., Jones, & Haan, 2000). The problem with electrical stimulation is that it cannot represent voluntary human muscle contraction as electrical stimulation circumvent the natural signal pathway as it directly stimulates the muscle nerve. A voluntary human contraction starts at the cortex wherefrom the signal travels down the central nervous system and finally reaches the alpha motor neuron. From there an action potential travels down its own axon, which finally leads to a muscle contraction. Hence, beside using electrical stimulation Lee and Herzog (2002) also used maximum voluntary activation (MVC) of the thumb adductor. They found an almost identical RFE of 16% compared with 17% using electrical stimulation. The aforementioned work completed the results from Cook and MCDonagh (1995) by giving proof that residual force enhancement is not only present in human muscles but can also be elicited during voluntary human muscle contractions.

To deny the importance of the investigated hand muscles regarding daily living would be wrong, but thinking about daily motion the issue becomes more complex. In 2007, two studies focused on the question if RFE was also part of big human muscles used for daily motion (Hahn, Seiberl, & Schwirtz, 2007; Pinniger & Cresswell, 2007). Hahn et al. (2007) failed to provide evidence for enhanced forces in their work for the quadriceps femoris (but found significant reduced muscle activation after active stretch up to 20%), in contrast to Pinninger and Creswell (2007) for the triceps surae and the tibialis anterior. Finally, Hahn, Seiberl, Schmidt, Schweizer and Schwirtz (2010) could show that during a multi-joint leg extension the force after an active eccentric contraction was enhanced compared to a pure isometric contraction. This study was a game changer when thinking about the presence of residual force enhancement in daily human motion. Simultaneous involvement of different joints and their muscles are a succinct characteristic of human movement.

Beside the simultaneous involvement of different joints, another point is distinctive for human motion or human behaviour in general. Muscles are not innervated maximally during daily life. Instead, it is mainly submaximal. The first study attended to this fact was done by Oskuei and Herzog (2005), again at the thumb adductor. In their study they used a muscle activation of 30% of the maximum activation level (MVA). As a result, they found enhanced forces of ~ 7% compared with a pure isometric contraction. Hence, also in submaximal conditions RFE was present. Another, perhaps more

important point of the study regarding daily living, was the second condition during the experiments. The authors also used a force feedback of 30% MVC and could show that the same force resulted in a lower muscle activation level of ~ 5% after an active stretch compared to a pure isometric contraction. To sum up, having higher forces might be good in some conditions but having an activation reduction (AR) means higher efficiency of the muscle contraction and thus probably an optimization of energetic processes inside a muscle. Until today only one *in vitro* study tested this hypothesis of reduced metabolic cost after active stretch on a muscle fibre level (Joumaa & Herzog, 2013). These authors demonstrated a reduction in the ATPase activity per unit force for the isometric contraction after active stretch, compared to the purely isometric contraction for a skinned fibre from rabbit psoas muscle.

The definition of RFE must be completed as follows:

*(1) Using the same level of muscle activation and muscle length, the isometric force after an active stretch is enhanced compared to an isometric contraction without a preceding stretch.*

In addition:

*(2) Using the same amount of force and muscle length, the activation of an isometric contraction after an active stretch is lower compared to an isometric contraction without a preceding stretch.*

The results from Oskouei and Herzog (2005), were verified by several authors. Altenburg, Ruiter, Verdijk, van Mechelen and Haan (2008) as well as Seiberl, Hahn, Herzog and Schwirtz (2012) confirmed the results for the quadriceps femoris. The range for the activation reduction after stretch was between ~8% to ~12% for the isometric contraction after active stretch compared to a pure isometric contraction, while using a muscle contraction level of 10% to 60% MVC.

Only during voluntary contraction did another phenomenon come up, which highlights the need for voluntary activated human muscle studies. In some studies (Hahn et al., 2007; Oskouei & Herzog, 2005; Seiberl et al., 2012; Seiberl, Hahn, Kreuzpointner, Schwirtz, & Gastmann, 2010; Tilp, Steib, & Herzog, 2009), a portion of subjects did not show enhanced forces or reduced activation in the isometric phase after an active stretch, compared with a pure isometric contraction. Hence, there is a responder – non-responder phenomenon during voluntary studies. The number of non-responder is ranging between ~10% up to ~30% in the aforementioned studies. By now, there is no valid explanation for this phenomenon. One theory is about the influence of fibre

type distribution among the subjects. According to Oskouei and Herzog (2005) responders showed a higher post activation potentiation which might be attributed to a greater fast-twitch fibre proportion in those subjects compared with non-responders. Another theory is about subject specific thresholds regarding the level of muscle activation (Oskouei & Herzog, 2006). Some studies could show that with increasing activation level the number of non-responders decreased and was finally non-existing at 100% MVC. However, this result is not consistent across all studies. Hahn et al. (2007), Seiberl et al. (2010) and Tilp et al. (2009) had non-responders in their data even during maximal voluntary contractions. Another theory has not yet been tested is the possibility that some subjects might have a lack of certain muscle physiological abilities regarding neural control. There is only one study testing cortical and spinal excitability during an RFE setup (Hahn, Hoffman, Carroll, & Cresswell, 2012). The authors found that after an active stretch contraction the motor evoked potentials as well as the V-waves were enhanced, compared with a pure isometric contraction. Hence, beside mechanical aspects also neural aspects might modulate force production during and after active eccentric motion.

Finally yet importantly, it is worth mentioning that not only during *in vitro* research but also during *in viv*o research, RFE is present across the whole force-length relationship. This has been verified for example for the quadriceps femoris that uses the whole f-l-r (Power, Makrakos, Rice, & Vandervoort, 2013; Seiberl et al., 2010; Shim & Garner, 2012) or the triceps surae muscle (Pinniger & Cresswell, 2007), which predominantly works on the ascending limb.

To sum up: Residual force enhancement has been verified for voluntary human muscles regarding enhanced forces or reduced activation in the isometric phase after an active stretch, compared to a pure isometric contraction. Additionally, it is known to occur on the whole f-l-r of a muscle (Figure 2). With respect to human motion only one study tested RFE during a multi joint setup using maximum voluntary contractions (Hahn et al., 2010). It is not guaranteed that the results are transferable to submaximal multi-joint contractions. Shim and Garner (2012) did not find RFE on the ascending limb of the f-l-r from the quadriceps femoris. Hence, adding to the fact that during human movement the major joints of the lower extremity are only slightly flexed (Lafortune, Vavanagh, Sommer, & Kalenak, 1992; Winter, 1984), the question arises if RFE is present during multi-joint leg extensions at joint-angle configurations close to natural human motion. Another open question is, whether reduced activation in the

isometric stretch is beneficial regarding muscle fatigue. This would be a hint towards reduced energy consumption and, consequently from this, it could be deduced that an active stretch enhances the economisation of the following isometric phase compared with a pure isometric condition. Still this only can be regarded as an indirect evidence regarding energy consumption. Using a RFE setup while getting a direct view onto the oxygen consumption of a muscle could finally provide direct evidence for an enhanced muscle-energetic economisation. Figure 6 summarizes the current state of scientific research at the beginning of this thesis.

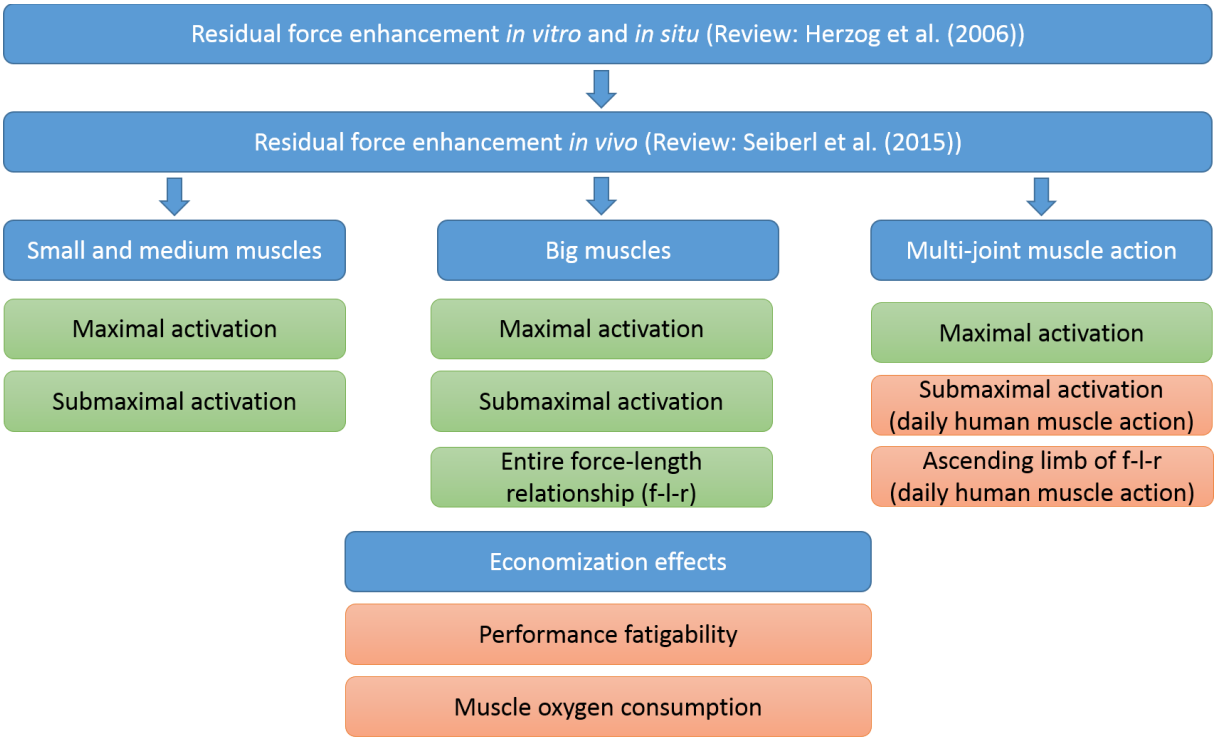


*Figure 6: Flowchart of solved und unsolved question in the research field of residual force enhancement at the beginning of the authors PhD thesis. Green: Solved questions. Red: Unsolved questions and main part of this thesis.*

## 1.3 Aims

In the following section, the aim and focus of the experiments of each paper included in this thesis are presented. The number in brackets represents the chapter of the respective publication.

“On the relevance of residual force enhancement for everyday human movement” (2.1)
The aim of the study was to figure out if residual force enhancement is present during a submaximal multi-joint setup. We hypothesized that for the external reaction force as

well as for the knee and ankle joint torque RFE was present and therefore plays a role during daily motion.

“Residual force enhancement during multi-joint leg extensions at joint-angle configurations clos to natural human motion” (2.2)
This study was designed to close the gap of previously made multi-joint studies (Hahn et al., 2010; Seiberl, Paternoster, Achatz, Schwirtz, & Hahn, 2013), which neglected the fact that human motion occurs only with slightly flexed joints (Lafortune et al., 1992; Winter, 1984). Hence, the research idea in this paper was to mimic joint angle configurations of daily locomotion and gain deeper insights on the relevance of RFE in human movement.

“Reduced activation in isometric muscle action after lengthening contractions is not accompanied by reduced performance fatigability” (2.3)
The aim was to gain insights if RFE in terms of activation reduction counteracts arising fatigue during an exhausting contraction. This would be an indirect evidence regarding the reduced ATPase activity per unit force recently shown in *in vitro* experiments (Joumaa & Herzog, 2013) and support the idea of enhanced neuromuscular efficiency proposed by several authors (Altenburg et al., 2008; Oskouei & Herzog, 2005; Seiberl et al., 2012).

“Oxygen consumption of gastrocnemius medialis during submaximal voluntary isometric contractions with and without preceding stretch” (2.4)
With this study we wanted to provide direct evidence that an active stretch prior to an isometric contraction influences the muscle oxygen consumption compared to a pure isometric contraction. This paper would be the first *in vivo* evidence that the presence of RFE result in an enhanced muscle economization of the following isometric phase, concerning muscle oxygen consumption.

## 1.4 Methods

The following section presents the used methods in the different studies. If a method is used in multiple studies, an appropriate indication will be given in the respective description.

### 1.4.1 Force and torque measurements

The basic measurement device used in all presented studies (2.1 – 2.4) was a motor-driven dynamometer (IsoMed 2000, D&R Ferstl GmbH, Germany). Using such a device enabled a high standardization for our studies with respect to the angular velocity as well as the range of motion of the investigated joint. For performing bilateral leg-extensions in the multi-joint leg extension studies (2.1, 2.2), we connected a leg-press adapter with the basic device, including two 3-D force plates top-mounted on the footrest (Figure 7).

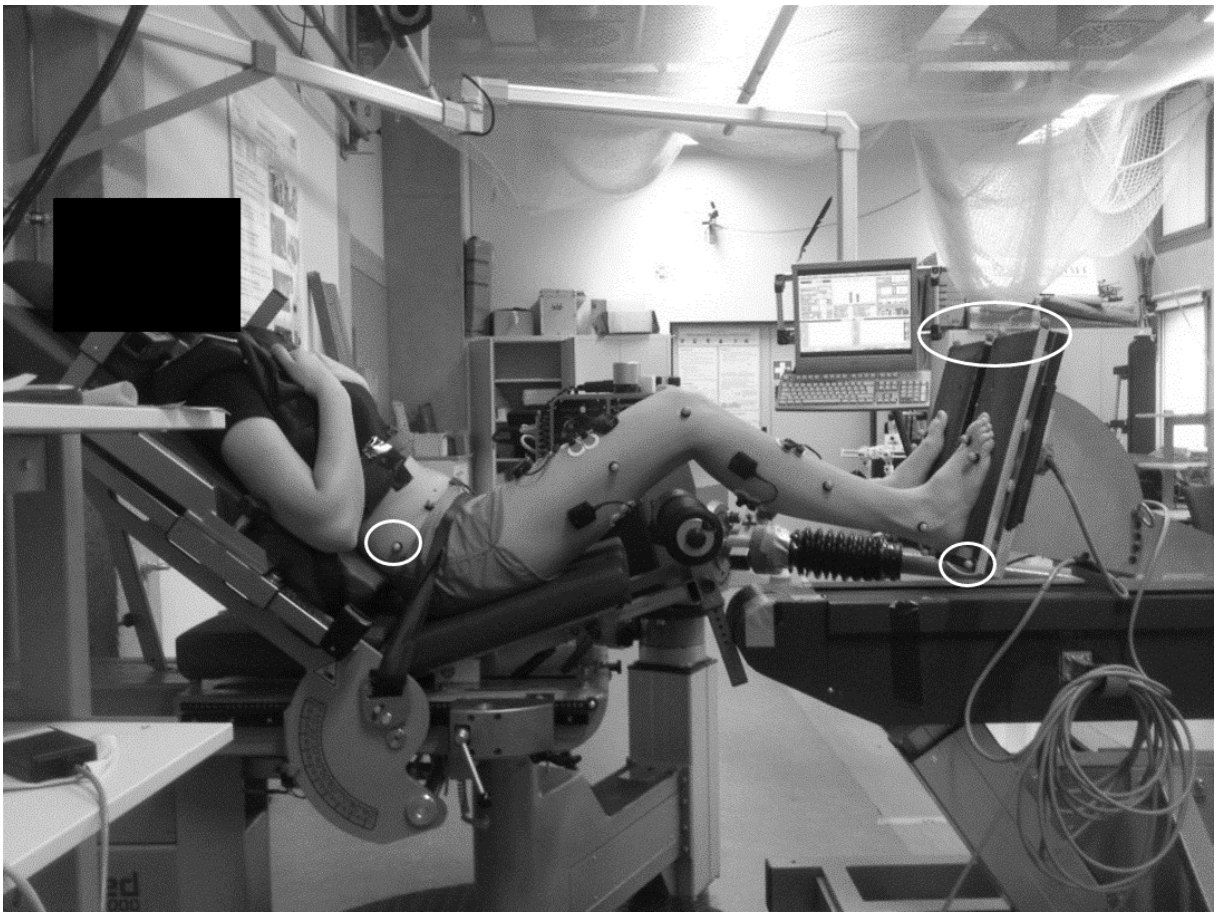

*Figure 7: Example figure of a subject during a multi-joint leg extension setup, including force plates top mounted on the footrest of the leg-press adapter. Note: White circles show the adaption of the used marker set-up exemplarily.*

To ensure the same angular-velocity at the region of interest across the subjects with different anthropometric properties, an anthropometric model for standardization of multiarticular leg extension movements was used (Hahn, Schwirtz, & Huber, 2005). For the measurement of ankle- or knee-joint we used specific adapters provided by the manufacturer (Figure 8) (2.3, 2.4).

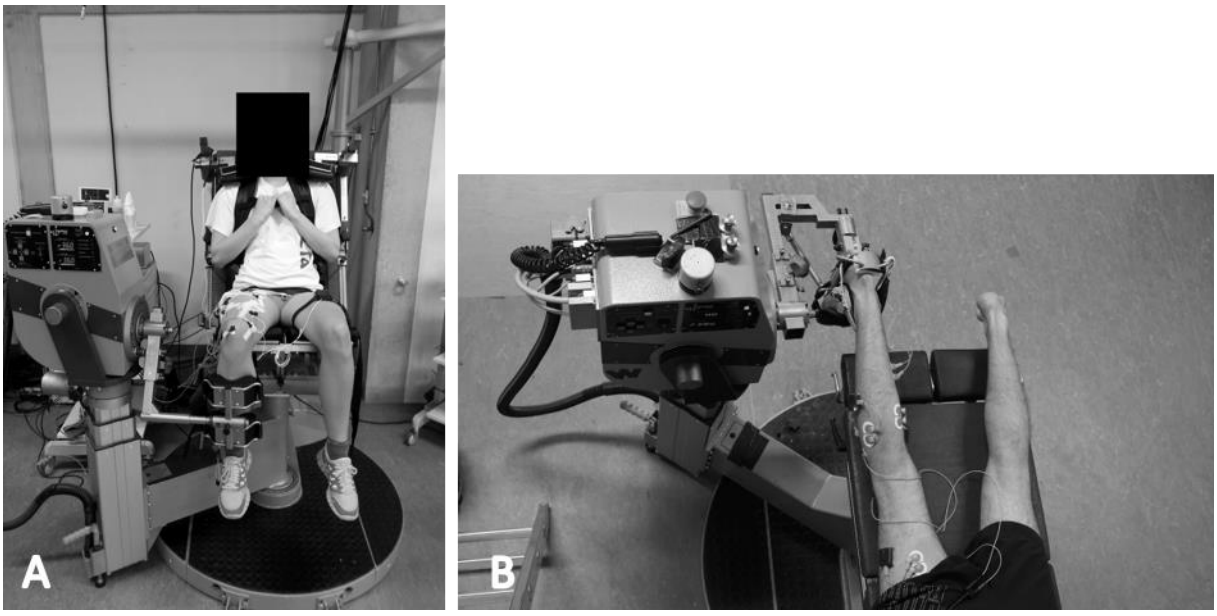


*Figure 8: A) Showing the position of a subject during a setup, measuring knee torque. B) Subject lying prone on the bench of the dynamometer for recording ankle torque data.*

During the different measurement setups the subjects were fixed with several belts as well as shoulder pads to avoid displacements of the body or the investigated joint. The torque data was measured with 1000 Hz. The same is true for the sample frequency of the force plates. Force and torque data were smoothed with a zero-lag second order low-pass filter (10 Hz or 5 Hz).

Hence, the motor-driven dynamometer provided the basis for our measurements of controlled isometric as well as isometric-eccentric-isometric muscle actions.

### 1.4.2 Muscle activation and electrical stimulation

The muscle activities of different muscles were measured using surface electromyography (sEMG). The placement of the electrodes was according to the SENIAM recommendations (Hermens et al., 1999) using an interelectrode distance of 2 cm and a corresponding skin preparation. The sampling frequency was set to 1000 Hz, except for study number three (2.3). In this study, the sampling rate was 4000 Hz due to the use of the interpolated twitch technique (ITT) to classify fatigue (Merton, 1954). Briefly, electrical evoked supramaximal twitches (1ms pulse doublets 10 ms apart) were given onto the corresponding muscle nerve at the peak of a maximal voluntary contraction (superimposed twitch) as well as after deactivation of the muscle in the relaxed state (resting twitch) (Figure 9). Out of this, it is possible to calculate the voluntary activation level of a subject:

$$voluntary\ activation = \left(1 - \frac{superimposed\ twitch}{resting\ twitch}\right) * 100$$

The aim of this calculation is to get an idea of the extent of central fatigue. The individual consideration of the resting twitch represents the occurred peripheral fatigue. The stimulation was done with a constant voltage stimulator (DS7AH Digitimer, United Kingdom). The sEMG signals were processed by using a zero-lag second order butterworth lowpass and highpass filter (500/400 Hz and 10 Hz), a rectification of the signal and finally followed by moving average smoothing.

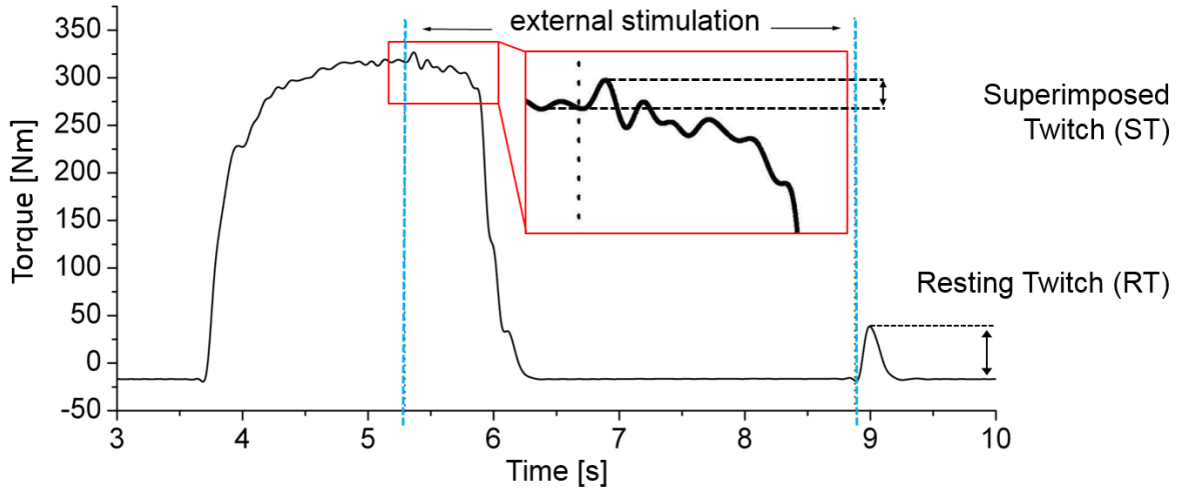


*Figure 9: Example plot of interpolated twitch technique. The horizontal dotted blue lines represent the supramaximal electrical evoked twitches. The superimposed twitch occurred at the plateau region of the torque signal, whereas the resting twitch appeared ~3 s after muscle deactivation.*

### 1.4.3 Kinematic and kinetics analysis

During the multi-joint leg-extension studies (2.1, 2.2), a 6-camera motion analysis system (Vicon Peak, United Kingdom) was used to record (200 Hz) the kinematic data of the lower leg. The marker set-up was based on a slightly adjusted Newington-Helen Hayes model (Charlton, Tate, Smyth, & Roren, 2004) with additional markers on the force plates and adjusted positioning of the left and right posterior superior iliac spine markers onto the left and right side of the crista iliaca (Figure 7). The calculation of the joint kinetics and kinematics was done using a customized biomechanical model with integrated moving force plate (Figure 10). Kinematic data were smoothed with a Woltring filter (5 MSE).

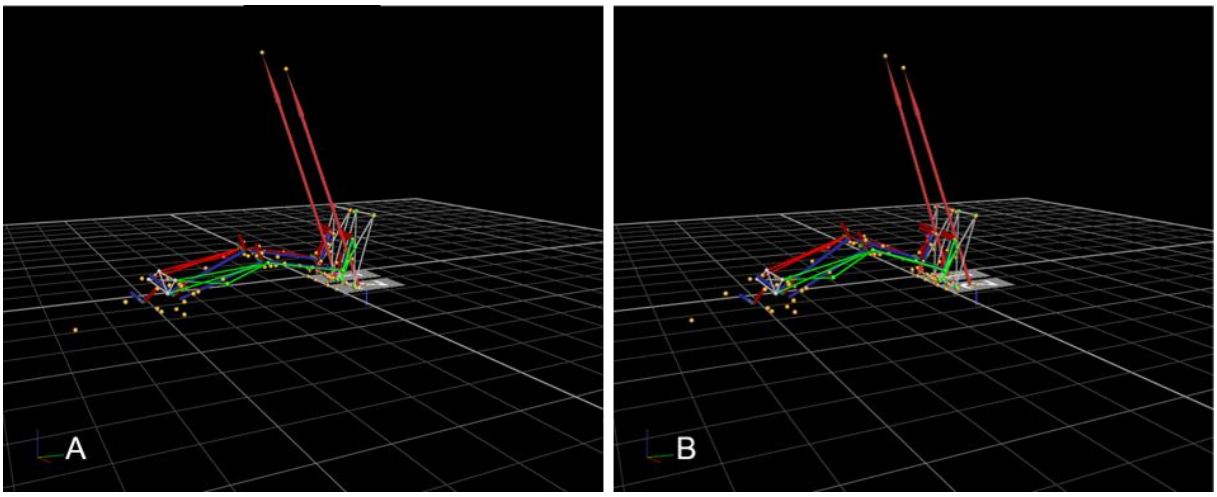


*Figure 10: Exemplar view on VICON Nexus 3-D perspective. A) Represent starting position of the isometric-eccentric-isometric contraction. B) Reference position for the pure isometric and isometric-eccentric-isometric condition. A customized biomechanical model with integrated moving force plate was used for the calculation of the joint kinetics and kinematics.*

### 1.4.4 Muscle oxygen consumption

To estimate the oxygen consumption within the investigated muscle a wireless continuous-wave near-infrared spectroscopy device (NIRS) was used (PortaMon, Artinis Medical Systems, the Netherlands) (2.4). The device consists of three light sources and one light detector and uses wavelengths of 780 and 855 nm. It has a maximal penetration depth of about 2 cm and a sample frequency of 10 Hz. NIRS systems can measure wavelength-specific changes in the optical density of the tissue, reflecting the tissue-oxygenation level in primarily small blood vessels (Mancini et al., 1994) using the modified Lambert-Beer law (Delpy & Cope, 1997). As haemo- and myoglobin are the main absorbers of light and additionally overlap in the absorption spectrum, it is not possible to distinguish between these two proteins. The density changes were transformed into concentration changes of oxygenated haemoglobin ($O_2$Hb), deoxygenated haemoglobin (HHb) and total haemoglobin (tHb) (Figure 11).
NIRS also provides the tissue saturation index (TSI) representing a percentage measurement of tissue oxygen saturation which is independent of the photon path length. The TSI was used as a standardization parameter to exclude different oxygen states at the beginning of the contractions.
Another standardization tool used was a high-pressure cuff (Hokanson 10D, United States). By applying 400 mmHg, using a rapid cuff inflator, an arterial occlusion was established at the region of interest resulting in a constant blood volume. Hence confounding variables like a heterogeneous inflow of oxygenated blood could be

minimized. The NIRS signals were smoothed by using a Loess filter (span 10%). The mean of the linear slopes was taken as representative of muscle oxygen consumption (Ruiter, Goudsmit, van Tricht, & Haan, 2007). Linearity was defined as $r^2 > 0.99$ (Figure 11).

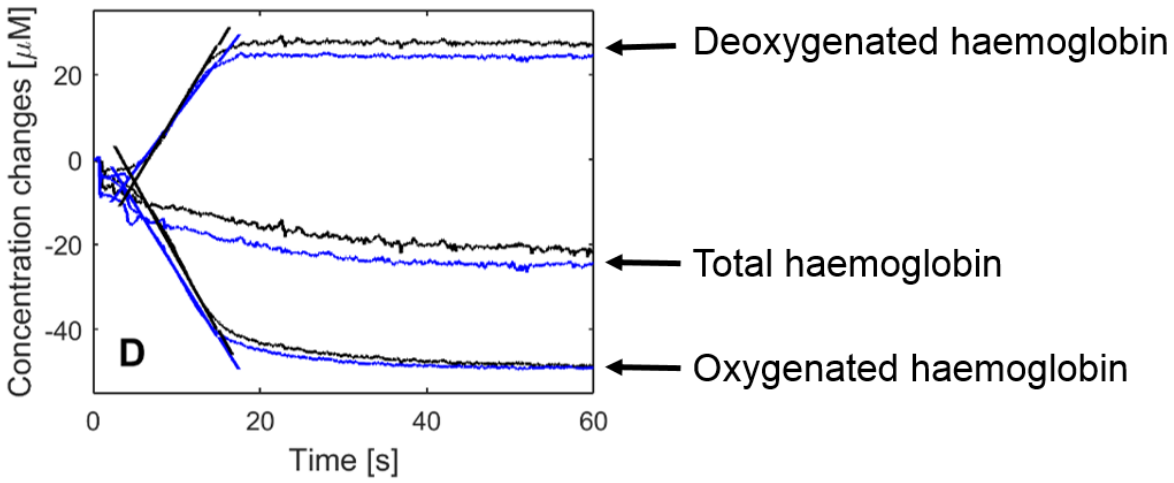


*Figure 11: Example plot of near infrared spectroscopy measurement. Blue: Isometric-eccentric-isometric contraction. Black: Pure isometric contraction. The mean out of the slopes from the oxy- and deoxygenated haemoglobin of the two contraction was calculated as representative of muscle oxygen consumption (Ruiter et al., 2007).*

### 1.4.5 Submaximal contraction level

To ensure the same submaximal contraction level between the isometric and isometric-eccentric-isometric condition, a feedback target curve was provided on a screen in front of the subject (Figure 12). If the presented feedback was muscle activity a rectification and smoothing was applied (1 s moving average) to ensure the traceability of the stochastic sEMG signal. A feedback system was used in all four studies (2.1 – 2.4).


*Figure 12: Experimental Setup: A) Motor-driven dynamometer. B) Electromyography system. C) Near-infrared spectroscopy device. D) High Pressure cuff. E) Shoulder pads. F) Screen for biofeedback*

# 2 Publications

In the following section, the papers underlying this thesis are presented. Thematically the studies can be divided into two-subject areas. The first two papers are dealing with the question of residual force enhancement and its relevance for daily human movement. Therefore a study design and setup was used which mimics the level of muscle activation (2.1) as well as joint angle configurations (2.2) with respect to daily human movement. Study number three and four focused on beneficial effects of RFE regarding muscle efficiency. Using neuromuscular tests, like the interpolated twitch technique, the goal was to estimate possible positive effects of RFE regarding enhanced fatigue resistance (2.3). Meanwhile the last presented publication aimed to figure out if RFE positively influences the energy demands inside the muscle by estimating muscle oxygen consumption (2.4).

## 2.1 Submaximal multi-joint setup (Study One)

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# On the relevance of residual force enhancement for everyday human movement

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ABSTRACT

Although residual force enhancement (RFE), i.e. enhanced force after active muscle stretch, is shown to be present in voluntarily activated human muscles, its relevance for everyday human movement is still elusive. Natural human motion is mainly composed of voluntarily submaximally activated muscle contractions driving coordinated multi-joint movements. Up to now there has been no study that directly investigated the presence of RFE following stretch when performing a submaximal multi-joint movement. For this purpose, $n=13$ subjects performed feedback controlled bilateral leg extensions at the level of 30% maximum voluntary activation in a motor-driven leg press dynamometer. Isometric–eccentric–isometric and purely isometric contractions were arranged in a randomized experimental protocol. Kinematics, forces and muscular activity were measured using optical motion tracking, 3d force plates and EMG of 9 lower extremity muscles. ANOVA identified significant RFE of external reaction force, and knee extension and plantar flexion torque (calculated by inverse dynamics). Enhanced force and torque ranged between 3% and 22% and was present for up to 22 s post-stretch. In spite of motor redundancy for solving a given task, no differences between contraction conditions were observed for any of the analyzed muscles, except for tibialis anterior. On the basis of our results, RFE is present in everyday alike human movement and might be an evolutionary optimization mechanism to enhance muscular performance at a given amount of energetic effort.



### 1. Introduction

Residual force enhancement (RFE), that means enhanced force of a muscle after active muscle stretch compared to purely isometric force at the same muscle length and activation level, has been constantly observed over the last decades in *in vitro* as well as in *in vivo* experiments (Edman et al., 1982; Hahn et al., 2010; Lee and Herzog, 2002; Oskouei and Herzog, 2005). Although the underlying mechanisms of RFE are not exactly known yet, the opinion prevails that sarcomere length non-uniformities, passive structures and half-sarcomere kinetics play a major role in stretch-induced RFE (Joumaa et al., 2007; Rassier, 2012a). For more detailed information on proposed mechanisms please refer to recent review papers (Campbell and Campbell, 2011; Edman, 2012; Herzog, 2013; Rassier, 2012b).

In general, RFE is present at all structural levels of muscle and over the entire range of the force-length relationship (Joumaa et al., 2008; Leonard et al., 2010; Peterson et al., 2004; Shim and Garner, 2012). It is shown to increase with increasing sarcomere length (on the descending limb of the F-l-r) (Edman et al., 1982) and with amplitude of stretch (Abbott and Aubert, 1952; Cook and McDonagh, 1995; Edman et al., 1978, 1982; Sugi, 1972), but RFE is not influenced by the speed of stretch (Edman et al., 1978; Sugi and Tsuchiya, 1988). For electrically stimulated muscle, RFE can be observed as long as the muscle is kept active (Abbott and Aubert, 1952).

Although RFE has continuously been shown for voluntarily activated human muscles (Lee and Herzog, 2002; Seiberl et al., 2010; Shim and Garner, 2012; Tilp et al., 2009), its relevance for everyday human movement remains elusive. Properties of RFE of voluntarily activated human muscles have been found to be different compared to those observed during *in vitro* or animal studies, e.g. total amount of RFE, dependence on stretch amplitude or long lasting effects (Hahn et al., 2007; Lee and Herzog, 2002; Seiberl et al., 2012a). Moreover, these differences occurred albeit previous human studies tried to reproduce results from *in vitro* or animal studies but not to investigate RFE under conditions relevant for human movement. Hence, the role of RFE in real life is still unclear. Natural human motion like walking or several sport techniques are mainly characterized by repetitive muscle contractions performed with submaximal effort that drive coordinated multi-joint movements. Thus, fundamental characteristics for real life scenarios appear to be (i) contractions at a submaximal level of

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activation and (ii) coordination of several large muscles during multi-joint movements.

Latest research revealed data showing RFE to be present in large human muscles (Seiberl et al., 2010; Shim and Garner, 2012; Tilp et al., 2009), during single-joint contractions at submaximal activation level (Oskouei and Herzog, 2005; Pinniger and Cresswell, 2007; Seiberl et al., 2012a) and also during maximum voluntary multi-joint muscle action (Hahn et al., 2010). However, to our knowledge there have been no studies that investigated RFE following stretch when performing a submaximal multi-joint contraction.

Therefore the aim of this study was to investigate the presence and the characteristics of RFE for a submaximal multi-joint leg extension, which is a typical pattern of human movement. Based on the findings from former *in vivo* RFE studies (Hahn et al., 2010; Oskouei and Herzog, 2005; Pinniger and Cresswell, 2007; Seiberl et al., 2012a) we hypothesized that enhanced force (at the level of external reaction forces) as well as enhanced joint torques (calculated by inverse dynamics) are present after eccentric multi-joint leg extension, compared to isometric reference contractions at the same joint-angle configurations.

## 2. Methods

### 2.1. Subjects

Thirteen healthy subjects (3♀, 10♂) with no history of ankle, knee or hip joint injury or neurological disorder participated in the study. The study was approved by the local Ethics Committee of the Technische Universität München and conducted according to the Declaration of Helsinki.

### 2.2. Experimental set-up

The setup was configured according to a former study by Hahn et al. (2010). Briefly, bilateral leg extensions were performed on a motor-driven leg press dynamometer (IsoMed2000, D&R Ferstl GmbH, GER), backrest was reclined to 50° and pelvis and upper body were secured using safety belts and shoulder pads. Stretch amplitude and velocity were arranged according to previous investigations (Hahn et al., 2010; Seiberl et al., 2012a, 2010) aiming at 20° range of motion (ROM) and a mean angular velocity of 60°/s (initial start position of 80°; end position 100° knee flexion; and 0° refers to full knee extension). Acceleration and translational velocities of the motor-driven leg press were adjusted individually according to an anthropometric standardization model (Hahn et al., 2005) to result in the desired angular velocity of 60°/s.

### 2.3. Force measurement, EMG and kinematics

Two 3d-force plates (Kistler, CH) mounted to the leg press footrest adapter were used for measurements of external reaction forces ($F_{ext}$). In addition, wireless surface electromyography (EMG) (myon RFTD, Myon AG, CH) served for quantification of muscular activity of mm. vastus lateralis (VL), rectus femoris (RF), vastus medialis (VM), biceps femoris (BF), semi-tendinosus (ST), gastrocnemius medialis (GM), gastrocnemius lateralis (GL), soleus (SOL), and tibialis anterior (TA). Skin preparation and electrode (Ambu, Denmark) placement were done according to the SENIAM recommendations (Hermens et al., 1999). Lower extremity kinematics were measured with a 9-camera motion tracking system (Vicon Peak, Oxford, UK) using a slightly adjusted Newington–Helen Hayes model marker set with additional markers on the force plates (Charlton et al., 2004; Hahn et al., 2010). A sample rate of 1000 Hz and 250 Hz was used for analog signals (force plates, EMG) and kinematic data, respectively.

### 2.4. Experimental protocol

Subjects were familiarized with testing procedures in at least 2 training sessions in order to perform maximum voluntary contractions (MVC) and to maintain submaximal muscle activation of 30% maximum voluntary activation (MVA) (see Section 2.5). The test session started with 3 isometric leg extension MVCs at 100° knee flexion to obtain maximum voluntary reaction forces and maximal muscle activation. Thereafter, 6 submaximal trials at 30% MVA including 3 purely isometric submaximal leg extensions (at 100° knee flexion) and 3 isometric–eccentric–isometric (stretch from 80° to 100° knee flexion) were performed in a randomized order. The eccentric stretch was initiated 3 s after a stable EMG feedback curve has been generated during the first isometric phase of the contraction and was followed by a second isometric phase of approximately 27 s. During pure isometric trials, subjects had to maintain constant VL activation for 30 s. Subjects got at least 3 min rest between all trials.

### 2.5. Biofeedback

In keeping similar with the single-joint setup of previous work (Seiberl et al., 2012a), visual feedback of VL muscle activation was given to control submaximal muscle activation. VL was chosen since according to Alkner et al. (2000) EMG-torque relation of VL is more linearly related to force compared to RF or VM. In addition, preliminary experiments revealed high correlation ($r > 0.8$) of thigh (VL) and shank (GM, GL) muscles to occur during multi-joint leg extension (Seiberl et al., 2012b). Feedback-information was preprocessed with 1 s root-mean-square smoothing (RMS) in order to reduce stochastic characteristics of EMG signal. Submaximal activation level was set to 30% MVA, with MVA calculated as mean maximum activation (RMS 1000 ms) of the 3 MVC trials.

### 2.6. Modeling

Lower extremity kinematics and kinetics were calculated by inverse dynamics using a customized biomechanical model with integrated moving force plates (Hahn et al., 2010). Individual inertial properties were accounted for by linear regression of weight and body height (Zatsiorsky et al., 1984). In addition, Zatiorsky's segment inertia parameters were adjusted according to de Leva (1996).

### 2.7. Data analysis

The best trial for each contraction condition, determined by the lowest standard deviation (SD) from the target level, and data from the right leg only were used for analysis. Kinematics were smoothed using Woltring filtering routine (MSE 5) and force data was processed using a Butterworth low-pass filter (25 Hz) and moving-average smoothing (100 ms). Thereafter, modeling of joint torques was done (see Section 2.6) based on preprocessed dynamic and kinematic data. EMG signals were band-pass filtered (Butterworth, 10–500 Hz), smoothed (RMS 500 ms) and normalized to MVA as calculated from mean individual activation of MVC trials. Parameters for statistics (force, torque, EMG, kinematics) were assessed over intervals of 2 s between 4–6 s, 8–10 s, and 20–22 s after stretch (AS1-AS3). "After stretch" was defined as the instant in time when the end of stretch was reached during the isometric-eccentric-isometric contractions. Initial starting joint angles were defined over 2 s intervals from 3 s to 1 s before the end of stretch. Thereafter, ROM of knee and ankle joints was calculated as angular displacement between initial starting angles and joint angles at AS1. RFE is presented as percentaged difference between isometric and post-eccentric force and torque at corresponding instances in time.

### 2.8. Statistics

Normality of the data was tested using the Kolmogorov–Smirnov test and a two way repeated ANOVA (factors 'contraction condition' and 'contraction time') and Bonferroni–Holm post hoc comparisons were used to identify characteristics of RFE. Since TA data distribution was not normal, non-parametric statistics (Friedmann and Wilcoxon) were used for this variable. Alpha level was set to $p < 0.05$.

## 3. Results

We found significant RFE at the level of $F_{ext}$, knee and ankle torque at all instances in time, whereas no differences in EMG data, except for TA, could be found between contraction conditions. Detailed mean values and standard deviation of all analyzed data can be found in Table 1. Typical graphs of analyzed signals are shown in Fig. 1.

### 3.1. Biofeedback, kinematics and EMG

We did not find any differences in VL activation level within contraction conditions and time intervals. According to the given submaximal activation level of 30% MVA, for both contraction conditions mean VL activity ranged between $29.1 \pm 2.2\%$ and $29.8 \pm 2.5\%$ MVA. Initial knee flexion angle before stretch was $79.7 \pm 5.0°$ and was followed by a stretch of $17.4 \pm 2.2°$. In the final reference position, significant differences of about 0.5° between post-eccentric and pure isometric knee flexion angles were found

**Table 1**
Means and standard deviation (SD) of measured parameters during isometric–eccentric–isometric (iso–ecc–iso) and purely isometric multi-joint leg extensions.

| Parameters | 4–6 s after stretch | | | | 8–10 s after stretch | | | | 20–22 s after stretch | | | | *p*-values ANOVA | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | iso-ecc-iso | | isometric | | iso-ecc-iso | | isometric | | iso-ecc-iso | | isometric | | | | |
| | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | cond. | time | *X* |
| $F_{ext}$ [N] | **368.0** | 99.2 | **313.0** | 89.9 | **347.1** | 94.1 | **305.3** | 87.6 | **327.9** | 85.5 | **299.6** | 87.6 | **0.00** | **0.00** | **0.00** |
| $M_k$ [Nm] | **63.4** | 24.8 | **55.4** | 20.8 | **58.6** | 23.2 | **53.4** | 20.1 | **51.4** | 20.7 | **49.4** | 18.2 | **0.01** | **0.00** | **0.00** |
| $M_a$ [Nm] | **32.4** | 10.4 | **26.9** | 7.5 | **31.5** | 9.6 | **27.1** | 7.8 | **31.9** | 9.2 | **28.0** | 8.5 | **0.03** | **ns** | **ns** |
| COP [mm] | 179.2 | 26.4 | 182.2 | 22.5 | 181.9 | 25.6 | 185.0 | 22.7 | 187.4 | 26.6 | 188.0 | 23.5 | **ns** | **0.01** | **ns** |
| Knee angle [°] | **97.1** | 4.0 | **97.7** | 3.9 | **97.3** | 4.0 | **97.8** | 4.0 | **97.3** | 4.0 | **97.8** | 4.0 | **0.01** | **0.00** | **ns** |
| Ankle angle [°] | **19.8** | 2.9 | **19.2** | 3.3 | **19.8** | 3.0 | **19.1** | 3.3 | **19.7** | 3.1 | **19.1** | 3.3 | **0.01** | **ns** | **ns** |
| Line of action [°] | 9.6 | 4.6 | 10.3 | 5.5 | 9.5 | 5.0 | 10.4 | 5.6 | 9.0 | 5.8 | 9.6 | 5.7 | **ns** | **ns** | **ns** |
| EMG [%MVA] | | | | | | | | | | | | | | | |
| VL | 29.8 | 2.5 | 29.7 | 1.5 | 29.4 | 2.9 | 29.2 | 2.0 | 29.1 | 2.2 | 29.6 | 2.7 | **ns** | **ns** | **ns** |
| VM | 25.0 | 6.1 | 22.6 | 7.7 | 23.0 | 5.8 | 23.4 | 6.6 | 24.0 | 6.6 | 22.9 | 6.6 | **ns** | **ns** | **ns** |
| RF | 16.2 | 9.7 | 14.3 | 10.1 | 15.8 | 8.9 | 14.9 | 10.2 | 15.4 | 8.9 | 15.5 | 8.6 | **ns** | **ns** | **ns** |
| ST | 35.1 | 18.5 | 35.7 | 21.5 | 36.3 | 20.3 | 36.5 | 23.0 | 42.6 | 24.7 | 40.8 | 23.6 | **ns** | **0.01** | **ns** |
| BF | 32.5 | 6.3 | 33.5 | 7.2 | 31.7 | 6.4 | 32.7 | 6.7 | 32.0 | 6.4 | 33.1 | 7.0 | **ns** | **ns** | **ns** |
| GL | 25.4 | 8.2 | 23.8 | 7.6 | 25.2 | 8.6 | 24.6 | 8.4 | 26.7 | 9.7 | 25.7 | 8.5 | **ns** | **0.04** | **ns** |
| GM | 23.4 | 6.2 | 22.4 | 5.7 | 23.2 | 6.0 | 22.5 | 6.2 | 24.2 | 6.4 | 23.7 | 5.9 | **ns** | **0.02** | **ns** |
| SOL | 16.8 | 6.6 | 16.6 | 7.2 | 16.7 | 6.5 | 17.1 | 7.3 | 19.1 | 7.8 | 18.7 | 7.9 | **ns** | **0.02** | **ns** |
| TA | **19.4** | 24.4 | **8.0** | 10.2 | 19.6 | 23.6 | 9.5 | 12.4 | 23.8 | 31.1 | 14.8 | 16.6 | **Friedman $p$=0.02** | | |

*P*-values and non-significant results (ns) of repeated measures ANOVA are presented for the factors contraction conditions (cond.) and time, and their interaction (***X***). After Bonferroni–Holm post hoc comparisons, significant differences between contraction conditions of parameters at specific time intervals are displayed in bold letters. Alpha level was set to $p<0.05$.

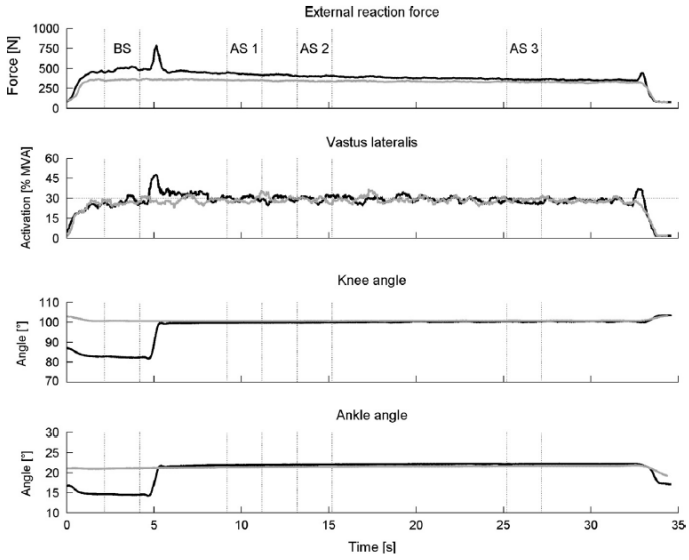


**Fig. 1.** Exemplar ($n=1$) data of typical experimental results of isometric–eccentric–isometric (black) and pure isometric (gray) multi-joint leg extensions before stretch (BS) and at analyzed time intervals of 4–6 s (AS 1), 8–10 s (AS 2) and 20–22 s (AS 3) after stretch. There is considerable enhanced external reaction force after stretch compared to isometric reference. Feedback control of rectified and smoothed activation of vastus lateralis was set to 30% of maximum voluntary activation (MVA).

(Table 1). Ankle joint angles were calculated to be $12.2^\circ \pm 4.0^\circ$ dorsi flexion (with $0^\circ$ defining the position when the tibia/fibula axis is perpendicular to the plantar aspect of the foot) at initial starting position and mean ROM during stretch was $7.6^\circ \pm 1.3^\circ$. This resulted in $19.8^\circ \pm 2.9^\circ$ dorsi flexion after stretch and there was a significant difference of about $0.7^\circ$ to isometric reference trials (Table 1).

None of the analyzed muscles showed any differences between contraction conditions, except TA showing increased activation 4–6 s after stretch (19.4 ± 24.4% MVA) compared to purely isometric trials (8.0 ± 10.2% MVA). Concerning contraction time, ANOVA identified significant increase of activation from AS1 to AS3 for GL, GM, SOL and ST (see Table 1).

### 3.2. Force and calculated joint torques

During MVCs, maximum $F_{ext}$ was 1207 ± 222 N. This resulted in calculated joint torques of 166.7 ± 43.0 Nm and 111.1 ± 19.7 Nm in

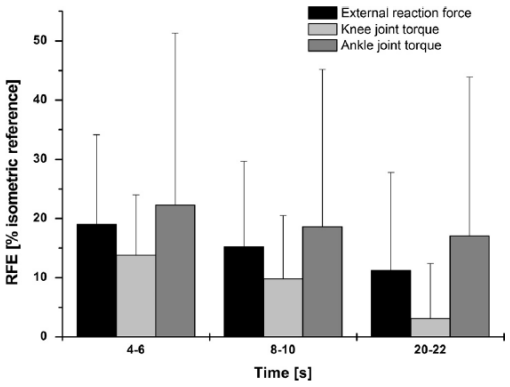


**Fig. 2.** Means and standard deviation of residual force enhancement (RFE) for external reaction force, knee and ankle joint torque at the analyzed time intervals of 4–6 s, 8–10 s, and 20–22 s after stretch. RFE is displayed as percentage enhancement after stretch in relation to the isometric reference. Significant RFE was found for every parameter at any analyzed time interval, although there is a significant decrease in RFE of external reaction force and knee joint torque.

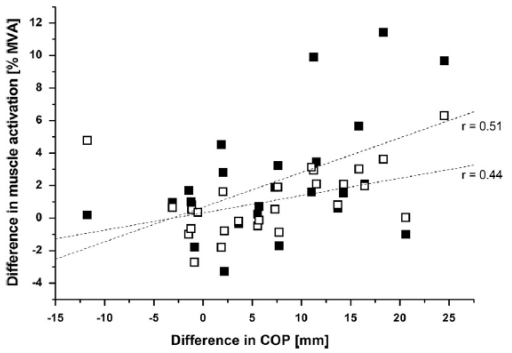


**Fig. 3.** Correlation between rising activity and increasing vertical shift of the center of pressure (COP) with ongoing contraction time. Differences were calculated by subtraction of data at time interval 4–6 s after stretch (AS1) from data of interval 20–22 s after stretch (AS3). Significant correlations with COP were only found for *m.* soleus (black squares) ($r=0.51$) and *m.* gastrocnemius medialis (white squares) ($r=0.44$).

knee ($M_k$) and ankle joint ($M_a$), respectively. In submaximal trials, force as well as torques were always significantly enhanced in post-eccentric states compared to isometric references (Fig. 2) resulting in RFE of $19.2 \pm 15.1\%$, $15.2 \pm 14.5\%$ and $11.2 \pm 16.6\%$ for $F_{ext}$, $13.7 \pm 10.2\%$, $9.8 \pm 10.7\%$ and $3.1 \pm 9.3\%$ for $M_k$, and $22.3 \pm 29.1\%$, $18.6 \pm 26.6\%$ and $17.0 \pm 26.9\%$ for $M_a$ in AS1–AS3, respectively. However, the amount of RFE significantly decreased over contraction time for $F_{ext}$ and $M_k$.

## 4. Discussion

While the underlying mechanisms of RFE still remain a matter of debate, its existence has been proven in many experimental setups (Edman et al., 1982; Lee and Herzog, 2002). Although even single sarcomere experiments identified RFE to be an essential part of muscle function (Leonard et al., 2010), a simple transfer of results to *in vivo* human movement is crucial. Therefore the purpose of this study was to analyze the relevance of RFE for everyday alike human muscle action. In this work we found significant RFE for submaximal multi-joint leg extensions at the level of external reaction forces as well as joint torques for up to 22 s after stretch. Hence, we believe that RFE is also a substantial part of muscle function in complex human movement at moderate intensities.

In order to describe RFE for voluntary muscle action *in vivo*, definition criteria like identical activation level and muscle length/joint angles need to be met very carefully. Standardization of contraction intensity was controlled via biofeedback of VL at a target level of 30% MVA. Actually measured VL activity was almost exactly 30% MVA and there were no differences concerning contraction conditions or time. Analyzed uncontrolled muscles showed variable activation intensities from 8% (TA) to 43% (ST) MVA. This basically reflects the motor redundancy phenomenon (Bernshtein, 1967) for complex motion tasks like multi-joint leg extension, as contribution to overall force differs among involved muscles. Nevertheless, except for TA, there were no differences in muscular activation according to contraction conditions. As TA activity was higher during post-eccentric contractions, if at all, additional dorsi flexion torque due to higher TA activity would counteract plantar flexion, and RFE of ankle joint might be slightly underestimated.

Throughout contraction time there was a significant increase of activation of GM, GL, SOL and ST muscles (see Table 1), which came along with a slight vertical COP shift towards the ball of the foot of $8.1 \pm 8.2$ mm and $5.8 \pm 8.3$ mm in post-eccentric and isometric states, respectively. However, we only found significant and moderate correlations between COP shift (differences of COP between AS1 and AS3 in mm) and increased activation (differences of activation between AS1 and AS3 in % MVA) for SOL ($r=0.51$) and GM ($r=0.44$) (Fig. 3). In addition, the line of action of $F_{ext}$ did not change throughout all trials and $M_a$ was almost constant during AS1, AS2 and AS3 in corresponding contraction conditions. Therefore increasing plantar flexor and ST muscle activity might have originated from raising fatigue (Moritani et al., 1986) rather than from changes in motor performance.

Concerning the criteria of identical muscle length, for single-joint experiments Seiberl et al. (2010) reported that after stretch fascicle length of VL was the same as in purely isometric reference contraction. A finding by Tilp et al. (2011) also confirmed this for TA. Therefore control of external joint angles seems to be a valid method to standardize underlying muscle length. Statistically significant differences of knee and ankle joint angles between contraction conditions in this study therefore might indicate differences in muscle length.

According to Hahn et al. (2010) greater knee flexion angles after stretch are due to higher forces on soft tissues and seat cushion. Using linear interpolation in maximum voluntary leg extensions they found differences of 1° knee flexion to led to an overestimation of RFE by 2% (Hahn et al., 2010). Although mean differences of about 0.5° in this study on submaximal contractions with 30% MVA are unlikely to have a meaningful influence on RFE interpretation, difference in knee angle might led to slightly overestimated RFE. Concerning the increased post-eccentric ankle dorsi flexion of about 0.7°, Hahn et al. (2011) showed that in multi-joint leg extension force and torque increases with increasing plantar flexion. Therefore ankle joint angle after stretch is disadvantageous in terms of torque production, which probably led to a light underestimation of RFE. Nevertheless, as differences in angle configurations were very small ($< 1°$) this is considered to be negligible. Hence, clearly enhanced forces and torques after stretch are thought to be directly related to proposed mechanisms like structural non-uniformities, engagement of titin, or changes in

cross-bridge kinetics (Campbell and Campbell, 2011; Edman, 2012; Herzog et al., 2008; Rassier, 2012b).

Maximum values of $F_{ext}$, $M_k$ and $M_a$ are within the range of data reported for similar multi-joint leg extension setups (Hahn et al., 2011, 2010). Reduction of contraction intensity to 30% MVA led to 33% and 38% MVC in isometric and post-eccentric $M_k$, which corresponds directly to results Seiberl et al. (2012a) found in EMG controlled single-joint experiments. In this context, $F_{ext}$ and $M_a$ were slightly lower and ranged between 24% and 30% MVC. The variety of possibilities to perform submaximal multi-joint movements with one and the same target criteria gets obvious in high SDs (Table 1) and poor correlations of muscle activation with force, as EMG data pooled over contraction condition and time did not show any resilient relation to $F_{ext}$ (Fig. 4), except for GL ($r=0.63$).

With RFE of 13% to 3%, data of $M_k$ is in good agreement with joint torques measured directly during single-joint experiments at the same level of activation (Seiberl et al., 2012a). In contrast, with up to 22% RFE, $M_a$ as observed here was about twice the values reported for single-joint experiments (9% RFE: Hahn et al., 2012; 7% RFE: Pinniger and Cresswell, 2007) or multi-joint setups (12% RFE: Hahn et al., 2010). Interestingly, this mismatch to literature seems not to be related to contraction intensity as Pinniger and Cresswell (2007) analyzed RFE in voluntary plantar flexion at about the same intensity (28% MVA), whereas Hahn et al. (2010, 2012) investigated contractions at maximum effort. Despite statistical significance, Fig. 2 reveals extreme SD for RFE of $M_a$, which can be explained by some subjects having RFE of up to 70% whereas others did not show enhanced but reduced post-eccentric torque of some 20%. As there is clear RFE for $F_{ext}$, we speculated that there might be a negative correlation between RFE of knee and ankle joint, depending on leg extension technique preferring force transmission via the ball of the foot or the heel. However, against our expectations data only showed a moderate positive correlation ($r=0.42$) (Fig. 5). In addition, there was no correlation ($r=-0.09$) between COP-shift and RFE in ankle joint. Therefore RFE in $M_a$ seems to be highly affected by extreme values of single cases since no systematical behavior was found. However, there was only one subject which did not show enhanced torque neither in knee nor in ankle joint (see Fig. 5).

In addition to high RFE, another interesting finding was that the amount of RFE in the ankle joint did not decrease significantly over contraction time and still was 17% at AS3. This reflects a long lasting effect that has also been reported in literature (Abbott and Aubert, 1952; Herzog and Rassier, 2002), but is barely supported by other *in vivo* human experiments. If analyzed at all, most

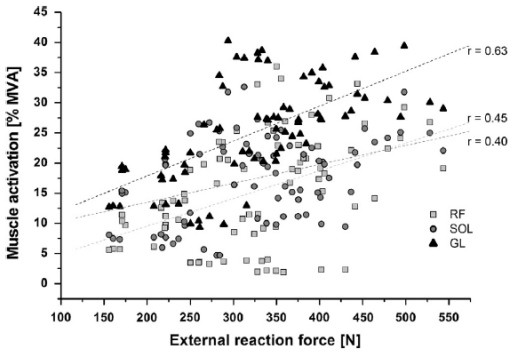


**Fig. 4.** Correlation of external reaction force with EMG of leg extending muscles, pooled over contraction time and conditions. Significant correlations can only be found with m. rectus femoris (RF, $r=0.45$), m. gastrocnemius lateralis (GL, $r=0.63$) and m. soleus (SOL, $r=0.40$).

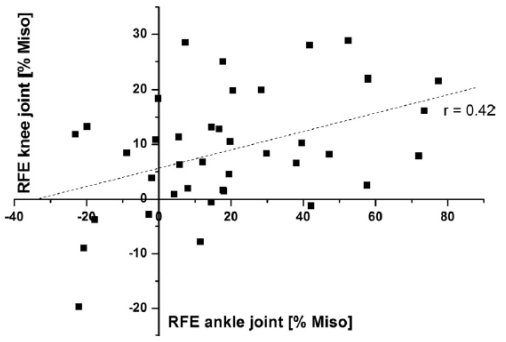


**Fig. 5.** Significant correlation ($r=0.42$) between residual force enhancement (RFE) of knee and ankle joint torque, pooled over contraction time. Note, only four data points in the bottom left corner describe no RFE neither in knee nor in ankle joint, in which three of them belong to one and the same subject.

studies reported force or torque to decrease more rapidly after stretch-contractions than during isometric references (Hahn et al., 2007; Seiberl et al., 2010; Shim and Garner, 2012). The reason for this remains unclear but might be due to the multi-joint experimental setup. To the author's knowledge this is the only paper describing RFE during multi-joint leg extensions over a time period of more than 20 s. Therefore, observations need to be confirmed in similar setups and further investigation on phenomenological characteristics is needed.

Despite obvious limitations of *in vivo* experiments concerning the analysis of underlying mechanisms of RFE, its existence in real life human movement is almost incontrovertible. Analog to enhanced forces, literature also reports reduced activation after stretch compared to purely isometric contractions (Oskouei and Herzog, 2005; Seiberl et al., 2012a). Provided that activation reduction and RFE originate from the same mechanism(s), Seiberl et al. (2012a) assumed that RFE is beneficial in saving metabolic energy while executing a given task. Just recently Joumaa and Herzog (2013) verified this hypothesis for single muscle fiber energetics, where ATPase was reduced after stretch-contractions. They further speculated that this reduced metabolic cost might be an important property in the evolution of muscles (Joumaa and Herzog, 2013).

Nevertheless, the question arises why and when RFE is present in real life. Normally, muscle function incorporates a combination of eccentric and concentric actions forms, so called stretch-shortening cycles (SSC) (Komi, 2000). Whereas preceding shortening decreases RFE in a dose-dependent manner, preceding stretch is reported to not inhibit force depression (Herzog and Leonard, 2000). Therefore RFE might not be beneficial in SSC movements. On the other hand, there is strong evidence showing stretch to increase force production during subsequent concentric muscle action, resulting in enhanced performance that is supposed to originate from stored elastic energy or myoelectrical potentiation (Bosco et al., 1982; Cavagna et al., 1968; Harrison et al., 2004; Komi, 2000). Although literature treats proposed mechanisms of SSC and RFE disparately, at the latest when it comes to multi-joint stretch-shortening, one has to think of similarities.

## 5. Conclusion

In this work we could show that RFE is present in everyday alike human muscle action. Enhanced force or torque during submaximal leg extensions at 30% MVA ranged between 3% and 22% and was present for up to 22 s post-stretch. Therefore RFE

might be an evolutionary optimization mechanism to increase muscular power at constant or reduced energetic costs. However, this has to be proven by future *in vivo* work to get a more detailed view on the relevance of RFE in real life muscle function. For this purpose, experimental studies combining methods from neuromechanics and exercise physiology should concentrate on fatigue and energy consumption after stretch compared to purely isometric contractions. In addition, *in vivo* experiments should be focused on characteristics of SSC contractions in relation to RFE and the force depression phenomenon.

## Conflict of interest statement

No conflict of interest.

## Acknowledgments

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## 2.2 Joint-angle configurations close to natural human motion (Study Two)

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# Residual force enhancement during multi-joint leg extensions at joint- angle configurations close to natural human motion ☆

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ABSTRACT

The isometric steady-state forces following lengthening are greater than those produced at the same muscle length and activation level but without prior lengthening. Although residual force enhancement (RFE) has been investigated across a range of conditions, its relevance for daily human movement is still poorly understood. We aimed to study RFE in a setup imitating daily activity, i.e., submaximal activation of the lower extremity's muscles with slightly flexed knee joints comparable to human walking.

A motor-driven leg press dynamometer was used for randomly arranged purely isometric and isometric–eccentric–isometric contractions. Thirteen subjects performed multi-joint leg extensions, which were feedback-controlled at 30% of maximum voluntary vastus lateralis activation. Isometric–eccentric–isometric contractions incorporated a stretch from 30° to 50° knee flexion, while isometric contractions were performed at 50° knee flexion. Isometric contractions following stretch and purely isometric reference contractions were performed at 50° knee flexion. Kinematics, forces, and muscular activity were measured using 3D optical motion tracking, force plates, and surface EMG of 9 lower limb muscles of the right leg and joint torques were calculated by inverse dynamics. Variables of standardization (EMG, joint angles) showed no differences between contraction conditions. Eight of 13 subjects showed RFE of up to 24.8 ± 32.5% for external forces and joint torques. Because the remaining 5 non-responders failed to produce enhanced forces during the stretch, we believe that RFE is functionally relevant for muscle function comparable to everyday human motion but only if there is enhanced force during stretch that sufficiently triggers mechanisms underlying RFE.



### 1. Introduction

Stretch of an active muscle induces a change in muscular properties, influencing the post-eccentric isometric phase. Abbott and Aubert (1952) first described this phenomenon known as residual force enhancement (RFE). RFE describes isometric muscular force production after an active muscle is stretched; this force is greater than the isometric force produced at a similar muscle length and an equal level of muscular activation, without preceding stretch.

Notably, the origin of this muscle feature remains unclear (Edman, 2012; Edman and Tsuchiya, 1996; Herzog and Leonard, 2002; Pinniger et al., 2006; Rassier and Pavlov, 2012), although it has been experimentally verified using *in vivo* and *in vitro* techniques (Hahn et al., 2010; Joumaa et al., 2008; Oskouei and Herzog, 2005; Seiberl et al., 2013; Shim and Garner, 2012).

Initial *in vivo* studies primarily focused on confirming results from *in vitro* experiments (Cook and McDonagh, 1995; Lee and Herzog, 2002; Ruiter et al., 2000). However, several recent investigations have focused on examining RFE during multi-joint or submaximal contractions to approximate everyday human muscle action (Hahn et al., 2010; Pinniger and Cresswell, 2007; Seiberl et al., 2010, 2012, 2013). Especially during experiments with submaximal contractions, a discrepancy between the total number of participating subjects and those showing RFE has been noted (Oskouei and Herzog, 2005; Seiberl et al., 2012; Tilp et al., 2009). Thus far, absence of RFE in certain subjects cannot be explained.

Because human movements, such as walking, are characterized by simultaneous involvement of several joints and their muscles, it is unclear if and how mechanism underlying RFE affect net performance and studies have aimed to elucidate general roles of RFE in human movement. However, previous multi-joint studies (Hahn et al., 2010; Seiberl et al., 2013) have neglected that during such movements,

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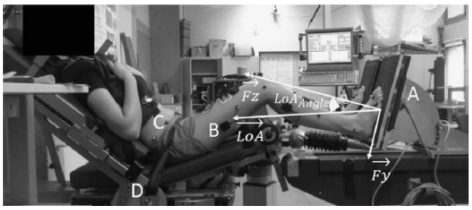


**Fig. 1.** Picture of the experimental setup of the study. A: Footrest of the leg-press including the top mounted 3D force plates. B: Wireless EMG system. C: Reflecting marker. D: Safety belts for the upper body. $\vec{F_z}$: Force perpendicular to the force plate. $\vec{F_y}$: Vertical Force along the force plate. $\vec{LoA}$: Resultant force vector resulting from $\vec{F_z}$ and $\vec{F_y}$. $LoA_{Angle}$: Angular direction of the $\vec{LoA}$ in relation to $\vec{F_z}$.

major joints of the lower extremity are only slightly flexed (Lafortune et al., 1992; Winter, 1984), so that quadriceps femoris and triceps surae are acting on the ascending limb of their torque-length relationships (T-l-r) (Kawakami et al., 1998; Pincivero et al., 2004; Power et al., 2013). Hence, in this study, we aimed to mimic joint angle configurations of daily locomotion and gain insights on the relevance of RFE in human movement.

## 2. Methods

### 2.1. Subjects

Thirteen healthy subjects (10 males, 3 females) with no history of ankle, knee, or hip joint injuries or neurological disorders participated in the study. This study was approved by the local Ethics Committee of the Technische Universität München and conducted according to the Declaration of Helsinki.

### 2.2. Experimental Setup

We used a setup based on previous studies (Hahn et al., 2010; Seiberl et al., 2013) with slight modifications (Fig. 1). Briefly, bilateral leg-extensions were performed on a motor-driven dynamometer (IsoMed 2000, D&R Ferstl GmbH, Germany). The backrest was reclined to 30° and the footrest with the force plates was rotated by 15° from the vertical toward plantar flexion and fixed. The pelvis and upper body were secured using safety belts and shoulder pads. Stretch amplitude and velocity corresponded to those in previous investigations (Hahn et al., 2010; Seiberl et al., 2013), aiming at a 20° range of motion (ROM) for the knee joint and mean angular velocity of 60°/s. This resulted in a ROM of $6.6 \pm 1.3°$ for the ankle joint starting from $-10.5 \pm 3.5°$ plantar flexion (0° defining the position when the tibia axis is perpendicular to the plantar aspect of the foot. Positive and negative angles refer to plantar and dorsi flexion, respectively). In contrast to previous studies, the initial start and end positions were set to 30° and 50° knee flexion, respectively (0° refers to full leg extension). Accordingly, the quadriceps femoris acted on the ascending limb of its T-l-r (Pincivero et al., 2004), same applies to the triceps surae (Hahn et al., 2012). In this context, ultrasound experiments from earlier studies (Seiberl et al., 2010; Tilp et al., 2011) showed that defining the knee joint angle is a valid method to standardize the underlying muscle length within subjects. Finally, the acceleration and velocity of the motor-driven leg press resulting in the desired angular velocity of 60°/s were adjusted individually, according to an anthropometric standardization model (Hahn et al., 2005).

### 2.3. Force measurement, electromyography (EMG), and kinematics

The external reaction force ($F_{ext}$) was measured by two 3-component force plates (Kistler, CH) top-mounted to the leg press footrest adapter. Activation of vastus medialis (VM), rectus femoris (RF), vastus lateralis (VL), biceps femoris (BF), semitendinosus (ST), gastrocnemius medialis (GM), gastrocnemius lateralis (GL), soleus (SOL), and tibialis anterior (TA) were recorded from the right leg using a wireless surface EMG system (myon RFTD, Myon AG, CH) (Fig. 1). After skin preparation, EMG electrodes (Ambu, Denmark) were placed on the muscles with an 20-mm inter-electrode distance, according to the SENIAM recommendations (Hermens et al., 1999). A 6-camera motion analysis system (Vicon Peak, Oxford, UK) was used to record kinematic data from the lower extremity. We used a slightly adjusted Newington-Helen Hayes model, with additional markers on the force plates (Hahn et al., 2010; Seiberl et al., 2013). All data were synchronized and sampled at 1000-Hz (analog data and EMG) and 250-Hz (kinematic data).

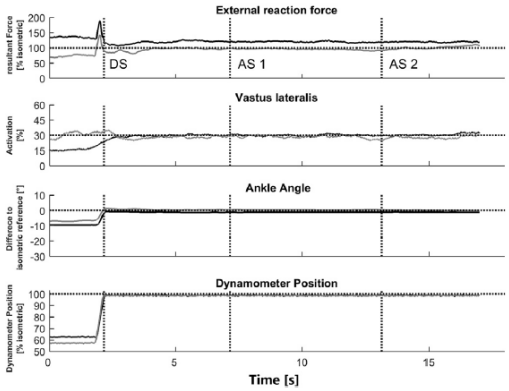


**Fig. 2.** Exemplar data of a responder (black) and a non-responder (gray) during multi-joint leg extension at the analyzed time intervals just before the end of stretch (DS) and 4–6 s (AS1) and 10–12 s (AS2) after stretch. The non-responder showed no enhanced force either at the end of stretch or at any time point after stretch (top trace). Feedback control of rectified and smoothed EMG of VL was set at 30% of maximum voluntary activation obtained at the reference position of 50° knee joint flexion. Muscle activation and kinematics after stretch showed no differences between subjects and in comparison to the purely isometric reference values. Different starting positions of the dynamometer were due to different leg lengths of subjects. To reach desired angular velocity of 60°/s, an anthropometric standardization model was used (Hahn et al., 2005). The dotted horizontal lines represent the reference values.

### 2.4. Biofeedback

Biofeedback was provided on a screen in front of the subjects represented by the EMG signal of VL muscle from the right leg. Due to the stochastic properties of EMG signals, muscle activity of VL was rectified and smoothed with a 1-s moving average (MOV) to ensure traceability. VL muscle was selected because it provides a more linear EMG-force relationship compared to RF or VM (Alkner et al., 2000; Seiberl et al., 2012, 2013)

### 2.5. Experimental protocol

Previous to the day of the experiments, subjects performed a training session to become familiar with the setup. This was particularly important to train the reproduction of submaximal contractions at 30% maximum voluntary activation (MVA). If there was concern regarding reproduction, additional training was held.

At the beginning of the experiment, subjects first performed three maximum voluntary leg extensions (MVC) at 50° knee flexion. MVA of VL and all other measured muscles was then defined as the mean of maximum activations within the three MVC trials. MVC contractions were followed by six randomized submaximal contractions (30 s each) comprising three purely isometric (50° knee flexion) and three isometric–eccentric–isometric (iso–ecc–iso) contractions. During iso–ecc–iso contractions, a stable feedback curve of 2 s was required during the first isometric phase before the eccentric phase was initiated (Fig. 2). The following isometric phase lasted 28 s. During purely isometric trials, subjects had to maintain 30 s of stable feedback. Between every trial, subjects rested as long as required; the minimum rest was for 3 min (Salles et al., 2009).

### 2.6. Modeling

Inverse dynamics using a customized biomechanical model with integrated moving force plates (Hahn et al., 2010) were used for calculating knee and ankle joint kinematics and kinetics. Individual inertial properties were determined by a linear regression of weight and body height (Zatsiorsky et al., 1987). Additionally, Zatsiorsky's segment inertia parameters were adjusted according to de Leva (1996).

### 2.7. Data analysis

Only data from the right leg were selected for analysis and only the trials with the lowest standard deviation (SD) from the biofeedback target level (i.e. the trial closest to 30% MVA and with least EMG oscillation) were taken for final processing. Force data were smoothed (10-Hz low-pass), whereas kinematics were processed

with a Woltring filter routine (MSE 5). EMG signals were band-pass filtered (10–499 Hz), rectified, and smoothed (0.5-s MOV). EMG of each muscle was normalized to respective MVA. The angular direction of the line of action (LoA) of the external force resulting from the y- and z-components was calculated using $\tan^{-1}$ of the division from the y-vector and z-vector of $F_{ext}$ (Fig. 1). Similar to previous studies (Hahn et al., 2010; Seiberl et al., 2013), parameters were determined during stretch (DS) just before the end of stretch, and at two specific times after stretch over a 2-s analysis window (AS1: 4–6 s, AS2: 10–12 s). RFE was calculated as percentage increase of force or torque (knee, ankle) over the isometric reference at corresponding joint angle, activation and time. Analyses were performed using the Biomechanical ToolKit (Barre and Armand, 2014) and MATLAB (The MathWorks, Inc., Natick, Massachusetts, United States).

### 2.8. Statistics

First, Shapiro–Wilk test was performed to check the normality of the data. A two-way repeated ANOVA was used to examine whether there were any statistical differences between "contraction time" and "contraction condition." If normality was rejected, non-parametric Friedmann and Wilcoxon tests were used. The alpha level was set to $p < 0.05$ and if needed, adjustments according to Bonferroni Holm post-hoc comparisons were applied. Analyses were performed using IBM SPSS statistics software (SPSS for Windows, SPSS Inc., Chicago, IL, United States).

## 3. Results

Although eight out of 13 subjects showed enhanced external reaction forces (AS1: $p=0.01$. AS2: $p=0.018$) after stretch compared to the purely isometric trials, no significant RFE was observed analyzing the overall subject group (AS1: $p=0.247$. AS2: $p=0.331$). Remaining five subjects not showing RFE ($p=0.681$) are termed 'non-responders' in the following (Fig. 3). Mean and SD values of all analyzed data are presented in Tables 1–3.

### 3.1. Force enhancement during stretch

Just before the end of stretch, forces were significantly enhanced compared to the purely isometric trial ($p=0.001$), whereas torques for the ankle ($M_a$) ($p=0.188$) and knee ($M_k$) ($p=0.144$) remained unchanged. Enhanced activation of RF ($p=0.05$), ST ($p=0.004$) and GL ($p=0.039$) were observed at the end of stretch compared with the purely isometric trial.

For responders, $F_{ext}$, $M_a$, and $M_k$ were significantly enhanced compared to the isometric trial ($F_{ext}$: $p=0.001$; $M_a$: $p=0.008$; $M_k$: $p=0.001$). All other variables showed no differences between contraction conditions, except GM, which showed an enhanced activation at the end of stretch compared with that of the purely isometric contraction ($p=0.012$).

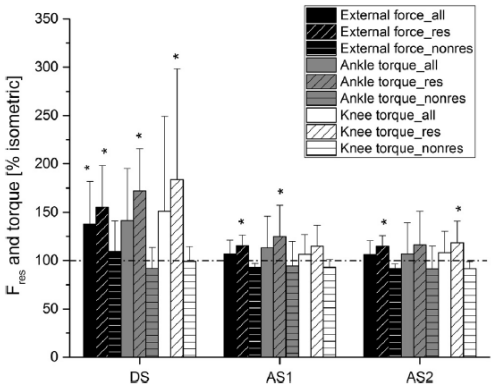


**Fig. 3.** External reaction force (black) and knee (gray) and ankle (white) torques for responders (angled striped bar), non-responders (horizontal striped bar), and overall subject group (full filled bars) at different time points (DS=during stretch, AS1=4–6 s after stretch, AS2=8–10 s after stretch). Asterisks indicate significant differences compared to the isometric reference values, represented by the dotted horizontal line.

Non-responders showed no enhancement in external reaction force or torque. RF ($p=0.017$) as well as ST ($p=0.024$) showed an enhanced activation for stretch contraction. Additionally, we found significant differences ($p=0.024$) regarding ankle angle between contraction conditions, resulting in a slightly less plantar flexed angle (Table 3) for the iso–ecc–iso trial.

### 3.2. Residual force enhancement

Overall, activity of VL did not show any significant differences between contraction conditions ($p=0.142$). Similarly, no significant differences were observed for ankle ($p=0.769$) or knee ($p=0.438$) joint angles. Concerning the appearance of RFE, $F_{ext}$ (AS1: $p=0.247$. AS2: $p=0.331$) or joint torques (Ankle: $p=0.188$, Knee: $p=0.144$) did not show differences across contraction conditions. RF activation (AS1: $p=0.038$. AS2: $p=0.009$) as well as ST (AS1: $p=0.046$. AS2: $p=0.046$) showed an enhancement during the iso–ecc–iso trial compared with that during the isometric trial.

After stretch, responders showed significantly enhanced $F_{ext}$ (AS1: $p=0.01$. AS2: $p=0.018$), $M_k$ (AS2: $p=0.004$), and $M_a$ (AS1: $p=0.031$). Further, activity of GL ($p=0.036$) and SOL ($p=0.012$) was significantly enhanced at AS1 during the post-eccentric phase.

For non-responders, there were no significant differences between isometric and isometric–eccentric–isometric trials regarding $F_{ext}$ ($p=0.681$), $M_a$ ($p=0.255$), or $M_k$ ($p=0.190$). Nevertheless, ankle angle significantly differed between isometric condition after stretch and the purely isometric condition at AS1 ($p=0.011$) and AS2 ($p=0.010$) as well as ST showed higher activation after stretch for AS1 ($p=0.039$) and AS2 ($p=0.033$).

Neither responders ($p=0.295$) nor non-responders ($p=0.069$) showed differences regarding VL activation between contraction conditions.

## 4. Discussion

The aim of this study was to clarify whether RFE occurs during multi-joint leg extensions in an experimental setup that mirrors daily human movement. These leg extensions are primarily characterized by knee and ankle joint angle configurations comparable to human walking, running, or hopping, and submaximal voluntary muscle activations.

For the overall subject group, no RFE was observed. However, as reported previously for submaximal human stretch-contractions (Hahn et al., 2007, 2010; Oskouei and Herzog, 2005, 2009; Seiberl et al., 2010), we observed clear RFE for approximately 60% of our subjects, referred to as "responders". These showed enhanced forces up to 15% (~5% MVC), enhanced knee torques up to 18% (~4% MVC) and enhanced ankle torques up to 24% (~7% MVC) could be found after lengthening contractions. The results of responders are in accordance to previously published data of submaximal (30%MVA) multi-joint leg extensions (Fres: RFE 19%. ~5% MVC, $M_k$: RFE 14%. ~5% MVC, $M_a$: RFE 22%. ~7% MVC: Seiberl et al. 2013) and amount of RFE is also comparable to submaximal single joint contractions for the knee (RFE 9%. ~3% MVC: Seiberl et al, 2012) and ankle joints (RFE 6.5%. 3% MVC: Pinniger and Cresswell, 2007).

A requirement for analyzing RFE is to check the data for standardization between contraction conditions. The variability of solutions to successfully resolve an experimental task is a crucial point that needs to be discussed, particularly for multi-joint leg extensions. Classically, *in vivo* RFE experimental setups control for

**Table 1**
Parameters measured in the isometric–eccentric–isometric (iso–ecc–iso) and purely isometric (iso) multi-joint contractions for the overall subject group.

| Parameters | DS | | | | AS1 | | | | AS2 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | iso–ecc–iso | | iso | | iso–ecc–iso | | iso | | iso–ecc–iso | | iso | |
| | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* |
| Fres [N] | 1342.11 | *426.38* | 1091.45 | *458.78* | 1125.16 | *447.58* | 1075.51 | *434.95* | 1090.75 | *426.06* | 1050.25 | *420.26* |
| Ankle torque [Nm] | 75.67 | *32.31* | 64.78 | *42.17* | 73.76 | *45.92* | 67.75 | *40.96* | 69.53 | *40.18* | 67.96 | *40.52* |
| Knee torque [Nm] | 128.51 | *37.71* | 111.05 | *51.27* | 107.91 | *45.04* | 107.54 | *47.87* | 105.55 | *43.53* | 104.31 | *47.15* |
| VL [%MVA] | 30.81 | *6.80* | 28.53 | *2.01* | 29.51 | *1.00* | 29.56 | *1.27* | 29.97 | *1.24* | 29.13 | *0.96* |
| VM [%MVA] | 27.10 | *8.46* | 25.17 | *6.95* | 26.09 | *7.19* | 25.84 | *7.24* | 26.02 | *7.47* | 25.21 | *7.43* |
| RF [%MVA] | 23.74 | *10.74* | 20.01 | *6.12* | 21.10 | *6.14* | 19.90 | *5.39* | 21.34 | *6.05* | 19.58 | *5.39* |
| GM [%MVA] | 30.00 | *19.67* | 21.83 | *16.47* | 18.35 | *11.61* | 19.72 | *13.41* | 16.04 | *8.78* | 21.46 | *14.55* |
| GL [%MVA] | 25.77 | *20.41* | 16.79 | *11.20* | 16.62 | *8.96* | 16.24 | *10.60* | 15.76 | *9.22* | 18.04 | *12.56* |
| SOL [%MVA] | 25.44 | *11.52* | 23.54 | *13.48* | 24.45 | *11.28* | 23.92 | *13.36* | 23.18 | *10.51* | 25.18 | *14.61* |
| TA [%MVA] | 21.40 | *10.02* | 23.96 | *21.50* | 18.81 | *9.87* | 20.51 | *16.36* | 19.06 | *9.89* | 21.80 | *18.83* |
| ST [%MVA] | 64.96 | *50.97* | 34.20 | *22.12* | 47.17 | *31.11* | 31.25 | *17.86* | 40.66 | *13.05* | 30.94 | *18.64* |
| BF [%MVA] | 47.26 | *36.57* | 33.86 | *23.62* | 30.02 | *13.96* | 33.43 | *21.92* | 29.90 | *12.59* | 34.29 | *22.11* |
| CoP_horz [mm] | 353.32 | *8.58* | 356.19 | *10.30* | 355.05 | *10.03* | 356.81 | *10.23* | 355.28 | *10.18* | 357.27 | *10.25* |
| CoP_vert [mm] | 159.55 | *32.33* | 161.96 | *37.09* | 165.87 | *35.27* | 166.86 | *38.24* | 164.96 | *32.36* | 169.76 | *37.75* |
| Fres_loa [deg.] | 17.70 | *3.24* | 16.48 | *5.29* | 17.22 | *4.64* | 17.69 | *4.94* | 17.23 | *4.32* | 17.89 | *4.92* |
| Ankle angle [deg.] | −4.00 | *3.11* | −4.16 | *2.80* | −3.93 | *3.17* | −4.03 | *2.88* | −3.95 | *3.09* | −4.09 | *2.83* |
| Knee angle [deg.] | 49.48 | *4.51* | 50.02 | *4.44* | 49.44 | *4.46* | 50.07 | *4.40* | 49.44 | *4.47* | 50.05 | *4.41* |

DS: during stretch. AS1: 4–6 s after stretch. AS2: 10–12 s after stretch. Fres: resultant force.VL: vastus lateralis. VM: vastus medialis. RF: rectus femoris. GM: gastrocnemius medialis. GL: gastrocnemius lateralis. SOL: soleus. TA: tibialis anterior. ST: semitendinosus. BF: biceps femoirs. CoP_horz: horizontal center of pressure. CoP_vert: vertical center of pressure. Fres_loa: angle of the line of action.

**Table 2**
Parameters measured in the isometric–eccentric–isometric (iso–ecc–iso) and purely isometric (iso) multi-joint contractions for responders.

| Responder | DS | | | | AS1 | | | | AS2 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | iso–ecc–iso | | iso | | iso–ecc–iso | | iso | | iso–ecc–iso | | iso | |
| | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* |
| Fres [N] | 1279.68 | *482.88* | 934.92 | *503.73* | 1085.69 | *559.34* | 947.85 | *497.97* | 1055.44 | *527.48* | 930.61 | *488.15* |
| Ankle torque [Nm] | 74.61 | *44.14* | 51.05 | *43.86* | 68.85 | *53.48* | 57.25 | *46.67* | 63.14 | *46.10* | 57.25 | *46.67* |
| Knee torque [Nm] | 128.70 | *48.46* | 97.82 | *59.90* | 104.30 | *56.96* | 97.69 | *57.44* | 102.63 | *54.17* | 94.37 | *56.41* |
| VL [%MVA] | 31.04 | *8.78* | 28.94 | *1.91* | 29.74 | *1.19* | 29.92 | *1.49* | 30.59 | *0.98* | 29.30 | *0.98* |
| VM [%MVA] | 26.92 | *9.60* | 24.66 | *8.15* | 25.70 | *7.41* | 26.19 | *8.21* | 25.90 | *8.23* | 26.22 | *8.10* |
| RF [%MVA] | 22.69 | *13.49* | 18.65 | *6.73* | 20.27 | *6.71* | 19.00 | *6.05* | 20.49 | *6.35* | 18.41 | *5.90* |
| GM [%MVA] | 22.82 | *18.16* | 14.71 | *15.81* | 13.71 | *8.31* | 14.88 | *14.74* | 11.38 | *4.86* | 15.41 | *14.87* |
| GL [%MVA] | 16.68 | *12.14* | 10.41 | *5.03* | 13.01 | *5.74* | 10.15 | *4.67* | 11.42 | *4.33* | 10.75 | *5.36* |
| SOL [%MVA] | 20.10 | *8.49* | 15.34 | *8.99* | 19.31 | *9.12* | 15.53 | *7.73* | 17.71 | *8.16* | 16.39 | *8.24* |
| TA [%MVA] | 18.98 | *8.56* | 20.21 | *21.20* | 17.47 | *10.24* | 14.90 | *10.57* | 17.28 | *9.92* | 15.08 | *10.62* |
| ST [%MVA] | 77.29 | *61.45* | 38.87 | *25.39* | 53.69 | *37.43* | 35.73 | *20.17* | 43.01 | *11.68* | 36.71 | *21.11* |
| BF [%MVA] | 53.45 | *44.40* | 36.67 | *29.92* | 32.64 | *17.14* | 35.05 | *27.52* | 32.02 | *15.28* | 35.86 | *27.52* |
| CoP_horz [mm] | 352.40 | *8.64* | 353.60 | *11.00* | 353.26 | *9.20* | 354.02 | *11.06* | 353.47 | *9.34* | 354.43 | *11.15* |
| CoP_vert [mm] | 157.86 | *41.15* | 146.21 | *36.85* | 157.80 | *40.95* | 153.78 | *41.89* | 154.98 | *36.01* | 153.31 | *41.56* |
| Fres_loa [deg.] | 17.38 | *4.09* | 14.32 | *5.76* | 15.53 | *5.26* | 15.35 | *5.27* | 15.41 | *4.79* | 15.41 | *5.12* |
| Ankle angle [deg.] | −3.83 | *2.88* | −3.49 | *1.98* | −3.85 | *3.00* | −3.35 | *2.08* | −3.80 | *2.80* | −3.42 | *1.95* |
| Knee angle [deg.] | 49.96 | *5.16* | 51.50 | *4.07* | 49.83 | *5.17* | 51.56 | *3.92* | 49.84 | *5.13* | 51.57 | *4.03* |

DS: during stretch. AS1: 4–6 s after stretch. AS2: 10–12 s after stretch. Fres: resultant force. VL: vastus lateralis. VM: vastus medialis. RF: rectus femoris. GM: gastrocnemius medialis. GL: gastrocnemius lateralis.SOL: soleus. TA: tibialis anterior. ST: semitendinosus. BF: biceps femoirs. CoP_horz: horizontal center of pressure. CoP_vert: vertical center of pressure. Fres_loa: angle of the line of action.

joint angle configuration and the intensity of muscle contraction via biofeedback of force or muscle activation (Oskouei and Herzog, 2005; Seiberl et al., 2012, 2013). In this study, we found no difference in the final knee joint angle when comparing forces and torques after stretch nor different activation levels of analyzed muscles, except for RF and ST. As RF activation was only 2% increased after stretch compared to isometric reference contraction we don't assume a meaningful influence on force generation in this submaximal setup. When it comes to antagonistic (ST, BF) muscles activation our data seems to indicate conspicuously high amounts of activation ranging between 37% and 77% MVA (Tables 1–3). It is important to note that all EMG data was normalized to maximum voluntary leg extension. Thus, a high MVA-percentage activation of antagonistic muscles still derives from a very low absolute activation level in comparison to the agonistic muscles.

Additionally, we analyzed the displacement of the center of pressure (CoP) on the force plates in the vertical and horizontal directions and the resulting LoA during experimental conditions after stretch and purely isometric leg extensions. Significant differences in LoA between contraction conditions would indicate different strategies of pushing against the foot plate, which can result in different external reaction forces as well as joint torques. Although difficult to control during an experiment, analysis of mean CoP and LoA did not reveal any differences between stretch and isometric leg extensions during the steady-state isometric phases after stretch. While the criteria of standardization therefore appear to be sufficiently fulfilled for the overall group, there have

**Table 3**
Parameters measured in the isometric–eccentric–isometric (iso–ecc–iso) and purely isometric (iso) multi-joint contractions for non-responders.

| Non-responder | DS | | | | AS1 | | | | AS2 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | iso–ecc–iso | | iso | | iso–ecc–iso | | iso | | iso–ecc–iso | | Iso | |
| | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* | Mean | *SD* |
| Fres [N] | 1442.00 | *342.16* | 1341.89 | *244.88* | 1188.30 | *213.02* | 1279.78 | *221.02* | 1147.24 | *226.29* | 1241.69 | *195.98* |
| Ankle torque [Nm] | 83.54 | *13.34* | 93.82 | *20.11* | 84.85 | *25.65* | 90.63 | *16.76* | 82.85 | *21.85* | 91.32 | *13.69* |
| Knee torque [Nm] | 128.20 | *12.58* | 132.20 | *26.43* | 113.68 | *18.47* | 123.30 | *24.38* | 110.22 | *22.47* | 120.22 | *24.18* |
| VL [%MVA] | 30.45 | *1.81* | 28.85 | *0.71* | 29.14 | *0.68* | 28.92 | *0.76* | 28.83 | *0.71* | 28.72 | *0.97* |
| VM [%MVA] | 27.39 | *7.30* | 26.00 | *5.23* | 26.70 | *7.64* | 25.28 | *6.21* | 26.22 | *6.98* | 23.60 | *6.76* |
| RF [%MVA] | 25.40 | *4.71* | 22.20 | *4.86* | 22.42 | *5.54* | 21.37 | *4.34* | 22.69 | *5.95* | 21.45 | *4.11* |
| GM [%MVA] | 41.46 | *17.78* | 33.22 | *10.64* | 25.76 | *13.11* | 27.46 | *6.12* | 23.50 | *8.76* | 31.13 | *7.62* |
| GL [%MVA] | 40.31 | *23.73* | 27.01 | *10.94* | 22.39 | *10.74* | 26.00 | *10.30* | 22.70 | *11.14* | 29.72 | *12.10* |
| SOL [%MVA] | 33.98 | *11.14* | 36.66 | *7.37* | 32.68 | *9.93* | 37.33 | *8.08* | 31.92 | *7.70* | 39.25 | *11.00* |
| TA [%MVA] | 25.27 | *11.94* | 30.00 | *22.95* | 20.95 | *9.97* | 29.50 | *21.07* | 21.90 | *10.23* | 32.56 | *25.12* |
| ST [%MVA] | 45.24 | *19.90* | 26.72 | *15.07* | 36.75 | *15.15* | 24.07 | *11.83* | 36.90 | *15.61* | 21.71 | *9.44* |
| BF [%MVA] | 37.35 | *19.01* | 29.36 | *8.11* | 25.84 | *5.90* | 30.84 | *10.13* | 26.53 | *6.64* | 31.78 | *11.39* |
| CoP_horz [mm] | 354.79 | *9.27* | 360.33 | *8.46* | 357.92 | *11.71* | 361.27 | *7.71* | 358.18 | *11.81* | 361.83 | *7.44* |
| CoP_vert [mm] | 162.25 | *12.50* | 187.15 | *21.48* | 178.80 | *21.38* | 187.78 | *20.67* | 180.93 | *18.50* | 191.29 | *17.59* |
| Fres_loa [deg.] | 18.21 | *1.32* | 19.95 | *1.30* | 18.44 | *1.33* | 19.81 | *0.99* | 18.69 | *1.05* | 20.21 | *0.64* |
| Ankle angle [deg.] | −4.24 | *3.81* | −5.22 | *3.80* | −4.06 | *3.81* | −5.12 | *3.86* | −4.19 | *3.85* | −5.15 | *3.89* |
| Knee angle [deg.] | 48.71 | *3.64* | 47.65 | *4.33* | 48.81 | *3.46* | 47.68 | *4.28* | 48.81 | *3.61* | 47.63 | *4.25* |

DS: during stretch. AS1: 4–6 s after stretch. AS2: 10–12 s after stretch. Fres: resultant force.VL: vastus lateralis. VM: vastus medialis. RF: rectus femoris. GM: gastrocnemius medialis. GL: gastrocnemius lateralis.SOL: soleus. TA: tibialis anterior. ST: semitendinosus. BF: biceps femoirs. CoP_horz: horizontal center of pressure. CoP_vert: vertical center of pressure. Fres_loa: angle of the line of action.

also been significant variations concerning the sub-groups that will be addressed later in the discussion.

The results concerning eccentric forces and torques generated at the end of stretch are only partly in accordance with previously published papers. Although we found enhanced external reaction forces of up to 38% above isometric references that are well in agreement with results from single joint (Tilp et al., 2009) and multi-joint (Hahn et al., 2010) studies, these forces did not cause enhanced mean torques in the knee and ankle joint.

Because steady control of muscle activation level was not possible during the ~330-ms lasting stretches, absence of enhanced mean torques during stretch may be a result of varying activation level during stretch that resulted in extremely high SD values (Fig. 3).

Furthermore, the overall statistics did not identify differences among the contraction conditions in the steady-state phase after stretch concerning $F_{ext}$, $M_k$, and $M_a$, indicating there was no RFE. These results are in contrast to previous studies on multi-joint leg extensions. Hahn et al. (2010) as well as Seiberl et al. (2013) found RFE of up to 19.2% for $F_{ext}$, 13.7% for $M_k$, and 22.3% for $M_a$. The main difference between the present and previous studies is the angular position of the ankle and knee joint. Although in previous studies on multi-joint leg extension, RFE occurred on the descending limb of the T-l-r of the quadriceps femoris, the present study was designed for RFE to occur on the ascending limb of the T-l-r (Pincivero et al., 2004; Power et al., 2013). Generally, RFE is assumed to occur on the entire working range of a muscle (Herzog, 2014); nevertheless, when it occurs specifically on the ascending limb, results deviate substantially from the consistent findings of RFE on the descending limb. Shim and Garner (2012) and Power et al. (2013) studied RFE of human quadriceps femoris in a single joint setup on the ascending and descending limbs of the T-l-r during maximum voluntary effort. Although both found RFE on the descending limb, only Power et al. (2013) also found RFE on the ascending limb. These differences might be explained by stretch amplitudes, which were 60° and 30° for stretches in Power et al. (2013) and Shim and Garner (2012), respectively. Because RFE is sensitive to the magnitude of stretch (Edman et al., 1978), the increased stretch amplitude in the setup of Power et al. (2013) may have enabled generation of RFE. Additionally, in the study of Power et al. (2013), stretches ended more closely to the plateau region of the T-l-r than stretches reported in Shim and Garner (2012), which could also support the appearance of RFE. In our experimental setup, we used a stretch amplitude (30°–50° knee flexion) comparable with that used by Shim and Garner (2012) so that quadriceps femoris is acting on the ascending limb of its T-l-r (Hahn, 2011). Similarly, the ROM in the ankle joint also refers to the ascending limb of the triceps surae T-l-r (Pinniger and Cresswell, 2007).

Notably, eight out of 13 subjects showed clearly enhanced forces across all analyzed time windows for $F_{ext}$ and enhanced torques for at least two analyzed time windows (Fig. 3). Our results of responders are well in line with previous results on submaximal multi-joint leg extensions (Seiberl et al., 2013), but exceed the amount of RFE compared to multi-joint experiment with maximum voluntary contraction level (Hahn et al., 2010).

RFE reportedly is not present in every subject but only in a subset of subjects, particularly during submaximal voluntary contractions (Oskouei and Herzog, 2005; Seiberl et al., 2012; Tilp et al., 2009). It is interesting to consider why submaximal voluntary contractions particularly divide a sample of subjects into responders and non-responders; multiple potential factors have been discussed (Seiberl et al., 2015a). However, it is unclear whether muscle physiological factors (such as fiber type) or neural mechanisms contribute to this responder versus non-responder phenomenon or whether non-responders are simply limited in performance and task-specific motor control during eccentric muscle actions (Seiberl et al., 2015a). Accordingly, several points need to be considered when discussing the results concerning responders and non-responders.

First, non-responders showed significant differences according to ankle angle when performing an iso–ecc–iso contraction compared to when performing a purely isometric contraction. An alteration in ankle angle might result from a change of the pushing technique between the tasks, consequently affecting standardization of experimental settings. Nevertheless, because differences in ankle angle configurations were very small ($< 1.2°$), they were considered negligible. Additionally, neither the line of action nor the center of pressure showed a significant difference between contraction conditions.

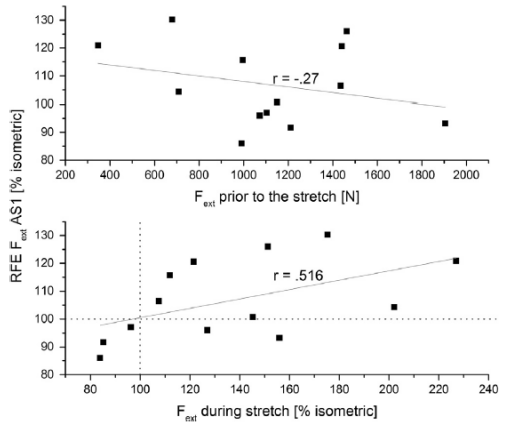


**Fig. 4.** Correlations between RFE at the first analyzed time point and (1) force prior to the eccentric stretch (top figure, $p=0.359$, $r=-0.277$) and (2) the force enhancement during stretch (bottom figure, $p=0.071$, $r=0.516$). The dotted horizontal and vertical lines indicate the isometric references. Data points above and below the horizontal line represent responders and non-responders respectively. Data points to the left and right of the vertical line further show if subjects achieved enhanced forces during stretch (right) or not (left).

Second, responders showed a significant difference regarding activation of shank muscles after stretch. EMG data of GL and SOL (AS1) revealed an increased activation of 3% and 4% in post-eccentric contractions, which might have caused a slight overestimation of RFE. However, this difference in shank muscle activation may not sufficiently explain the entire absence of RFE for non-responders in general, and specifically cannot explain the absence of RFE in some subjects regarding knee torques.

Third, the isometric force level prior to stretch as well as the eccentric forces during stretch differed between responders and non-responders. To examine the influence of the force level prior to the stretch, we calculated correlations between RFE at AS1 and force prior to stretch and between RFE at AS1 and the FE during stretch (Fig. 4). Despite a moderate but insignificant correlation between FE during stretch and RFE (Fig. 4, lower plot), there is evidence according to our data that enhanced forces during stretch are a necessity for the occurrence of RFE. Every responder (squares above horizontal dotted line, Fig. 4, lower plot) had enhanced forces. This trend in the correlation is supported by Bullimore et al. (2007) who showed that RFE is highly related to the forces at the end of the stretch. Notwithstanding, forces during stretch cannot solely explain the occurrence of responders and non-responders in our study since also two non-responders had enhanced forces during stretch (Fig. 4, lower plot). On the other side, the resultant force prior to the stretch even showed a negative although non-significant correlation (Fig. 4, upper plot). This result is in accordance with the work of de Ruiter et al. (2000). They showed that RFE is unaffected by the initial isometric force over a broad range for non-fatigued muscles. Hence, we believe that in our study the occurrence of RFE is not influenced by the deviations in forces prior to stretch as shown in Fig. 2.

## 5. Conclusion

Based on our results, we conclude that RFE can be observed for submaximal multi-joint leg extension at joint angle configurations comparable with everyday human movement, provided there is enhanced force during stretch and that standardization criteria are matched. However, this only applied to approximately 60% of our subjects and enhanced forces at the end of stretch are insufficient to exclude the occurrence of non-responders so that the reason (s) for the phenomenon of non-responders remain unclear.

Furthermore, although mimicking activation level and joint angle configurations of everyday locomotion, daily locomotion like walking and running involve stretch-shortening cycles (SSC) (Komi, 2000), rather than stretch and hold contractions. To further elucidate the relevance of RFE for human locomotion, it is necessary to investigate whether the mechanisms of RFE contribute to enhanced performance during the shortening phase of a SSC (Cavagna et al., 1968). For *in vivo* human adductor pollicis this has been confirmed (Seiberl et al., 2015b), but further verification is needed for multi-joint contraction conditions as presented here.

## Conflict of interest statement

None.

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## 2.3 Fatigability after active lengthening (Study Three)

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# Reduced activation in isometric muscle action after lengthening contractions is not accompanied by reduced performance fatigability

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**After active lengthening contractions, a given amount of force can be maintained with less muscle activation compared to pure isometric contractions at the same muscle length and intensity. This increase in neuromuscular efficiency is associated with mechanisms of stretch-induced residual force enhancement. We hypothesized that stretch-related increase in neuromuscular efficiency reduces fatigability of a muscle during submaximal contractions. 13 subjects performed 60 s isometric knee extensions at 60% of maximum voluntary contraction (MVC) with and without prior stretch (60°/s, 20°). Each 60 s trial was preceded and followed by neuromuscular tests consisting of MVCs, voluntary activation (VA) and resting twitches (RT), and there was 4 h rest between sets. We found a significant ($p = 0.036$) 10% reduction of quadriceps net-EMG after lengthening compared to pure isometric trials. However, increase in neuromuscular efficiency did not influence the development of fatigue. Albeit we found severe reduction of MVC (30%), RT (30%) and VA (5%) after fatiguing trials, there were no differences between conditions with and without lengthening. As the number of subjects showing no activation reduction increased with increasing contraction time, intensity may have been too strenuous in both types of contractions, such that a distinction between different states of fatigue was not possible anymore.**

When an active muscle is stretched the resulting post-eccentric steady-state force is greater than an isometric force at corresponding muscle length and activation[1,2]. Numerous observations on all structural levels of muscle confirm specific characteristics of this phenomenon, referred to in the literature as residual force enhancement (RFE). Most findings show RFE to increase with increasing lengthening amplitudes[1,3–6] and to be independent of velocity of stretch[5,7]. RFE occurs at all muscle lengths[1,8,9], lasts as long as the muscle is kept active (long lasting) and is instantaneously eliminated by deactivation of the muscle[3,10].

Research working with animal models and isolated fiber preparations in combination with histological examinations focuses on decoding the mechanisms generating RFE[11–14]. Underlying mechanisms are still not fully understood and a combination of active and passive components are discussed in literature, including half sarcomere non-uniformities, increase in the number of attached cross-bridges or in the average cross-bridge force, and $CA^{2+}$-dependent titin stiffness modulation[2,15–17].

Besides the identification of RFE mechanisms, the role that RFE plays in natural *in vivo* muscle function is subject of investigation. There is broad evidence that RFE is present in stimulated as well as voluntary muscle action of small and large human muscles, as well as in multi-joint leg extensions[18–26]. From an evolutionary point of view, it is questionable if benefits concerning RFE lay in the increase of the maximum force capacity of an isomeric contraction following eccentric lengthening. Recent studies[27,28] confirm early proposed but barely addressed ideas that mechanisms underlying RFE contribute to performance enhancement associated with muscles undergoing stretch-shortening cycles[29]. Furthermore, it is well documented that on a submaximal level, for a given amount of force, less muscle activation is required after active lengthening for maintaining a given force output[30–33]. The characteristics of this stretch-induced activation reduction (AR) were associated with increased neuromuscular efficiency and reduced metabolic costs[30,32,34], presumably optimizing the economy of muscle

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function[35]. If so, it may be reasoned that AR is beneficial for the resistance to neuromuscular fatigue during or after prolonged muscle action that is preceded by an eccentric lengthening contraction.

Muscle fatigue is described as an exercise-induced limitation of performance and measurable as a reduction in the ability of a muscle or muscle group to maintain a certain force over time, or a change in the myoelectric pattern of muscle activation[36–38]. The causes of muscle fatigue may be manifold, but primary mechanisms are associated with disturbances of the central nervous system[36] and/or impairments of the contractile machinery within the muscle[39,40], referred to as central and peripheral fatigue, respectively. Just recently, terms of performance fatigability and perceived fatigability were suggested to better describe the broad phenomenology of fatigue during human performance[41,42]. According to this, performance fatigability depends on the contractile and nervous capabilities to maintain a task against factors modulating the development of fatigue, such as calcium kinetics or activation patterns[41]. Concerning voluntary muscle activation, an influence of RFE-mechanisms on factors modulating performance fatigability was shown in several *in vivo* studies[30,32,43].

The findings that active lengthening of a muscle leads to stretch-induced optimization of neuromuscular efficiency[18,20,30–33,44] and reduced ATPase activity per unit of force in skinned muscle fibers[34] may lead to the conclusion that RFE mechanisms counteract the development of fatigue. However, none of the listed studies on voluntary submaximal lengthening contractions lasted for more than 30 s and it is unclear if shown short term effects persist over time. Therefore, we speculated that if stretch-induced reduction of muscle activity can be sustained over an exhausting period of time (>50 s), this increase in neuronal efficiency should have a positive influence on the resistance to the development of peripheral and/or central fatigue. Hence, the aim of this study was to address the question if mechanisms associated with stretch-induced residual force enhancement counteract arising fatigue. We hypothesized active lengthening prior to submaximal exhausting contractions of the human m. quadriceps femoris would lead to reduced muscle activation and reduced fatigability as compared to a pure isometric contraction of identical intensity.

## Methods

**Subjects.** Sixteen healthy subjects (7 ♀, 9 ♂; 27 ± 4 years) voluntarily participated in this study and gave written informed consent. None of them had any history of leg and particular knee injury or neurological disorders. The study was approved by the local Ethics Committee of the Technical University of Munich and conducted according to the Declaration of Helsinki.

**Experimental set-up.** During all tests, single leg knee extension torque was measured using a motor driven dynamometer (Isomed 2000, D&R Ferstl GmbH, Germany) in isometric or isokinetic mode (60°/s). All subjects were seated upright on the dynamometer with a hip flexion angle of 100° and they were firmly fixed with safety belts. Isometric contractions were performed at 100° knee flexion angle (0° referring to fully extended knee), eccentric contractions were performed over a 20° range of motion, ending at 100°. Bipolar surface electrodes were attached to subjects following the guidelines for preparation and electrode placement of the SENIAM-group[45]. Inter-electrode distance was 2 cm, and EMG data of m. vastus lateralis (VL), m. rectus femoris (RF) and m. vastus medialis (VM) were amplified no further than 10 cm from the recording site (OT bioelettronica, Italy). All data was recorded at a sampling rate of 4 kHz.

**Neuro-mechanical testing.** For the assessment of neuromuscular function, voluntary peak torque (MVC) was measured and electrically evoked twitches (femoralis nerve stimulation; 1ms pulse doublets 10ms apart, DS7AH Digitimer constant voltage stimulator, UK) were recorded during the plateau of MVCs (superimposed twitch, SIT) and after deactivation of the muscle in a relaxed state (resting twitch, RT). Electrical stimulus intensity was assessed during twitch-response tests with increasing stimulus current. Supra-maximal stimulus intensity for further tests was set to 150% of the single-pulse stimulus current needed to evoke maximum twitch-torque and maximum VL M-wave peak-to-peak amplitude. The interpolated twitch technique[46] was used to calculate voluntary activation (VA) as $[1 - (SIT / RT)] \times 100\%$.

**Experimental Protocol.** All subjects were familiarized with the dynamometer and had to train MVCs and submaximal knee extensions in isometric and isometric-eccentric modes in at least one training session.

On test day subjects were prepared with EMG electrodes and performed a 10 min general warmup on a bicycle ergometer (100 W), followed by a local warmup on the dynamometer. Thereafter, a set of neuromuscular tests (MVC-ISO-pre) including three MVCs with SITs and RTs were conducted with 3 min rest in between each. After another 5 min rest subjects had to perform a 60 s isometric contraction at an intensity of 60% of previously measured maximum voluntary torque (Fig. 1). During this sub-maximal contraction subjects got visual real-time feedback of their torque output and were asked to match and maintain the given 60% MVC torque level as precisely as possible. Immediately after this fatiguing contraction another neuromuscular test (MVC-ISO-post) was executed in identical manner as MVC-ISO-pre.

Thereafter subjects got four hours of rest in order to fully recover from the first block of experiments. All measurement equipment stayed on subjects, attached to identical positions on the thigh muscle. The second block of experiments also started with a set of three neuromuscular tests (MVC-DYN-pre), identical to MVC-ISO-pre. Subsequently subjects performed a second isometric fatiguing contraction identical to fist block but preceded by a 20° lengthening contraction (60°/s). Once again, fatiguing contraction was immediately followed by a neuromuscular test (MVC-DYN-post).

The order of tests was identical for all subjects and randomization was purposely not undertaken. Although all subjects had a rest of 4 h, we cannot guarantee that all body systems totally recovered. The test design therefore is biased on purpose and a measurable effect of RFE would always have to outperform possible limitations of muscle function due to incomplete recovery.

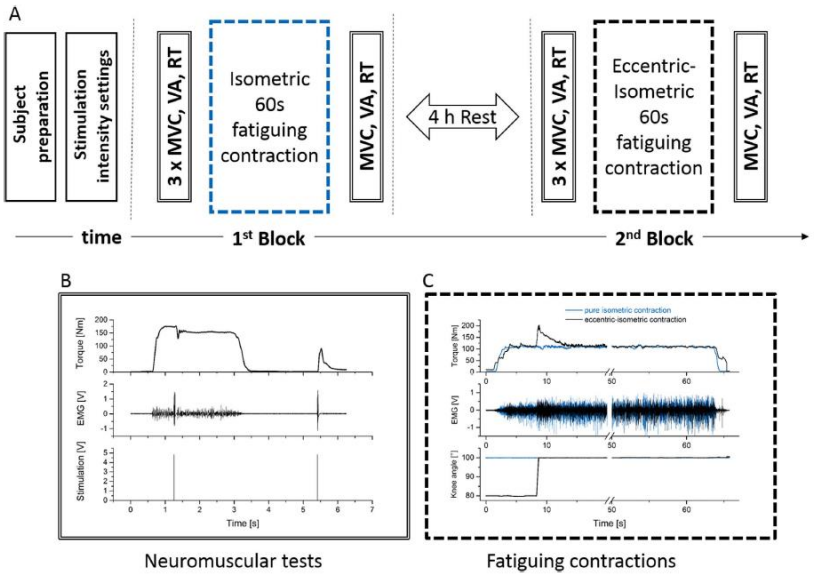


**Figure 1. Experimental parts and time line.** (**A**) after subject preparation and settings for electrical stimulation, neuromuscular tests (**B**) consisting of maximum voluntary torque (MVC), voluntary activation (VA) and resting twitch torque (RT) were carried out. Thereafter, a 60 s fatiguing contraction (**C**) with (black) and without (blue) preceding lengthening at 60% of MVC was performed in the first and second block, respectively. After fatiguing trials another set of neuromuscular tests was performed. Blocks were separated by four hours rest.

**Data reduction and analysis.** Torque data was smoothed with 20ms moving average and EMG data were bandpass filtered (10-400 Hz, 2nd order Butterworth), rectified and smoothed (250ms moving average). As presented in detail in earlier work[30], a simplified net-EMG model (i) was used to account for the structural complexity of m. quadriceps femoris. EMG signals of VL, RF and VM were weighted based on literature data on physiological cross-sectional area (PCSA)[47,48] and muscle volume[49], that is reported to be directly related to maximum muscle force[50]. The used weighting factors in this model are 0.17 for RF, 0.35 for VL and 0.25 for VM. The sum of weighted EMGs is considered as 'net' overall activation of the QF (m. vastus intermedius was not taken into account as this part was not measureable via surface EMG).

$$weighted\ EMG = (RF_{measured} \cdot 0.17) + (VL_{measured} \cdot 0.35) + (VM_{measured} \cdot 0.23) \quad (1)$$

Peak torque of each set of neuromuscular tests was calculated from MVCs and defined as the maximum value before SIT. The set of MVC, SIT and RT of the test with the highest peak torque was used for further statistics. SIT and RT peak torque was derived from the maximum peak-to-base torque difference, with the base defined as mean torque (10ms) at the time point of 10ms before stimulation. The rate of force development in RTs (RFD-RT) was calculated from the maximum slope of torque increase after stimulation. Half-relaxation time (HRT) of evoked RTs was defined as the time from RT peak-torque until torque dropped to50% of peak RT torque.

The pure isometric and eccentric-isometric 60 s endurance trials were synchronized to the beginning of the contraction (50 Nm) and torque, angle, EMG amplitude and EMG median frequency data were then analyzed at five instances in time, every 10 seconds, beginning at the time point corresponding to 10 s after lengthening. EMG data of the 60 s fatiguing trials were normalized to the mean of maximum EMG values measured during the three MVCs preceding respective 60 s trial. Median frequency was assessed using MATLAB codes on power spectral density estimates based on fast Fourier transformations. The mean of five seconds at each time point was used for statistical analysis.

**Statistics.** All data was checked for normality (Kolmogorov–Smirnov test) and depending on the outcome either repeated measures ANOVA or nonparametric Friedman tests with post hoc comparisons (Students t-tests or Wilcoxon test) were used to identify significant differences in our data ($\alpha \leq 0.05$). Comparisons between neuromuscular tests were assessed between pre vs post fatiguing exercise as well as between pre ISO vs pre DYN, and post ISO vs post DYN. Fatiguing trials were analyzed as within trial comparisons over time, and between trial comparisons concerning contraction conditions: time (5) x condition (2).

| n=13 | before ISO | | after ISO | | before ECC-ISO | | after ECC-ISO | |
|---|---|---|---|---|---|---|---|---|
| | mean | SD | mean | SD | mean | SD | mean | SD |
| MVC torque [Nm] | 139.2 | *41.9* | **95.6** | *29.2* | 136.6 | *40.8* | **95.5** | *26.7* |
| RT [Nm] | 43.1 | *22.0* | **29.4** | *16.6* | 43.4 | *21.9* | **30.3** | *17.3* |
| VA [%] | 94.8 | *4.5* | **90.5** | *6.9* | 95.9 | *4.3* | **90.1** | *9.7* |
| RFD-RT max [Nm/s] | 1029.9 | *493.1* | **673.8** | *350.4* | 1070.2 | *508.8* | **691.4** | *355.7* |
| HRT [ms] | 78.7 | *25.8* | **132.7** | *54.1* | 82.9 | *36.0* | **133.4** | *55.2* |

**Table 1. Data show neuromuscular tests before and after fatiguing trials with (ECC-ISO) and without (ISO) prior lengthening.** Data shows means and SD of maximum voluntary torque (MVC), resting twitch torque (RT), voluntary activation (VA), rate of force development in RTs (RFD-RT), and half-relaxation times of RTs. Bold values indicate significant difference to corresponding parameter before fatigue ($p<0.01$).

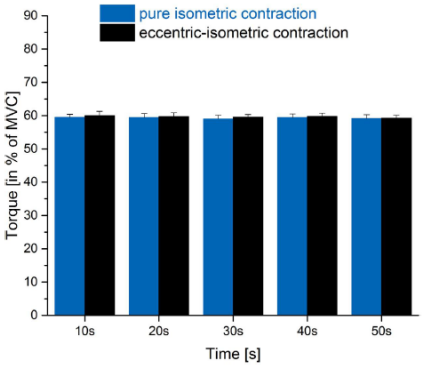


**Figure 2. Feedback controlled torque level.** Mean and SD of torque (in % of MVC) during 60 s fatiguing trials with (black) and without (blue) prior lengthening. ANOVA identified significant differences in torque control between conditions.

## Results

One subject showed incorrect EMG recordings (missing data), and two subjects were not able to keep torque level within 5% of target level throughout the 60 s trial length. These three subjects were discarded from further analysis, resulting in a sample size of $n = 13$.

**Neuromuscular tests.** ANOVA identified statistical differences in MVC, VA, RT, HRT, and RT-RFD when compared over time (before vs after fatiguing trials; $p < 0.01$), but there were no differences in any of these parameters between conditions before fatiguing trials with and without prior lengthening, and between conditions at time point after fatiguing trials with and without prior lengthening (see Table 1).

**Fatiguing trials.** ANOVA statistics identified statistical but negligible differences concerning feedback torque control between conditions ($p = 0.015$) but not over time ($p = 0.113$). Mean torque ranged between $59.0 \pm 1.1\%$ and $60.0 \pm 1.3\%$ of MVC and was slightly higher (<1%) during post-eccentric contractions (Fig. 2).

Median frequency was significantly ($p < 0.005$) decreasing over time from about 57 to 47 Hz and 64 to 52 Hz for VL and VM, respectively, thereby showing no differences between conditions and no interaction effects. For RF, ANOVA identified a significant decrease ($p < 0.005$) of median frequency over time from about 56.5 to 40.8 Hz in pure isometric trials, and 56.8 to 43.0 Hz in isometric trials preceded by stretch. There were no interaction effects between time and condition according to RF median frequency, however, a trend ($p = 0.067$) of difference between conditions with less decrease in RF median frequency after stretch-contraction (Table 2).

Analysis of VL, RF and VM activity revealed a significant increase in activity over time for both fatiguing trials ($p < 0.002$) and no interaction effects between contraction time and condition. Concerning individual activation reduction in muscle parts, ANOVA identified no differences in conditions for VL ($p = 0.259$), a trend for VM ($p = 0.051$), and significantly ($p = 0.024$) reduced activity of RF after lengthening (Table 2). Paired t-test analysis revealed significantly reduced mean individual activity that reached $83.8 \pm 18.7\%$ ($p = 0.020$), $85.6 \pm 14.4\%$ ($p = 0.007$), $87.9 \pm 15.3\%$ ($p = 0.017$), and $89.6 \pm 17.8\%$ ($p = 0.047$) of the isometric RF reference activation at 10, 20, 30, and 40 s after lengthening, respectively. A non-significant ($p = 0.139$) RF activation reduction ($91.7 \pm 22.1\%$ of isometric reference) was found 50 s after lengthening.

| EMG parameter | | | 10 s | | 20 s | | 30 s | | 40 s | | 50 s | | p value ANOVA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | mean | *SD* | mean | SD | mean | *SD* | mean | *SD* | mean | *SD* | condition | time |
| Amplitude [% MVA] | VL | iso | 53.4 | *9.5* | 56.2 | *10.6* | 59.1 | *10.0* | 67.0 | *12.2* | 74.3 | *14.6* | 0.26 | <0.01 |
| | | ecc-iso | 48.7 | *7.9* | 52.9 | *9.2* | 57.3 | *9.9* | 63.9 | *10.8* | 70.1 | *10.5* | | |
| | RF | iso | 60.6 | *24.0* | 70.0 | *26.0* | 74.4 | *26.3* | 84.9 | *34.0* | 97.8 | *45.1* | **0.024** | <0.01 |
| | | ecc-iso | **48.4** | *14.4* | **57.7** | *16.8* | **63.5** | *19.3* | **73.8** | *28.3* | 85.9 | *40.9* | | |
| | VM | iso | 50.3 | *13.5* | 52.8 | *15.9* | 57.8 | *20.8* | 68.0 | *29.2* | 81.6 | *40.1* | 0.051 | <0.01 |
| | | ecc-iso | 47.5 | *9.7* | 50.0 | *13.9* | 55.1 | *17.1* | 63.6 | *24.1* | 73.8 | *30.9* | | |
| | net-EMG | iso | 40.6 | *9.1* | 43.7 | *10.8* | 46.6 | *12.2* | 53.5 | *16.0* | 61.4 | *20.3* | **0.036** | <0.01 |
| | | ecc-iso | **36.2** | *5.9* | **39.8** | *8.1* | 43.5 | *9.5* | **49.5** | *12.6* | 56.1 | *14.5* | | |
| median frequency [Hz] | VL | iso | 56.5 | *7.6* | 53.7 | *7.4* | 52.0 | *7.6* | 50.4 | *9.7* | 46.7 | *8.7* | 0.29 | <0.01 |
| | | ecc-iso | 57.2 | *6.9* | 54.3 | *5.7* | 53.4 | *6.3* | 51.3 | *6.7* | 48.2 | *7.1* | | |
| | RF | iso | 56.5 | *5.8* | 52.3 | *6.9* | 50.0 | *6.3* | 45.2 | *6.8* | 40.8 | *6.2* | 0.067 | <0.01 |
| | | ecc-iso | 56.8 | *6.3* | 53.1 | *6.6* | 50.9 | *6.1* | 46.1 | *7.8* | 43.0 | *6.0* | | |
| | VM | iso | 63.7 | *13.7* | 61.6 | *12.6* | 59.7 | *11.8* | 56.0 | *11.7* | 51.9 | *11.5* | 0.95 | <0.01 |
| | | ecc-iso | 64.7 | *13.1* | 61.1 | *11.6* | 58.9 | *11.1* | 55.7 | *11.3* | 52.2 | *12.2* | | |

**Table 2. EMG data of 60 s fatiguing trials with (ecc-iso) and without (iso) prior active lengthening.** Data shows mean and SD of EMG amplitude and frequeny parameters of vastus lateralis (VL), rectus femoris (RF) and vastus medialis (VM). Bold values indicate significant difference to isometric references ($p < 0.05$).

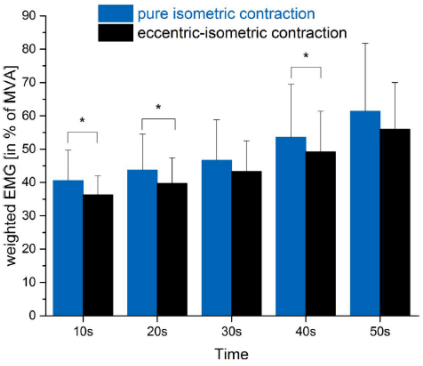


**Figure 3. Muscle activation during 60 s fatiguing trials with (black) and without (blue) prior lengthening.** Bars represent net quadriceps activations, calculated from weighted and summed EMG data of vastus lateralis, rectus femoris and vastus medialis. ANOVA (post-hoc tests) identified significantly reduced activation after lengthening (*$p < 0.05$).

Concerning weighted EMG, net activation was significantly ($p < 0.036$) different between fatiguing trials with and without lengthening, and stretch-induced activation reduction raged between 89 and 92% of pure isometric reference (Fig. 3). Paired t-test analysis identified differences at 10 s ($p = 0.018$), 20 s ($p = 0.019$) and 40 s ($p = 0.047$) after lengthening (Table 2).

## Discussion

The story of residual force enhancement started in the 50's of the last century and the last word is not spoken yet. Underlying mechanisms remain a matter of debate[2,15,16,51], and in addition, the relevance of RFE for natural human muscle function is still unclear[35]. Stretch-induced increase in neuromuscular efficiency could be shown in several *in vivo* human studies, indicating optimized muscle function[30,31].

Although mean activation of all measured QF muscle parts was constantly lower after lengthening in this study, only individual contribution of rectus femoris activation reduction was identified by statistical analysis. However, overall net activation of QF in terms of weighted EMG was showing stretch-induced activation reduction for up to 40 s after lengthening (Fig. 3), indicating that the same net torque was achieved with less net neural effort (EMG amplitudes)[30–32], likely related to reduced metabolic costs[34].

During fatiguing trials, the contraction intensity was feedback-controlled by subjects at 60% of individual maximum torque. Although there was a statistical difference in torque level between contractions conditions, this

difference is virtually of no relevance (Fig. 2). Additionally, it is important to note that there were no differences in peak torque, voluntary activation and potentiated resting twitches in neuromuscular tests before pure isometric and lengthening-isometric fatiguing tasks. This indicates that baseline values and neuromuscular start conditions were identical before fatiguing contractions with and without active lengthening. Furthermore, if there was any uncontrolled influence of insufficient rest between trials, our biased protocol with pure isometric contractions being always the first test would rather lead to an underestimation of stretch-induced activation reduction. Not all measured muscle parts showed statistically significant increases in neuromuscular efficiency, and if so significantly reduced activation was not found for all analyzed time points. This was likely due to the huge standard deviations, indicating a lot of variability in subjects' muscle activation for solving the task. This limitation may always be part of *in vivo* tests using voluntary muscle activation and needs to be kept in mind when following the discussion of our findings. However, despite obvious variance, the results on net activation are in accordance with previously published work on stretch-induced activation reduction[18,30–32] and add information on *in vivo* muscle function in history dependent scenarios.

It's highly plausible that the reduced EMG amplitudes found after lengthening trials result from reduced motor unit recruitment and/or lower firing rates during the submaximal muscle action[52]. Accordingly, as force was controlled at a constant level, median frequencies were identical, and net-EMG amplitudes were reduced, a reduced number of active motor units must have produced the controlled force output of 60% MVC. Thus, the force per motor unit and its corresponding muscle fibers was increased. This optimization in neuromuscular efficiency is well in line with the current understanding of which mechanisms might contribute to stretch-induced residual force enhancement. Enhanced force per fiber may partly derive from increased passive stiffness in sarcomeres due to calcium sensitive titin-actin interactions, or be a result of an increased proportion of strongly bound cross-bridges within the contractile machinery[2,12,15,51,53,54]. Concerning the latter, it seems unlikely that stretch-induced alterations of cross-bridge kinetics persist for 30 seconds and longer, as countless new cross-bridge-cycles take place in post-eccentric phase after lengthening[55]. For this reason and due to the fact that RFE effects are reported to be long-lasting in earlier work[3,56], we favor the idea of a stretch-loaded spring (like titin), that added the most to the force enhancement in active fibers. Consequently, this enhanced force per muscle fiber may have allowed for maintaining a certain load with a reduced number of active motor units and thus net muscle activation. However, this is highly speculative and the performed experiments in this work do not allow for direct conclusions on a microscopic level. Additionally, the used EMG model for net activation of QF muscle needs to be interpreted with caution. Direct evidence of correctness of underlying theoretical base is hardly possible, and although overall results are in accordance with literature, there is no guarantee that our model reflects real muscle activation or coordination. Furthermore, we cannot provide an answer to the questions if, how, and why discussed mechanisms brake up at a certain time, as we did not find reduced activation at the end of our trials. This needs further examination.

Separate from the stretch-induced activation reduction, at all analyzed muscle parts EMG amplitudes increased and median frequencies decreased during the 60 seconds of submaximal muscle action with and without prior lengthening. The continuously decreasing RF, VL and VM median frequencies were not different between contraction conditions at any of the analyzed time points. This indicates that due to earlier fatigue of fast twitch fibers, fiber type recruitment during prolonged muscle action may have changed to a higher proportion slow muscle fibers and decreased muscle fiber conduction velocity over time[57,58]. Prolonged half-relaxation times as well as reduced rate of force development in resting twitches after fatiguing trials are well in line with this line of arguments.

Hence, subjects showed typical signs of emerging fatigue over time[59–61] that resulted in a considerable amount of reduced muscle function. We found a 30% decrease in voluntary maximum torque after 60 s submaximal trials, that derived from reduced voluntary activation levels as well as from severe peripheral fatigue (resting twitches) (Table 1). Interestingly and totally against our expectations, we did not find any difference between neuromuscular tests after the two types of fatiguing contractions. Although neuromuscular efficiency was increased after lengthening, the resulting impairments, especially concerning structural muscle functionality (i.e. resting twitches), were identical after both fatiguing trials. This is in conflict with the idea that stretch-induced enhancement of neuromuscular efficiency counteracts performance fatigability.

To the authors' knowledge, there is only one study analyzing energetic cost after lengthening-contractions on a muscle fiber level and a decrease in ATPase activity per unit of force was found in isometric contractions following active lengthening[34]. During muscle action ATP is used to maintain $Na^+/K^+$ pumping in and out of a muscle cell after an action potential, to generate force and do work during cross-bridge cycling[62]. It is unclear if comparable mechanisms can be transferred to *in vivo* muscle action and performance fatigability. Concerning our results, it may be speculated that the total intensity and duration of the 60 s fatiguing task at 60% of maximum voluntary torque was too strenuous in both types of contractions, such that a distinction between different states of fatigue was not possible anymore. Indeed, the number of non-responders (i.e. subjects showing no activation reduction at specific time points) increased with increasing contraction time and to the end of the 60 s fatiguing contraction no differences in net activation could be found between conditions. As a result, this may have caused comparable amounts of severe disturbances in the excitation-contraction coupling, depletion of muscle glycogen or accumulation of metabolites, and our tests may not have been sensitive enough to distinguish. However, again, this needs further research.

In conclusion, a stretch-induced increase in neuromuscular efficiency can be supported at least for findings on net activation reduction after active lengthening contractions, although this was not found for all individual muscle parts. After 60 s of muscle action, fatigue signaling parameters were identified irrespective of prior eccentric lengthening and no differences were found between the two types of fatiguing contractions. Hence, no advantage of RFE mechanisms could be identified in terms of better resistance against the development of central or peripheral fatigue. This may be due to the strenuous protocol in this study or huge individual variability. Further work is needed to elaborate if results differ when analyzing additional submaximal contraction intensities in different muscles.

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## Author Contributions

W.S., D.H. and F.K.P. conceived and designed the experiments. F.K.P., E.H. and W.S. performed the experiments. W.S. and F.K.P. analyzed the data. All authors discussed the results and contributed to the elaboration of the manuscript.

## Additional Information

**Competing financial interests:** The authors declare no competing financial interests.

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## 2.4 Oxygen consumption of gastrocnemius medialis (Study Four)

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# Oxygen consumption of gastrocnemius medialis muscle during submaximal voluntary isometric contractions with and without preceding stretch

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**After an active muscle stretch, maintaining a certain amount of force in the following isometric phase is accompanied by less muscle activation compared to an isometric contraction without preceding active stretch at the corresponding muscle length. This reduced muscle activation might be related to reduced metabolic costs, such as the oxidative metabolism. Hence, the aim of this study was to clarify if mechanisms associated with stretch-induced activation reduction (AR) also influence oxygen consumption of voluntary activated human muscles after active stretch. Plantarflexion torque of 20 subjects was measured during 1) purely isometric and 2) active stretch contractions (26°, 60°/s), at a submaximal torque level of 30% MVC. Oxygen consumption ($m\dot{V}O_2$) of gastrocnemius medialis (GM) was estimated by near-infrared spectroscopy while applying arterial occlusion. Since the overall group did not show AR at GM after active stretch ($p > 0.19$), a subgroup was defined ($n = 10$) showing AR of $13.0 \pm 10.3\%$ ($p = 0.00$). However, for both purely isometric and active contractions $m\dot{V}O_2$ was the same ($p = 0.32$). Therefore, AR triggered by active stretch did not affect $m\dot{V}O_2$ of active human muscle.**

In 1952, Abbott and Aubert made experiments on the toad sartorius muscle and found enhanced forces in the isometric phase after active stretch compared to purely isometric contractions. The final isometric muscle length as well as the muscle stimulus intensity were the same for the two conditions[1]. This finding of the so-called "residual force enhancement" (RFE) provided the basis for a continual research.

Despite the growing number of studies, the underlying mechanism(s) of RFE is (are) still unknown[2–5]. From a phenomenological perspective the muscular feature is known to be independent of stretch velocity[6] but sensitive to the stretch amplitude[1,7]. RFE has been proven for the entire force-length relationship[8,9] and has been verified in *in vivo* studies for maximum voluntary[10–12] and submaximal voluntary contractions[13–16], for small[10] and large human muscles[17] as well as for multi-joint movements[11,14,15]. Beside the aforementioned lack of knowledge regarding the origin of RFE, especially studies on humans performing voluntary contractions reported a discrepancy between the total number of subjects involved in a study and those who showed enhanced forces after active stretch, referred to as responder vs. non-responder phenomenon[15,18,19].

In 2005, the definition of RFE was extended to submaximal contractions while keeping the applied force constant[20]. In 2005, Oskouei and Herzog found changes in the EMG signal in the isometric phase after active stretch, compared to pure isometric contractions at the same muscle length, resulting in a lower EMG signal for the isometric contraction preceded by an active stretch. Also in later work, this enhanced neuromuscular efficiency was assumed to be beneficial in terms of reduced metabolic cost during muscle contraction after active stretch[13,21]. However, only one study directly tested this hypothesis of reduced metabolic cost after active stretch on a muscle fibre level[22]. These authors demonstrated a reduction in the ATPase activity per unit force for the isometric contraction after active stretch, compared to the purely isometric contraction for a skinned fibre from rabbit

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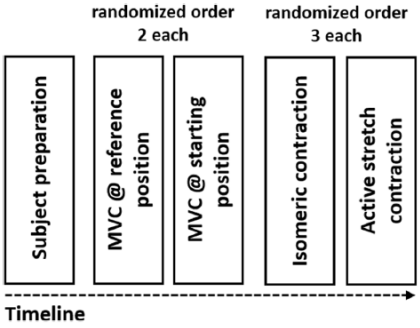


**Figure 1.** Schematic timeline of the performed experiment, measuring plantar-flexion torque. After the subject preparation, the participant did two maximum voluntary contractions (3–5 s) at the starting (13.3 ± 0.4° dorsiflexion) and reference position (13.0 ± 0.4° plantar flexion) in randomized order. These contractions were followed by either isometric (13.0 ± 0.4° plantar flexion) or active stretch contractions (Range of motion: 26.3 ± 0.4°. Angular velocity: 60°s$^{-1}$) executed in randomized order with an activation level of 30% MVC. Rest between the different contractions was set to a minimum of 3 minutes[30].

psoas muscle. They suggested that the average force per cross bridge or the engagement of a passive structure is responsible for this enhanced fibre efficiency. However, it is unclear if these results can be transferred to a complex system like *in vivo* human muscle contraction.

As one of the main methods of energy production in skeletal muscle is the oxidative metabolism, enhanced economisation triggered by active stretch contraction would positively influence the energy demands inside the muscle. A possibility to monitor processes of muscle metabolism non-invasively is provided by the use of near-infrared spectroscopy systems (NIRS). Such optical measurement systems are used in a variety of different settings, ranging from isometric to dynamic muscle contractions measuring variant muscles[23–25]. One of the first experiments calculating muscle oxygen consumption ($m\dot{V}O_2$) using light at different wavelength were done by Millikan[26] on the cat soleus. These days, using NIRS devices in combination with arterial occlusion enables the possibility to estimate $m\dot{V}O_2$ in active *in vivo* muscles[27–29].

Little is known regarding *in vivo* muscle oxygen consumption within the field of residual force enhancement and it is unclear if the rare information about metabolic benefits of RFE can be transferred to human muscle action. Therefore, the purpose of this study was to estimate oxygen consumption of gastrocnemius medialis (GM) during isometric, submaximal plantar flexion, with and without a preceding active stretch. The submaximal contractions were chosen because most everyday movements are based on non-maximal efforts.

## Methods

**Subjects.** Twenty healthy male subjects (29 ± 4 y, 80 ± 7 kg, 183 ± 6 cm) with no history of ankle joint injuries or neurological disorders participated in the study. The subjects had a mean adipose tissue thickness of 4.0 ± 1.9 mm at the gastrocnemius medialis. The study was approved by the local Ethics Committee of the Technical University of Munich and conducted according to the declaration of Helsinki. Subjects voluntarily participated and gave written informed consent.

**Experimental Protocol.** Previous to the experiment, subjects performed a training session to become familiar with the testing setup and procedure, especially to train the reproducibility of submaximal contractions at 30% maximum voluntary contraction (MVC). Biofeedback (proActive, prophysics AG, CH) was presented on a screen in front of the subjects showing the plantar flexion torque signal from the right ankle.

For further understanding of the study it is worth knowing that the starting positions represents the initial position of the active stretch contraction, whereas the reference position reflects the angular position where the parameters were assessed for the comparison of the two different contractions.

For calculation of the torque level throughout the submaximal contractions, the test session started with four maximum voluntary plantar flexion contractions, two at each position (starting position: 13.3 ± 0.4° plantar flexion, reference position: 13.0 ± 0.4° dorsiflexion. 0° defining the position when the tibia axis is perpendicular to the plantar aspect of the foot) in randomized order. To guarantee standardized conditions throughout the MVC contractions (~3 s each) the examiner gave maximum verbal encouragement. The torque curve was presented the whole time in front of the subject and the verbal starting signal was the same for all MVC contractions. In addition, the subjects were instructed to contract as fast and hard as possible.

The maximum torque value from the two contractions at each position was defined as peak torque and subsequently was used for calculation of the submaximal target level (~30% MVC). MVC contractions were followed by three submaximal pure isometric contractions in the reference position and three active stretch (isometric-eccentric-isometric) contractions with a stretch amplitude of 26.3 ± 0.4° at an angular velocity of 60°s$^{-1}$ (Fig. 1). The six contractions were performed in randomized order, each lasting 60 s. During active stretch contraction, a stable feedback curve of 2 s was required before the active stretch phase was initiated (Fig. 3A).

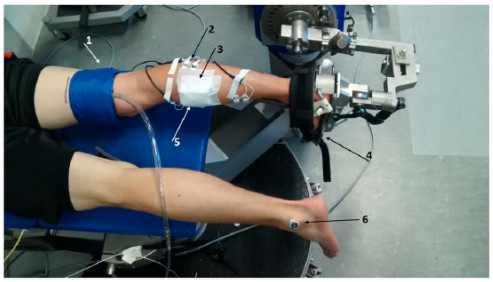


**Figure 2.** Experimental Setup. 1: Pressure Cuff. 2: EMG Electrodes. 3: Near-infrared spectroscopy device. 4: Footrest including safety belts and binding system. 5: Position of gastrocnemius medialis electrodes. 6: Reference electrode.

Hence, as the active stretch lasted ~0.5 s, the isometric phase in the reference position was about 57.5 s for the active stretch contraction and 60 s for the pure isometric contraction. Between every contraction, subjects rested as long as individual required; but a minimum of rest was set to 3 min[30].

**Experimental Setup.** Plantar flexion torque was measured (1000 Hz) on a motor-driven dynamometer (IsoMed 2000, D&R Ferstl GmbH, GER). Subjects lay prone on the bench of the dynamometer. The right foot was fixed with a binding system around the instep and the heel was secured with a safety belt to avoid heel displacement during the different contractions (Fig. 2). Additionally, the subjects were fixed with shoulder pads.

Muscle activation of gastrocnemius medialis (GM), gastrocnemius lateralis (GL), soleus (SOL), and tibialis anterior (TA) were recorded (proEMG, prophysics AG, CH) with 1000 Hz (USB-6218 BNC, 16-bit, National Instruments Corporation, USA) using a wired, surface EMG system (OT Bioelecttronica, I). Skin preparation (for EMG and NIRS measurement) as well as electrode placement were done according to the SENIAM recommendations[31]. Due to the usage of a near-infrared spectroscopy system on GM, EMG electrode placement was slightly adjusted regarding the SENIAM recommendations (Fig. 2). The reference electrode was placed on the lateral malleolus of the contralateral side as the experimental setup did not allow to place it on the ipsilateral side. (Figure 2). The NIRS probe was placed on the muscle belly of GM. A constant blood volume in the lower leg was ensured via arterial occlusion. Therefore, a pressure cuff (400 mmHg, Hokanson 10D, Bellevue, WA) was placed just above the knee and was rapidly inflated (~3 s) (Fig. 2) directly prior to the onset of the submaximal contractions. To ensure the same placement throughout the different contractions the cuff position was tagged with a permanent marker. In order to avoid varying blood volumes prior to the different contraction conditions, the pressure cuff was always inflated in the reference position. After reaching the target pressure, the subjects were passively brought into the starting position for active stretch contractions, whereas for the isometric contractions a passive movement across the whole ROM was done prior to the beginning of the contraction. The pressure cuff was immediately deflated at the end of the submaximal contractions.

**Near-infrared spectroscopy.** A wireless continuous-wave (CW) NIRS device (PortaMon, Artinis Medical Systems, NL) was used to estimate local oxygen consumption in GM during submaximal contractions. The interoptode distance of 40 mm as used in our setup resulted in a penetration depth of about 20 mm[32]. The wavelengths of the light source were 760 and 850 nm. Data were collected with a sample frequency of 10 Hz. The NIRS device was secured with adhesive tape and an elastic bandage to ensure the same placement throughout the test. In addition, a light-tight piece of cloth was placed around the NIRS system to avoid influence from ambient light.

CW NIRS systems can measure wavelength-specific changes in the optical density of the tissue, reflecting the tissue-oxygenation level in primarily small blood vessels[33] using the modified Lambert-Beer law[34]. As haemo- and myoglobin are the main absorbers for light of the applied wavelength, the density changes were transformed into concentrations changes of oxyhaemoglobin ($O_2Hb$) and oxymyoglobin ($O_2Mb$) as well as deoxyhaemoglobin (HHb) and deoxymyoglobin (HMb). Due to the overlap in the absorption spectrum it is not possible to distinguish between haemoglobin and myoglobin proteins. Therefore, in the present study $O_2Hb$ and HHb represents both oxygenated and deoxygenated proteins, respectively. Since the path-length of the photons travelling through the tissue is unknown when using CW NIRS, the measurements were done using a differential path length factor of 4 for calculation of absolute concentration changes.

Beside density changes, the NIRS device provides the measurement of the tissue saturation index (TSI) which is a percentage measurement of tissue oxygen saturation and independent of near-infrared photon path length. The TSI value was used to exclude different oxygenation levels at the onset of the two contraction conditions and is calculated as

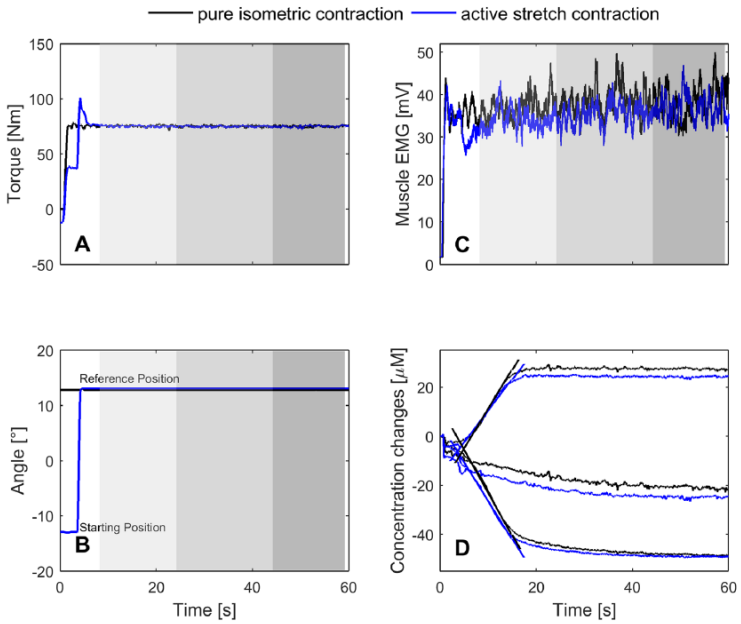


**Figure 3.** Exemplar data of measured parameters during an active stretch contraction (blue) and a pure isometric contraction (black). Different background colours in (**A**–**C**) represent three analysed time windows (Light grey: 4–20 s. Grey: 20–40 s. Dark grey: 40–55 s). A: Plantar flexion torque. B: Ankle angle. C: Muscle EMG of gastrocnemius medialis. (**D**) Near-infrared spectroscopy data. Upper-two lines represent deoxygenated haemoglobin. Mid-two lines represent total haemoglobin. Lower-two lines represent oxygenated haemoglobin. For these data the mean out of the slopes from the oxy- and deoxygenated haemoglobin of the two contraction conditions was calculated as representative of muscle oxygen consumption. Note: The time references in (**A**–**C**) are the same for both contraction conditions.

$$TSI = (O_2Hb/(O_2Hb + HHb))^*100. \quad (1)$$

Skinfold thickness was measured with a skinfold caliper (Harpenden, Baty International, GB). To obtain the adipose tissue thickness the results from the caliper measurements were divided by two[35].

**Modelling of triceps surae muscle activity.** To get a better overview across the EMG data during the force controlled setup and to account for the complexity of the m. triceps surae (TS), EMG data was weighted according to the physiological cross-sectional area and muscle volume[13] which is thought to be directly related to maximum muscle force[36]. The weighting factors for TS ($EMG_{TS}$) were taken from Albracht *et al.*[37]. Net EMG activation was calculated as follows:

$$EMG_{TS} = SOL_{measured}{}^*0.62 + GM_{measured}{}^*0.26 + GL_{measured}{}^*0.12 \quad (2)$$

**Data analysis.** Because the NIRS data was stored on a separate computer, signals were synchronized with an external device (PortaSync, Artinis Medical Systems, NL) and transferred to MATLAB (The MathWorks, Inc., USA) for further analysis.

For each contraction condition, the contraction with the lowest standard deviation from the biofeedback torque target curve was chosen for final processing. Angle and torque were filtered using a 5 Hz Low pass zero-lag filter. EMG signals were band-pass filtered (10–500 Hz) with a second order Butterworth zero-lag filter, rectified and smoothed (0.5 s moving average). For statistical analysis regarding differences of the two contraction conditions, each 60 s lasting contraction was divided into 3 sections starting after the end of stretch (T1: 4–20 s, T2: 20–40 s, T3: 40–55 s) (Fig. 3A–C). Since the start of each contraction was defined when the torque value exceeded 10 Nm, the time-points of the analysis section from the active stretch contraction could be assigned to the pure isometric contraction. Thereby we can ensure that the duration of the muscle activation was the same at each analysis section for each condition. For torque and angle data the mean of each section was calculated whereas

| Overall Group (n = 20) | T1_iso | ± | T1_as | ± | T2_iso | ± | T2_as | ± | T3_iso | ± | T3_as | ± |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Torque [Nm] | 75.5 | 11 | 75.6 | 11 | 75.5 | 10.9 | 75.5 | 10.9 | 75.5 | 10.9 | 75.6 | 11.0 |
| Angle [°] | 13.0 | 0.5 | 13.0 | 0.3 | 13.0 | 0.5 | 13.0 | 0.4 | 13.0 | 0.4 | 13.0 | 0.3 |
| $EMG_{TS}$ [mV*s] | 2.0 | 1.6 | 1.9 | 1.5 | 2.6 | 2.1 | 2.5 | 2.0 | 2.0 | 1.6 | 2.0 | 1.6 |
| GM [mV*s] | 3.1 | 2.3 | 3.0 | 2.4 | 3.9 | 3.1 | 3.8 | 2.4 | 2.8 | 2.2 | 2.8 | 2.2 |
| GL [mV*s] | 1.8 | 2.3 | 1.7 | 2.1 | 2.4 | 1.8 | 2.4 | 2.6 | 2.0 | 1.5 | 1.9 | 1.8 |
| SOL [mV*s] | 1.5 | 1.2 | 1.5 | 1.1 | 2.1 | 1.8 | 2.1 | 1.6 | 1.7 | 1.4 | 1.7 | 1.4 |
| TA [mV*s] | 0.4 | 0.3 | 0.4 | 0.3 | 0.5 | 0.3 | 0.5 | 0.3 | 0.5 | 0.4 | 0.4 | 0.3 |
| $*TSI_{start}$ [%] | 69.7 | 4.2 | 70.7 | 3.8 | | | | | | | | |
| $**TSI_{stretch}$ [%] | 67.8 | 3.7 | 68.8 | 3.5 | | | | | | | | |

**Table 1.** Mean and standard deviation (±) of all subjects during pure isometric (iso) and active stretch (as) contractions at three analysed windows. T1 = 4–20 s after stretch. T2 = 20–40 s after stretch. T3 = 40–55 s after stretch. Torque = Plantar flexion torque. Angle = Angular position at the reference position. $EMG_{TS}$ = Triceps surae. GM = Gastrocnemius medialis. GL = Gastrocnemius lateralis. SOL = Soleus. TA = Tibialis anterior. Torque and angle data represent mean data. GM, GL, SOL and TA represent integrated data. *TSI = Tissue saturation index just prior to the onset of the contraction. $**TSI_{stretch}$ = Tissue saturation index just after the end of stretch.

for EMG data the integral for each analysis section was computed using the trapezoidal numerical integration function of MATLAB.

Activation reduction for each analysis section was calculated as

$$AR = (1 - EMG_{active\_stretch}/EMG_{pure\_isometric}) \times 100. \quad (3)$$

Hence, positive values indicate activation reduction.

The baseline values of the NIRS data, calculated as mean over a 30 s time period prior to start of the contractions, were subtracted from the signal in a first step. Afterwards the data were smoothed using a Loess filter (span 10%) as the differentiation of the raw NIRS signal was too noisy for calculation of peak $m\dot{V}O_2$.

The peak $m\dot{V}O_2$ value was needed for an iteration method defining the linear slope of the $O_2Hb$ and HHb signal with a goodness of fit for $r^2 > 0.99$. The mean of the slopes was taken as representative of $m\dot{V}O_2$[27]. The calculation of the offset corrected slopes started at the beginning of the contraction, defined when torque exceeded 10 Nm. The slopes of $O_2Hb$ and HHb were normalized to the individual maximum value at the end of each contraction, to make our results comparable between subjects. Analogous to the calculation of the activation reduction, the relation between $m\dot{V}O_2$ from the pure isometric and the active stretch contraction was calculated as

$$m\dot{V}O_2\% = \left(1 - m\dot{V}O_{2\_active\_stretch} / m\dot{V}O_{2\_pure\_isometric}\right) \times 100. \quad (4)$$

Thus, positive values represent reduced oxygen consumption.

In addition, for the pure isometric as well as for the active stretch contraction, the tissue saturation index was calculated at the onset of the contraction ($TSI_{start\_iso}$, $TSI_{start\_as}$) as well as just after end of stretch ($TSI_{stretch\_iso}$, $TSI_{stretch\_as}$) for both contraction conditions.

**Statistics.** Data were tested concerning normal distribution using the Shaprio Wilk test. If normality was confirmed, a 2 × 3 (condition × time) repeated measure ANOVA was calculated and the results were corrected if sphericity was violated using Greenhouse-Geisser correction. In the case of only comparing two means, we used a student's t-test for paired groups. Once normality was rejected Friedmans's ANOVA was calculated. In the case of a significant result, a Wilcoxon test was used for further analysis. The alpha level was set to $p < 0.05$ (two-sided) and analysis was performed using IBM SPSS 23 software (SPSS for Windows, US).

**Data availability.** The dataset generated and analysed during the current study are available from the corresponding author on reasonable request.

## Results

Detailed descriptive data can be found in Tables 1 and 2. Data are presented as mean ± standard deviation.

**Overall group.** Maximum NIRS values ($O_2HB\_iso = 34.2 \pm 10.7\,\mu M$; $O_2Hb\_ecc = 35.5 \pm 9.9\,\mu M$; $HHb\_iso = 24.1 \pm 8.4\,\mu M$; $HHb\_ecc = 24.2 \pm 9.1\,\mu M$) used for normalization of $m\dot{V}O_2$ were statistically not different between contraction conditions ($O_2Hb$: $t(19) = -1.27$, $p = 0.22$. HHb: $t(19) = -0.36$, $p = 0.72$). The estimated muscle oxygen consumption ($m\dot{V}O_2$) showed no differences between the two conditions ($t(19) = -1.71$, $p = 0.10$). The tissue saturation index (TSI) at the onset of the contraction showed a trend towards higher values for the active stretch condition ($t(19) = -2.00$, $p = 0.06$), the same was true for the parameter $TSI_{stretch}$ ($t(19) = -2.05$, $p = 0.05$) (Table 1).

Friedmans's ANOVA indicated significant differences in overall angular positions of the ankle ($\chi^2(5) = 15.66$, $p = 0.01$). Wilcoxon post-poc tests did not identify differences of angle between contraction conditions at specific analyses windows (T1: $T = 55$, $p = 0.62$, T2: $T = 53$, $p = 0.52$, T3: $T = 99$, $p = 0.82$). Repeated measures ANOVA

| Subgroup (n = 10) | T1_iso | ± | T1_as | ± |
|---|---|---|---|---|
| Torque [Nm] | 75.8 | 8.7 | 75.5 | 9.0 |
| Angle [°] | 12.9 | 0.1 | 13.0 | 0.2 |
| $EMG_{TS}$ [mV*s] | **1.9** | 0.9 | **1.8** | 0.9 |
| GM [mV*s] | **3.3** | 1.6 | **2.9** | 1.6 |
| GL [mV*s] | 1.7 | 0.9 | 1.7 | 1.3 |
| SOL [mV*s] | 1.4 | 0.8 | 1.4 | 0.7 |
| TA [mV*s] | 0.4 | 0.2 | 0.5 | 0.2 |
| $*TSI_{start}$ [%] | 71.8 | 3.5 | 72.4 | 3.9 |
| $**TSI_{stretch}$ [%] | 68.8 | 3.81 | 70.3 | 3.5 |

**Table 2.** Mean and standard deviation (±) of all subjects during pure isometric (iso) and active stretch (as) contractions at T1. T1 = 4–20 s after stretch. Torque = Plantar flexion torque. Angle = Angular position at the reference position. GM = Gastrocnemius medialis. GL = Gastrocnemius lateralis. SOL = Soleus. TA = Tibialis anterior. Torque and angle data represent mean data. GM, GL, SOL and TA represent integrated data $*TSI_{start}$ = Tissue saturation index just prior to the onset of the contraction. $**TSI_{stretch}$ = Tissue saturation index just after the end of stretch. Bold numbers represent significant differences between contraction conditions at specific analysed time window.

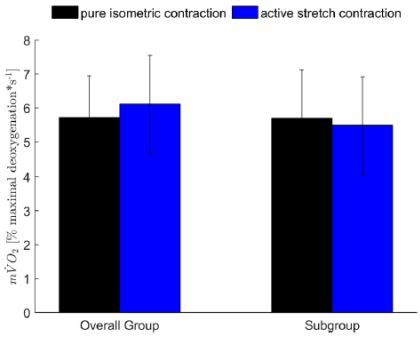


**Figure 4.** Results (mean ± standard deviation) for the estimated oxygen consumption for the overall subject group (n = 20) and the subgroup (n = 10). No significant differences were found between isometric and active stretch contraction.

showed no differences regarding the torque values for factor condition ($F(1, 19) = 0.24$, $p = 0.88$), time ($F(1.35, 25.70) = 0.40$, $p = 0.60$), and interaction of condition and time ($F(2, 38) = 0.70$, $p = 0.50$).

Regarding the EMG activity the modelled triceps surae activity ($EMG_{TS}$) ($\chi 2\ (5) = 72.77$, $p = 0.00$) as well as GM ($\chi^2\ (5) = 70.26$, $p = 0.00$), GL ($\chi^2\ (5) = 45.71$, $p = 0.00$), SOL ($\chi^2\ (5) = 75.80$, $p = 0.00$) and TA ($\chi^2\ (5) = 68.37$, $p = 0.00$) showed significant results. Calculating Wilcoxon tests, neither $EMG_{TS}$ (T1: T = 58, p = 0.62, T2: T = 72, p = 0.52, T3: T = 92, p = 0.82) nor the activity of GM (T1: T = 80, p = 0.35, T2: T = 70, p = 0.19, T3: T = 92, p = 0.63), GL (T1: T = 72, p = 0.22, T2: T = 71, p = 0.20, T3: T = 78, p = 0.31), SOL (T1: T = 91, p = 0.60, T2: T = 102, p = 0.91, T3: T = 75, p = 0.26) and TA (T1: T = 97, p = 0.77, T2: T = 82, p = 0.39, T3: T = 75, p = 0.26) showed differences between contraction conditions at the three different analysed time-windows.

A positive correlation was found between $m\dot{V}O_2\%$ and AR ($r = 0.69$, $p = 0.001$), whereas there was no correlation between $TSI_{stretch}$ and $m\dot{V}O_2\%$ ($r = -0.18$, $p = 0.46$) (Fig. 5).

**Subgroup.** To test the hypothesis whether an activation reduction in the post-isometric phase after an active stretch affects muscle oxygen consumption, a subgroup showing activation reduction (AR) in the GM during the first analysed time window (T1) was defined. 50% (n = 10) of the overall group fulfilled this criteria. T1 (4–20 s after stretch) was chosen as the plateau region of the O2Hb and HHb signal was reached about 15–20 s after contraction start (Fig. 3D). Hence, this gives us the opportunity to ensure that activation reduction was present in those subjects and to connect activation reduction with estimated oxygen consumption.

Statistical analysis at T1 showed no differences between contraction conditions regarding torque ($t(9) = -1.27$, $p = 0.35$) and EMG of GL ($t(9) = -0.40$, $p = 0.70$), SOL ($t(9) = -1.27$, $p = 0.31$) and TA ($t(9) = -1.27$, $p = 0.36$), $TSI_{start}$ ($t(9) = -1.27$, $p = 0.52$) and $TSI_{stretch}$ ($t(9) = -2.00$, $p = 0.076$). For the ankle angle there was a significant but irrelevant difference at T1 ($T = 6$, $p = 0.03$) between the pure isometric contraction and the active stretch contraction (12.9 ± 0.1° vs. 13.0 ± 0.2° dorsiflexion).

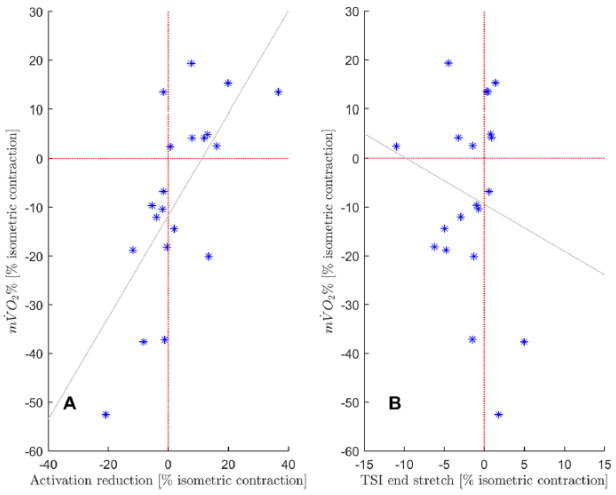


**Figure 5.** (**A**) Scatter plot between activation reduction (x-axis) and oxygen consumption ($m\dot{V}O_2$) (y-axis). Positive values on the y- and x-axis are attributed to activation reduction (AR) and reduced $m\dot{V}O_2$ compared to pure isometric contraction. Data shows a significant correlation between $m\dot{V}O_2$% and activation reduction. ($r = 0.69$, $p = 0.001$). (**B**) Scatter plot between TSI value at the end of stretch (x-axis) and oxygen consumption ($m\dot{V}O_2$%) (y-axis). Positive values on the y- and negative values on the x-axis are attributed to reduced $m\dot{V}O_2$% and enhanced TSI values after end of stretch compared to pure isometric contraction. TSI at the end of stretch was not correlated to $m\dot{V}O_2$ in following isometric states. ($r = -0.18$, $p = 0.46$). Note: Each symbol represents one subject.

There was a significant difference for the muscle activity of $EMG_{TS}$ ($t(9) = 4.76$, $p = 0.00$) and GM ($t(9) = 4.12$, $p = 0.00$). Showing an AR after active stretch of $7.7 \pm 4.8$% and $13.0 \pm 10.3$% compared with the pure isometric contraction, respectively. However, $m\dot{V}O_2$ showed no significant difference between contraction conditions ($t(9) = 1.05$, $p = 0.32$, Fig. 4).

## Discussion

The purpose of the present study was to clarify if AR during an isometric contraction following an active stretch is associated with a reduced muscle oxygen consumption in comparison to a pure isometric contraction without preceding active stretch. This purpose is based on the repeatedly reported finding of enhanced neuromuscular efficiency after active stretch compared to a pure isometric contraction[13,20,38]. Although never measured for an *in vivo* muscle, it was concluded from these results that the observed reduced AR in the isometric phase after active stretch is accompanied by reduced metabolic cost[13,21].

As a requirement for testing our hypothesis, two criteria must be fulfilled for the analysis of $m\dot{V}O_2$ regarding activation reduction in GM in our setup:

1) Subjects must be responders regarding activation reduction after active stretch at GM.
2) Activation reduction must occur in the GM concerning the detection of reduced $m\dot{V}O_2$. At the same time, the remaining investigated muscles of the triceps surae should not show an enhanced muscle activation during the active stretch compared to the pure isometric contraction. This is necessary to exclude a compensation of AR at GM by muscle redundancy[39].

The overall subject group did not fulfil the first criterion. There was no AR in the target muscle GM even so the second criterion was fulfilled as GL and SOL showed no difference when comparing the isometric phase after active stretch with the pure isometric condition. Likewise, $m\dot{V}O_2$ showed no difference between contraction conditions (Fig. 4). To overcome the problem of muscle redundancy[39] during a specific task, Seiberl *et al.*[13] modelled the overall EMG-activity of the involved muscles by calculating a net muscle activity according to the physiological cross-sectional area and the muscle volume of the involved muscles. However, applying this approach to the triceps surae did not show enhanced neuromuscular efficiency in terms of activation reduction after active stretch. Hence, our data is different regarding the existence of activation reduction compared to previously published data of muscles involved in human locomotion[13,38]. Especially the number of non-responders is higher than reported for comparable work: 20–30% in Seiberl *et al.*[13], ~30% in Oskuei and Herzog[18], ~10% in Tilp *et al.*[19]. In our study, 50% of the subjects showed no activation reduction after active stretch for GM. Despite numerus reports that especially

during submaximal contractions only a part of the subjects is showing reduced activation or enhanced torque after active stretch in comparison to a pure isometric contraction[15,18,19], by now no existing explanation gives a valid and satisfying answer for these observations. Fibre type distribution, subject specific individual threshold regarding the level of muscle activation or the lack of certain muscle physiological abilities are among the discussed theories[40]. Unfortunately, our data does not allow to draw any conclusions regarding that phenomenon.

For testing whether the estimated oxygen consumption is different between a pure isometric and an isometric contraction preceded by an active stretch, a subgroup was chosen according to the predefined criteria.

50% of our participants fulfilled the first criteria showing AR in the GM at T1. T1 (4–20 s after stretch) was chosen as the time point when the NIRS signals reached the plateau phase was between 15 to 20 s after contraction start (Fig. 3D). Thus, this time window allows direct connection of activation reduction with estimated oxygen consumption. Standardized condition for this subgroup were given regarding torque production. Ankle angle showed a significant difference at T1. As the calculated angle difference between the contraction conditions was less than 0.1°, the discrepancy is supposed to have no influence on the interpretation. For the other parts of the triceps surae we found no differences between contraction conditions, therefore fulfilling the second criteria. The same was true for the antagonistic muscle TA. Hence, the subgroup satisfied both criteria as well as the standardization criteria between the contraction conditions and showed an activation reduction of 13% in the gastrocnemius medialis and about 7% for the modelled net EMG-activity data at T1. For the active stretch contraction, Oskouei and Herzog[18,20] showed an activation reduction for the thumb ranging between 7 and 11%, Altenburg *et al.*[38] found a reduction of about 10% and the data of Seiberl *et al.*[13] revealed a AR of about 8% both obtained for the knee extensor muscle.

To guarantee the same oxygen status of the investigated tissue, the tissue saturation index was taken just prior to the onset of the contraction. The results showed no difference and a tissue saturation of about 72% for both contractions which is in the range of previously published work[41,42]. For the subgroup, oxygen consumption estimated for GM showed a reduction of 3.2% for the isometric phase after active stretch compared to the pure isometric contraction but was statistically not different. This is in contrast to the study published from Joumaa and Herzog[22] who found a reduced ATPase activity per unit force in the isometric phase after an active stretch compared to a pure isometric contraction for a skinned rabbit psoas muscle fibre. They assumed, inter alia, that an enhanced force per cross-bridge is associated with the results. This is line with Altenburg *et al.*[38] suggesting a derecruitment of active motor units after active stretch. Referring to de Ruiter *et al.*[27] proposing a reduced $m\dot{V}O_2$ as indicator towards the number of force generating cross-bridges, our results do not support the theories from Joumaa and Herzog[22] and Altenburg *et al.*[38].

The rate of oxygen consumption (5.6% maximum deoxygenation*$s^{-1}$) is in accordance with previous published data from Kooistra *et al.*[43] and Ruiter *et al.*[27], investigating quadriceps femoris at 30% of maximum torque capacity. Although there was a strong positive correlation between muscle activation and $m\dot{V}O_2$ (Fig. 5A), statistics revealed no difference regarding the oxygen consumption between an active stretch contraction and a pure isometric contraction. Hence, for our subgroup the results are contrary to published literature where reduced muscle activation was associated with lower $m\dot{V}O_2$, when comparing different levels of muscle activation[43–45].

Praagman *et al.*[46] showed a high positive correlation between muscle activation and $m\dot{V}O_2$ ranging between $r = 0.81$ and $r = 0.94$ for m. biceps brevi and m. brachioradialis. These are higher values than in our study (Fig. 5A, $r = 0.69$, $p = 0.001$). Nevertheless, there seems to be a relation between activation reduction caused by an active stretch and oxygen consumption of the investigated muscle. Reasons of possible mechanism triggered during an active stretch are still under debate. The idea of a stretch-loaded (active) spring within the sarcomere would help to explain reduced metabolic demands of a muscle to maintain a certain amount of force. However, this is highly speculative and way beyond methodologically based conclusions of this study.

Alterations of blood-volume while applying arterial occlusion can sometimes occur due to an ongoing redistribution of blood within the limb and has been described in literature as an increase in tHb[23,44,47]. Such an increase in tHb is associated with an ongoing re-oxygenation of the area under the investigated muscle. A constant blood volume under the optode will result in mirrored graphs for $O_2Hb$ and HHb, while tHb, calculated out of the sum of $O_2Hb$ and HHb nearly stays constant. A re-oxygenation might mask changes in the NIRS signal regarding the resulting slopes representing muscle oxygen consumption. Visually inspecting the graphs of tHb we found no re-oxygenation of blood volume during the individual trials (Fig. 3D) which suggests a fully occluded lower leg in our study. In addition, the pressure of the cuff used to establish arterial occlusion is in the range of previous studies[27,28] regarding the lower limb. Another point to discuss is the possible influence of the active stretch regarding the NIRS region of interest. Despite inflating the pressure cuff always in the reference position and performing the same amount of ankle joint motion for each condition (passive shortening and an active stretch for dynamic task; passive shortening-stretch prior to the pure isometric contraction), we cannot exclude that an active stretch had different effects on the underlying tissues in comparison to a pure isometric contraction. To clarify a possible influence, we additionally calculated the TSI values for both contraction types at the time point "end of the stretch" to evaluate if the region of interest had the same oxygen status. Results revealed a slightly enhanced ($p = 0.05$) TSI directly after stretch for the active stretch condition ($68.8 \pm 3.5\%$) compared to the pure isometric contraction ($67.8 \pm 3.5\%$) at the corresponding time point. Correlation between $m\dot{V}O_2$ and TSI at the end of stretch provided no additional information ($r = -0.18$, $p = 0.46$, Fig. 5B). Therefore, the initial contraction phase until the time point end of stretch does not affect the two contraction conditions in a different manner. Consequently, estimated differences regarding $m\dot{V}O_2$ during the isometric phase after active stretch compared with the pure isometric contraction can be attributed to mechanisms triggered by active stretch.

In general, using near-infrared devices has always some limitations. The estimation of $m\dot{V}O_2$ via near-infrared spectroscopy is limited because it primarily reflects concentration changes in small blood vessels, such as the capillary or arteriolar and venular beds[33]. Therefore, no direct conclusion can be drawn about deep parts of

muscle tissue. In this context, adipose tissue thickness is known to additionally affect the measurement of $m\dot{V}O_2$, as the path of the light is different in adipose tissue compared with muscle tissue. Hence, a high amount of subcutaneous fat will result in an underestimation of $m\dot{V}O_2$[35]. However, as this study is based on a repeated within-subject measure design, effects of tissue thickness variability should not have any influence on the presented results.

To our knowledge, this was the first study in the field of residual force enhancement testing the assumption of a stretch-induced energetic optimization in *in vivo* human muscles using near-infrared spectroscopy. Our data did not confirm reduced metabolic cost in terms of oxygen consumption, as there was no difference between active stretch condition and pure isometric contraction. As muscle redundancy could have influenced our data, for future studies it is suggested to focus on less complex muscles in first instance to assess the basic phenomenological relations.

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## Author Contributions

F.K.P., W.S., D.H. and F.S. conceived and designed the experiments. F.K.P., A.G. performed the experiments. F.K.P. and W.S. analysed the data. All authors discussed the results and contributed to the elaboration of the manuscript.

## Additional Information

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# 3 Summary

The current thesis could show that residual force enhancement is present in everyday alike human muscle action and support the idea of a stretch-induced increase in neuromuscular efficiency after active stretch, at least for surface electromyography measurements.

One of the main characteristics of daily human movement, like walking, is the simultaneous involvement of different joints and hence the coordination of several large muscles. In addition, daily activity is mainly occurring on a submaximal activation level and finally yet importantly human motion only occurs with slightly flexed joints. The results of this thesis could show that residual force enhancement plays a role in a setup close to natural moment. In a first step (2.1), it was shown that under submaximal conditions there were enhanced forces and joint-torques after an eccentric-isometric-eccentric contraction compared to a pure isometric contraction under submaximal conditions. In total 13 subjects performed feedback controlled bilateral leg extensions for 30 s with an activation level of 30 % of maximal voluntary activation. The analyzation of three time intervals showed significantly enhanced force and torque levels for the measured parameters after stretch ranging from 3 % to 22 % up to 22 s post-stretch. In detail, residual force enhancement regarding force was between 19 % and 16 %, for ankle torque between 22 % to 17 % and for knee torque between 14 % and 3 %. The EMG values of the antagonistic muscles as well as the centre of pressure were not different between the contraction conditions. Hence, for the first time it was shown that residual force enhancement is present during a submaximal multi-joint leg-extension setup.

The second step (2.2) included beside a multi-joint leg-extensions setup and a submaximal activation level also slightly flexed joint angles. This is due to the fact that human motion mainly occurs with slightly flexed joints (Lafortune et al., 1992; Winter, 1984). Hence, this work closed the gap not only regarding the muscle activation level but also regarding daily-like joint-angle configurations. The results of this study showed on the on hand residual force enhancement of up to 25 % for forces and joint torques but on the other hand 5 subjects did not show residual force enhancement. The analysis showed a missing of enhanced forces during stretch for the non-responders. Hence, enhanced force during the stretch phase seems to be a requirement for the

occurrence of residual force enhancement. This highlights the need for studies focusing on the responder – non-responder phenomenon (possible research approaches can be found in chapter 4.1, 4.2). Hence, the authors concluded that RFE is present for submaximal multi-joint leg-extension at joint angle comparable to human movement. Notwithstanding, a necessity for the occurrence is the appearance of enhanced forces during the active stretch contraction.

These published studies are a consistent further development from the work of Hahn et al. (2010). Including the study from Hahn et al. (2010), it is very likely that residual force enhancement occurs in daily human movement.

The verification regarding the presence of RFE in a daily-like setup raised the question about the influence of the phenomenon on muscle economy optimization. Therefore, we did a study investigating the influence of RFE with respect to muscle fatigue (2.3). The study included a 60 s fatiguing task with an activation level of 60 % MVC. In addition, we estimated peripheral as well as central fatigue using the interpolated twitch technique. The design was biased as there was always the pure isometric condition before the isometric-eccentric-isometric contraction. We used this design because we could not exclude that beside a four-hour break between the contraction conditions some of the body systems did not fully recovery. Hence, the effect of RFE always had to outperform possible limitations of muscle function in the case of incomplete fatigue. In accordance to e.g. Oskuei and Herzog (2005) we found increased neuromuscular efficiency in the EMG results regarding amplitude parameters. The EMG signal of the rectus femoris and the modelled EMG data of the quadriceps femoris showed a reduction of ~17% and ~11% in the isometric phase after an active stretch contraction in comparison with a pure isometric contraction. Against our hypothesis neither peak torque nor any fatiguing parameter were different between contraction conditions. These parameters were measured immediately after the fatiguing trials. Hence, no advantage of RFE mechanism could be identified in terms of better resistance against fatigue. The authors suspected that this was due to the strenuous protocol in the study or due to huge individual variability. More research is needed to answer that question.

The goal of a follow-up study was to gather information regarding metabolic benefits of RFE estimating muscle oxygen consumption (2.4). In addition, this was the first *in vivo* study testing this assumption. Therefore, a near-infrared spectroscopy device was used and placed on the gastrocnemius medialis muscle. In this study, the subject had to perform plantar-flexion contraction with a submaximal activation level of 30 %. The

study showed significant reduced EMG data for the modelled triceps-surae activity as well as for the gastrocnemius medialis (7.7 ± 4.8%, 13.0 ± 10.3%). Restrictively, one must say that this was only the case for a subset of subjects (n = 10). The subgroup was defined according to criteria allowing detecting the influence of RFE with respect to estimated oxygen consumption. The criteria were:

*“1) Subjects must be responders regarding activation reduction after active stretch at GM.*

*2) Activation reduction must occur in the GM concerning the detection of reduced mV̇O2. At the same time, the remaining investigated muscles of the triceps surae should not show an enhanced muscle activation during the active stretch compared to the pure isometric contraction. This is necessary to exclude a compensation of AR at GM by muscle redundancy” (Paternoster, Hahn, Stöcker, Schwirtz, & Seiberl, 2017, p. 7).*

The subgroup showed a reduced oxygen consumption of 3.2% after an active stretch compared to pure isometric contraction. Nevertheless, statistics showed no differences between the contraction conditions ($t(9) = 1.05$, $p = 0.32$).

With this work, we could not prove a connection between activation reduction and reduced metabolic cost in terms of oxygen consumption. We hypothesized that maybe muscle redundancy could have influenced our results. A possibility to circumvent the muscle redundancy is presented in chapter 4.3.

Figure 13 summarizes the questions that were dealt with in this thesis and gives an overview of research questions resulting from this work.

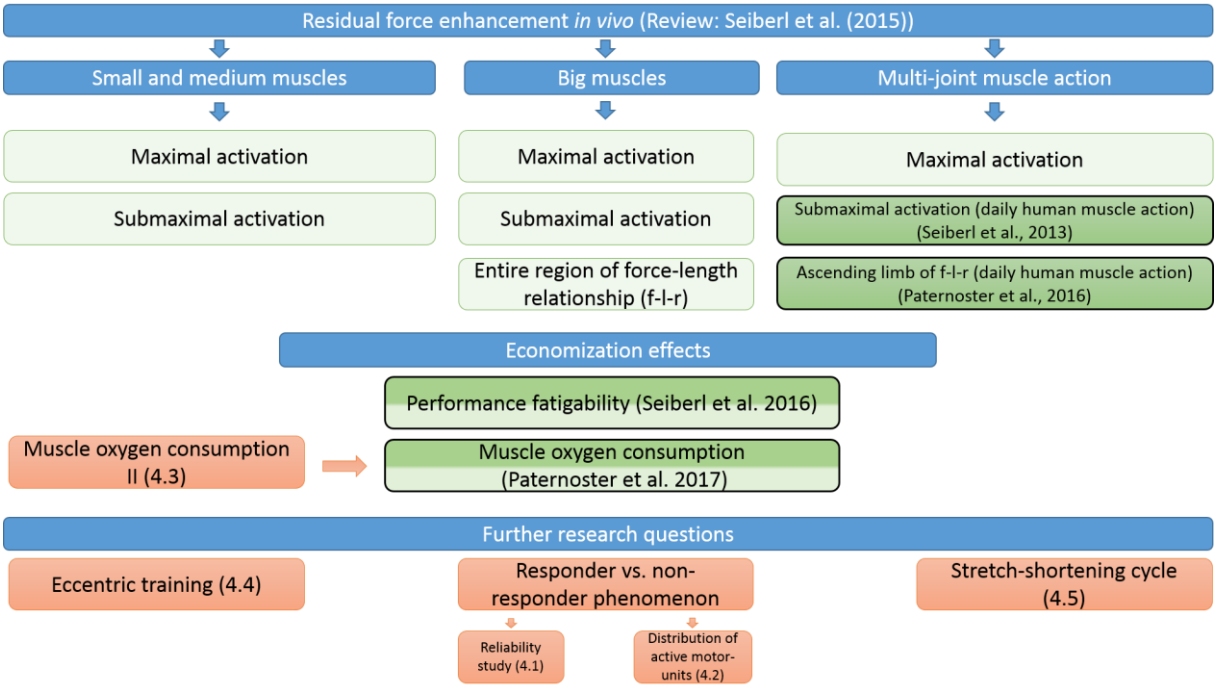


*Figure 13: Flowchart summarizing the research questions the author worked on during his PhD thesis and presentation of questions arising from it. Light green: Existing knowledge at the beginning of the PhD thesis. Dark green: Solved questions during the thesis. Mixture of light and dark green: Hypothesis partially confirmed. Light red: Research questions which result from the work. The number in brackets represents the chapter with additional information in the manuscript.*

# 4 Outlook

In the following, research questions are presented with the aim to gain further insights into the investigated muscle phenomenon. One the one hand, the research questions are based on the results of the presented thesis (4.1 – 4.3) and on the other hand questions are presented which could enhance the knowledge regarding residual force enhancement but were not directly part of this thesis (4.4, 4.5).

## 4.1 Reliability and the responder vs. non-responder phenomenon

Still one of the most challenging questions is the responder vs. non-responder phenomenon. To the author's knowledge, there is only one study with a kind of reliability design. Oskouei and Herzog (2005) showed that non-responders during the first test were non-responder during the second test, too. The second test was several weeks after the first. Hence, this study can give a first evidence that the missing of RFE might be attributed to the lack of certain physiological muscle abilities or insufficient task specific motor control. On the other hand, the term "[…] several weeks after the first testing session […]" (Oskouei & Herzog, 2005, p. 2091) as used by the authors for a description of the time delay between the test sessions, might not be precise enough to completely answer that question. Confirming the results from Oskouei and Herzog (2005), would give new insights into the distribution of RFE during voluntary contractions. In a first step, as usual the subject should be trained to ensure that the execution of the task is correct. For example, the muscle should not be deactivated at the beginning or during the eccentric phase. During the first test session, electrical stimulation can be used to ensure that the subject's muscle is able to show residual force enhancement in general. In the following, each subject is measured for example 2 times per week for 3 weeks. A predefined number of weeks after the last test session is another test session to ascertain whether possible changes in the characteristics of RFE were temporary or not. Such a designed study could provide novel insights into the question if the non-responders have a lack of certain muscle physiological abilities or an insufficient task specific control.

## 4.2 The use of multi-channel surface EMG in the context of residual force enhancement

Surface EMG (sEMG) analysis using two electrodes has the disadvantage that it can only measure the area between the placed electrodes. According to the SENIAM recommendations, the distance between the electrodes is recommended to be 2 cm (Hermens, Freriks, Disselhorst-Klug, & Rau, 2000). Hence, the rest of the muscle cannot be measured directly but is assumed to behave in the same way as the investigated muscle area. By using multi-channel surface electromyography (multi-sEMG), this problem can be overcome. Multi-sEMG uses multiple electrodes arranged on a grid and hence can give insights into the spatial distribution of electric potential over the skin during muscle contraction (Farina, Leclerc, Arendt-Nielsen, Buttelli, & Madeleine, 2008). Watanabe, Kouzaki and Moritani (2012) showed that during hip flexion and knee extension the central locus activation during knee extension was located at distal site comparing to that in hip flexion. Also during walking inhomogeneities were detected using a multi-channel EMG system (Watanabe, Kouzaki, & Moritani, 2014), inter alia, resulting in greater EMG amplitudes centro-distally in the rectus femoris muscle during the eccentric phase after heel strike. Gallina, Merletti and Vieira (2011) figured out that during a fatiguing task of the gastrocnemius medialis, the area were the fatigue occurred was regionally distributed. Therefore, beside a task dependence concerning the regional activation of a muscle, there is also evidence that fatigue occurs unevenly distributed on a muscle. This is linked to the results from Holtermann, Roeleveld and Karlsson (2005) showing that the spatial distribution of the EMG amplitude is inhomogeneous, underlining the heterogeneity of a muscle's strategy which motor units are recruited during a muscle contraction. Another possibility using multi-sEMG is to calculate the fibre conduction velocity (CV). It can provide insights about the conduction of action potentials along muscle fibres (Arendt-Nielsen & Zwarts, 1989). Piitulainen, Botter, Merletti and Avela (2013) showed in a study on the long and short head of the biceps brachii that the conduction velocity during an eccentric contraction is higher compared to an isometric contraction. Since the twitch torque and the conduction velocity correlates positively ($r = 0.87$) (Andreassen & Arendt-Nielsen, 1987), it seems that during an eccentric contraction more fast twitch fibres are recruited than during an isometric contraction.

Concerning residual force enhancement multi-sEMG can be a useful tool to gain further insights. First, it is not known how or if an active eccentric muscle action affects the

distribution of active motor units across the muscle in the following isometric phase compared to a pure isometric contraction. Hence, multi-sEMG can provide new insights regarding the history-dependence of muscle contraction and on the other side might explain the number of non-responder in voluntary studies especially investigating RFE in the context of activation reduction. Perhaps an active stretch only alters specific parts of a muscle in the following isometric phase compared to a pure isometric contraction. If this adjustment happens outside of the SENIAM recommendations this change would be missed using classic sEMG.

## 4.3 Neuromuscular efficiency - only present in EMG signals?

With this thesis we did not provide evidence that an active stretch results in enhanced neuromuscular efficiency in terms of muscle oxygen consumption. It was concluded that muscle redundancy (Bernstein, 1967) might have played a role. Muscle redundancy in this context means that the central nervous system can accomplish a task by changing the influence of different muscles involved in a specific task without changing the outcome like force or torque. For following studies, it should stay in the focus to exclude the influence of muscle redundancy a priori to assess basic phenomenological relations by using a less complex muscle like the tibialis anterior. For these basic insights, one could also imagine to use electrical stimulation in combination with a near-infrared spectroscopy device (NIRS) to get rid of the responder vs. non-responder phenomenon. The consequence would be an undiluted insight if *in vivo* measured muscles behave the same as isolated muscles fibres regarding enhanced muscle efficiency in the isometric phase after an active stretch compared with a pure isometric contraction (Joumaa & Herzog, 2013).
In general, using near-infrared devices has always some limitations. The estimation of oxygen consumption via near infrared spectroscopy is limited, because it primarily reflects concentration changes in small blood vessels, such as the capillary or arteriolar and venular beds (Mancini et al., 1994). In future, a recently developed method which allows the measurements of blood oxygen saturation in deep tissues could solve some of the problems associated with NIRS (Tzoumas et al., 2016).

## 4.4 Eccentric training and its influence on residual force enhancement

Being a sport scientist involves always the question if training has an influence on specific parameters. In the case of residual force enhancement, the specific parameter

could be the stiffness of titin. According to a discussed (Herzog et al., 2016) theory, titin binds to actin and becomes stiffer when a muscle is actively stretched. Hence, in the following isometric phase the force of titin is enhanced as it has become shorter and stiffer and thus RFE appears, when comparing with a pure isometric contraction (Rode, Siebert, & Blickhan, 2009, Herzog et al., 2016). Bellafiore et al. (2007) found variation of titin expressions after 6 weeks of endurance training. This is in contrast to Mc Guigan et al. (2003) which did not find changes in titin after eight weeks of explosive jump squat training. The same is true for Kyröläinen et al. (2005). After 15 weeks of power training, including explosive muscle actions the mean percentage of titin isoforms remained unchanged. Notwithstanding, "[…] the pattern of titin protein band expression in skeletal muscle between athletes and non-athletes is different" (McBride, Triplett-McBride, Davie, Abernethy, & Newton, 2003, p. 555). Siebert, Kurch, Blickhan and Stuzig (2016) investigated RFE comparing weightlifters with a reference group. The authors highlighted that weightlifters perform many submaximal eccentric contractions during their regular training. Against their hypothesis, the amount of RFE was the same for both groups. Beside this knowledge, a missing link regarding training studies is the fact, that no one ever did a training study in the field of residual force enhancement and none of the aforementioned studies included a real eccentric training. Hence, the question if a multi-week eccentric training intervention influences titin or influences residual force enhancement cannot be answered by now. Aside from new insights into basic phenomenological relations, this study can also provide new insights into the responder vs. non-responder phenomenon. In addition, one have to keep in mind that until today there is no final explanation for the phenomenon residual force enhancement. An eccentric training study in combination with histological measurements, could help to identify muscle structures responsible for residual force enhancement.

## 4.5 Stretch-shortening cycle

Daily activity like walking or running involving a continuous change between eccentric and shortening contractions, the so-called "stretch-shortening cycle" (SSC). Active shortening contraction result in reduced forces in an isometric phase after shortening compared to a pure isometric contraction (Herzog & Leonard, 1997), at the corresponding muscle length and level of activation. Hence, it is a kind of opponent to the investigated residual force enhancement in the context of history dependence of

muscle action. In addition, this force depression (FD) is known to be dependent on the magnitude, speed, force of shortening and is proportional to the amount of work performed (Herzog & Leonard, 1997). In recently published work (Fortuna, Groeber, Seiberl, Power, & Herzog, 2017; Seiberl, Power, Herzog, & Hahn, 2015) the authors could show that residual force enhancement counteracts FD during a SSC and thus contributes to the increased force/work in the shortening phase of SSC. In the past there were three primary mechanisms connected to enhanced force/work of muscles during the shortening phase of SSC: 1) Storage and reutilization of elastic energy. 2) Contribution of stretch reflexes. 3) Time available for force development (van Ingen Schenau, G J, Bobbert, & Haan, 1997). Residual force enhancement as the fourth mechanism highlights the importance of the underestimated muscle feature in the context of human muscle contraction and emphasize the need for an ongoing research within a SSC or pure RFE study design.

# 5 Abbreviations

AR .....activation reduction

CV ..... conduction velocity

FD.....force depression

f-l-r ..... force-length relationship

ITT ..... interpolated twitch technique

multi-sEMG..... multi-channel surface electromyography

MVA..... maximum voluntary activation

MVC.....maximum voluntary contraction

NIRS.....near-infrared spectroscopy device

RFE ..... residual force enhancement

sEMG..... surface electromyography

SSC .....stretch-shortening cycle

TSI.....tissue saturation index

# 6 Figures

# 7 References


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