Review

Advancements in Understanding Spasticity: A Neuromusculoskeletal Modeling Perspective

Mohammad S. Shourijeh *, Argyrios Stampas, Shuo-Hsiu Chang, Radha Korupolu, Gerard E. Francisco

Posted Date: 22 August 2025

doi: 10.20944/preprints202508.1608.v1

Keywords: spasticity; neuromusculoskeletal modeling; reflex hyperexcitability; muscle-tendon mechanics; computational modeling; gait analysis; cerebral palsy; stroke rehabilitation; spinal cord injury

 doi:10.20944/preprints202508.1608.v1

Review

Advancements in Understanding Spasticity: A Neuromusculoskeletal Modeling Perspective

Mohammad S. Shourijeh *, Argyrios Stampas, Shuo-Hsiu Chang, Radha Korupolu and Gerard E. Francisco

Department of Physical Medicine and Rehabilitation, McGovern Medical School at the University of Texas Health Science Center at Houston, Houston, TX, United States

* Correspondence: Mohammad.sharifshourijeh@uth.tmc.edu

Abstract

Spasticity, a complex consequence of upper motor neuron lesions, poses challenges for clinical assessment due to its neural and mechanical origins. Traditional scales like the Modified Ashworth and Tardieu Scales provide subjective, context-limited insights, often missing spasticity's dynamic nature. Neuromusculoskeletal (NMS) modeling offers objective, quantitative insights by integrating patient-specific muscle-tendon properties, reflex dynamics, and multi-joint biomechanics. This scoping review examines advancements in spasticity modeling, comparing mechanical, neurological, and integrated approaches, and their applications in conditions like cerebral palsy and stroke. We highlight barriers to clinical translation, including computational demands and regulatory challenges, and propose future directions, such as real-time simulation and machine learning integration, to enhance personalized assessment and treatment.

Keywords: spasticity; neuromusculoskeletal modeling; reflex hyperexcitability; muscle-tendon mechanics; computational modeling; gait analysis; cerebral palsy; stroke rehabilitation; spinal cord injury

1. Introduction

Spasticity is a complex sensorimotor disorder characterized by involuntary muscle hyperactivity in the presence of central paresis. While historically defined as a velocity-dependent increase in muscle tone due to hyperexcitable stretch reflexes, more recent frameworks broaden this concept to include rigidity, dystonia, spasms, and sensory abnormalities, reflecting the multifaceted nature of motor dysfunction following upper motor neuron injury [1–3]. This involuntary overactivity results not only from altered spinal reflex pathways but also from impaired voluntary motor control, maladaptive plasticity, and sensory disinhibition due to cortical and subcortical damage [1].

Spasticity is prevalent across a spectrum of neurological conditions, affecting approximately 25–40% of stroke survivors, 84–86% of individuals with multiple sclerosis (MS), 48–87% of those with spinal cord injury (SCI), and 69–80% of people with cerebral palsy (CP) [4,5]. A significant proportion develop severe or disabling spasticity, up to 79% in SCI, 47% in MS, and 9–10% post-stroke, resulting in complications such as pain, contractures, joint deformities, pressure ulcers, impaired mobility, falls, and sleep disturbances. These issues contribute to increased healthcare utilization, long-term disability, and reduced quality of life [4–6].

Functionally, spasticity impairs both posture and movement, often limiting independence. In CP, for instance, it can cause crouch gait and restrict ambulation, while in stroke survivors, it frequently affects upper limb function, interfering with activities of daily living such as dressing, grooming, and feeding. Despite its clinical significance and widespread impact, the pathophysiology of spasticity remains only partially understood, posing ongoing challenges for the development of effective and individualized interventions. However, emerging definitions that encompass its full

 doi:10.20944/preprints202508.1608.v1

clinical spectrum and recognize its neuroplastic and sensory components offer a more comprehensive foundation for therapeutic targeting and patient-centered management.

The complexity of spasticity arises from its dual neural and mechanical origins. Neural factors include hyperexcitability of stretch reflex pathways, reduced inhibitory control, and altered proprioceptive feedback, while mechanical factors encompass increased intrinsic muscle stiffness, altered tendon compliance, changes in the extracellular matrix, and joint contractures. These factors interact dynamically, varying across individuals, conditions, and even specific tasks, making standardized assessment and treatment difficult. Traditional clinical tools, such as the Modified Ashworth Score (MAS) and Tardieu Scale, rely on subjective evaluations of muscle tone and reflex responses, often failing to differentiate neural from biomechanical contributions (i.e., distinguishing passive tissue resistance from reflex-mediated active muscle force), and struggling to clearly separate spasticity from related but distinct motor impairments like rigidity or fixed contractures. This subjectivity can compromise treatment planning. For example, suboptimal botulinum toxin dosing or imprecise injection site selection may reduce treatment effectiveness and increase the risk of functional decline. Incorporating objective biomechanical modeling approaches may help address these challenges by providing more detailed insights into the underlying neural and mechanical impairments. When used alongside clinical judgment, such models have the potential to enhance assessment precision and support more informed intervention strategies ([6]).

To overcome these limitations, computational modeling has become a pivotal tool in spasticity research. Early modeling efforts included mechanical models focusing on passive tissue properties, neurological models simulating reflex pathways, and threshold control models quantifying reflex triggers like the Tonic Stretch Reflex Threshold (TSRT) and Dynamic Stretch Reflex Threshold (DSRT). While these approaches provided valuable insights, they often operated in isolation, lacking the integration needed to capture spasticity's complexity during functional tasks like walking or reaching. For instance, mechanical models could not replicate neural-driven phenomena like clonus, while neurological models often ignored biomechanical constraints (e.g., realistic muscle force-generating capacities, moment arms, or segmental inertial properties), reducing their clinical applicability.

The advent of NMS modeling has marked a significant leap forward, enabling integrated simulations of neural control and musculoskeletal dynamics. These models generate physiologically realistic representations of movement, reflex behavior, and resistance to stretch, offering a comprehensive framework to study spasticity. By incorporating patient-specific data, such as muscle geometry, reflex thresholds, and biomechanical properties (e.g., muscle optimal fiber lengths, tendon slack lengths, pennation angles, and segment inertial parameters), NMS models support personalized simulations that enhance clinical relevance. For example, a personalized model for a child with CP might simulate how increased gastrocnemius stiffness and heightened reflex sensitivity contribute to crouch gait, guiding targeted interventions like botulinum toxin injections or selective dorsal rhizotomy.

Computational platforms such as OpenSim (open-source; [7,8]) and the AnyBody Modeling System (commercial; [9]) have laid the groundwork for biomechanical simulation by enabling the estimation of joint kinematics, muscle forces, and movement dynamics across a variety of tasks. Building on these foundations, open-source frameworks like Moco [10] and SCONE [11] have introduced predictive simulation and optimal control capabilities, allowing researchers to simulate how movement might change in response to altered neuromuscular or musculoskeletal conditions. These tools have enhanced the ability to model impaired motor control and optimize interventions virtually. To address the specific complexities of spasticity, more targeted platforms have emerged. The Neuromusculoskeletal Modeling (NMSM) Pipeline, for example, integrates physics-based modeling with patient-specific parameter estimation and predictive simulations to replicate stretch-induced responses with high fidelity. Similarly, the Calibrated EMG-Informed Neuromusculoskeletal Modeling System (CEINMS; [12]) and its real-time extension CEINMS-RT [13] fuse EMG data with biomechanical modeling to enable personalized, real-time assessments of

 doi:10.20944/preprints202508.1608.v1

neuromuscular dynamics. These platforms support the extraction of spasticity-specific metrics such as impedance-based joint stiffness and damping, as well as reflex thresholds like TSRT and DSRT. These quantitative biomarkers exceed the diagnostic granularity of traditional clinical scales, enabling precise assessment and individualized treatment planning. For instance, impedance-based metrics can quantify dynamic joint resistance during gait, informing orthotic design and guiding targeted interventions.

Despite these advancements, clinical adoption remains limited by several barriers: the computational complexity of high-fidelity models, the need for extensive validation across diverse patient populations and clinical contexts, the lack of user-friendly interfaces for clinicians, and regulatory hurdles related to medical device approval and risk classification. These challenges hinder the transition from research to practice, perpetuating reliance on subjective assessment tools and reducing diagnostic and therapeutic precision. For instance, in the absence of clinically accessible modeling tools, clinicians may struggle to anticipate patient-specific treatment responses, such as functional improvements following interventions. Emerging technologies, including machine learning, wearable sensors, and multiscale modeling, offer promising solutions to enhance model scalability, usability, and clinical integration.

This review synthesizes the current state of spasticity modeling, identifies key methodological advancements, and proposes future directions, with a focus on personalized NMS approaches. We aim to differentiate these models from traditional frameworks, highlight their capacity for patient-specific simulation, and explore their potential to advance clinical assessment and treatment. Key enabling technologies, such as hybrid modeling, real-time sensor integration, and artificial intelligence (AI)-driven personalization, are discussed, alongside future directions like regulatory validation and translational applications in rehabilitation robotics. By contextualizing these advancements, we underscore the transformative potential of personalized NMS modeling in improving diagnostic accuracy, therapeutic precision, and patient outcomes across diverse neurological conditions.

Table 1. Modified Ashworth Scale.

Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, minimal resistance at end of range of motion (ROM)
1+	Slight increase in muscle tone, catch followed by minimal resistance through less than half of ROM
2	More marked increase in muscle tone through most of ROM, but affected part easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part rigid in flexion or extension

Table 2. Tardieu Scale: The Tardieu Scale assesses spasticity by evaluating muscle responses to passive movements at varying velocities. V1 (slow) measures passive range of motion without triggering the stretch reflex, V2 (medium, limb falling under gravity) detects mild spastic responses, and V3 (fast) elicits velocity-dependent spasticity. Muscle reaction is graded 0–4, from no resistance (0) to sustained clonus (4), with a "catch" indicating a sudden increase in tone at a specific angle. The angle of catch, measured in degrees via goniometer during V2 or V3, quantifies the spastic threshold. Fatigable clonus (Grade 3, <10s) or non-fatigable clonus (Grade 4, >10s) indicates severe spasticity.

Velocity of Movement	Quality of Muscle Reaction (Grade)	Description	Angle of Catch (R1) / PROM (R2)

 doi:10.20944/preprints202508.1608.v1

V1: Slow (as slow as possible)	N/A (or "No spastic reaction expected")	Baseline measurement of passive range of motion (PROM) under minimal stretch reflex activation.	R2 (Angle of full PROM) is recorded. No R1 (catch) is expected.
V2: Medium (limb falling under gravity)	A grade (0-4) is assigned based on the observed muscle response.	Assesses muscle response to stretch at a moderate speed. A catch (R1) indicates spasticity.	R1 (Angle of catch) is recorded if present.
V3: Fast (as fast as possible)	A grade (0-4) is assigned based on the observed muscle response.	Assesses muscle response to stretch at a fast speed. Elicits velocity-dependent spasticity (catch/clonus).	R1 (Angle of catch or clonus) is recorded if present.

Section 1: Overview of Spasticity Modeling Approaches

1.1. Mechanical, Neurological, and Threshold Control Modeling

Computational modeling of spasticity has historically followed three primary paths: mechanical, neurological, and threshold control models. Each approach targets distinct aspects of spasticity, passive biomechanical properties, reflex-mediated neural responses, and reflex thresholds, respectively, offering valuable insights but facing limitations when applied in isolation, particularly for simulating complex spastic behavior across diverse individuals and functional tasks.

Mechanical models represent muscle-tendon units and joints using simplified elements like springs and dampers to capture stiffness, viscosity, and resistance. Foundational studies by He et al. (1991) [14], Fee and Foulds (2004) [15] , and Alibiglou et al. (2008) [16] employed viscoelastic analogs in pendulum tests, quantifying increased muscle tone and altered damping in spastic limbs. More recent advancements by Wu et al. (2018) [17], Le Cavorzin et al. (2001) [18], and He et al. (1997) [19] incorporated nonlinear tissue behaviors to reflect responses under varied movement velocities and joint angles, enhancing accuracy for passive assessments ([20]), with some models even attempting to characterize the distinct phases of a spastic catch (e.g., pre-catch, catch, and post-catch) to better represent the dynamic joint resistance. These models excel in simulating static or low-velocity conditions, such as joint resistance during clinical exams, but fail to capture neural-driven phenomena like velocity-dependent reflex contractions or clonus. For example, mechanical models cannot replicate the dynamic interplay of reflex hyperexcitability and muscle activation during gait, limiting their utility for functional tasks.

Neurological models focus on the central and peripheral mechanisms underlying reflex responses, modeling stretch reflexes with threshold-based activation and neural gain parameters. Koo and Mak (2006) [21], de Vlugt et al. (2010) [22], and Shin et al. (2020) [23] advanced these models by incorporating muscle spindle feedback and reflex loop delays, improving simulations of velocity-dependent behaviors. These models have elucidated how altered reflex thresholds and delayed inhibitory responses contribute to spastic movement dysfunction, such as exaggerated elbow flexion in stroke survivors. However, their reliance on idealized or population-averaged parameters often overlooks individual variability. Moreover, by neglecting biomechanical context, such as joint mechanics, muscle-tendon compliance, or segmental inertia, neurological models produce abstract simulations that lack biomechanical fidelity for tasks like reaching or stair climbing, limiting their ability to predict how neural changes manifest as altered joint torques or movement patterns.

Threshold control models, developed by Levin and Feldman (1994) [24], Calota et al. (2008) [25] , and Bar-On et al. (2013) [26], emphasize reflex thresholds like TSRT and DSRT, which quantify the joint angle or velocity at which reflex activity is triggered. Applied in stroke and CP ([27–29]), these models provide insights into neural hyperexcitability and have been used to assess spasticity during passive and active movements. For instance, TSRT measurements can identify the elbow angle at

 doi:10.20944/preprints202508.1608.v1

which a reflex is elicited, helping clinicians determine which muscles exhibit heightened reflex sensitivity and should be targeted for botulinum toxin injections to maximize therapeutic effect. Conceptually, these thresholds can define a patient-specific 'spastic joint space,' illustrating the range of motion compromised by hyperreflexia. However, these models require integration with biomechanical data to simulate functional tasks accurately. Without accounting for muscle-tendon dynamics, joint constraints, and the inertial properties of the limb segments, they may not fully capture spastic behavior during complex movements like gait.

Recognizing these limitations, early hybrid models sought to combine mechanical and neural elements. Kamper et al. (2001) [30] integrated stretch reflex thresholds with intrinsic muscle stiffness to simulate reflex-mediated torques during limb motion, demonstrating how increased reflex gain amplifies joint resistance. These models highlighted the value of integration but were low-dimensional and lacked personalization, restricting their application to simple test scenarios, such as single-joint pendulum tests. More advanced hybrids have since emerged, incorporating multi-joint dynamics and patient-specific parameters, but early efforts laid critical groundwork.

The limitations of isolated modeling approaches have significant clinical implications. Mechanical models' inability to simulate neural dynamics can lead to incomplete assessments, missing critical reflex contributions to spasticity. Neurological models' lack of biomechanical grounding may result in unrealistic predictions, reducing their utility for treatment planning. While precise in quantifying reflex triggers, threshold control models require biomechanical integration to inform functional interventions. These gaps can lead to suboptimal diagnoses and one-size-fits-all treatments, such as generic botulinum toxin targeting or orthotic design, ultimately compromising patient outcomes. The shift toward personalized NMS modeling addresses these challenges, offering a comprehensive platform for simulating spastic behavior under realistic movement conditions and supporting precision rehabilitation.

In summary, mechanical, neurological, and threshold control models have provided foundational insights into spasticity but are constrained by their partial perspectives. Mechanical models excel in passive assessments but miss neural dynamics; neurological models capture reflex behavior but lack biomechanical context; threshold control models quantify reflex triggers but need biomechanical integration. The evolution toward integrated, personalized NMS modeling bridges these domains, enabling clinically meaningful simulations that enhance diagnostic accuracy and therapeutic precision across diverse patient populations.

Section 2: Neuromusculoskeletal Modeling in Spasticity

NMS modeling represents a paradigm shift in spasticity research, offering a comprehensive framework to simulate the interactions among neural control, musculoskeletal structure, and biomechanical response in both healthy and pathological states. Unlike isolated mechanical or neurological models, NMS approaches integrate anatomical fidelity, muscle dynamics, and reflex behavior within a unified computational environment, making them ideally suited to address spasticity's multifactorial nature. These models account for the complex interplay of neural hyperexcitability, altered muscle-tendon properties, and joint mechanics, providing a robust platform for studying spasticity across conditions. The recent shift toward personalized NMS simulations, which incorporate patient-specific parameters, has further enhanced their potential to predict individual motor responses and guide clinical decisions [23,31–33]. For example, simulations have been used to identify which muscles contribute most to gait abnormalities in cerebral palsy, demonstrating the potential to influence decisions on targeted botulinum toxin injections or orthotic prescriptions [26,34]. Such applications support more individualized and effective treatment planning.

2.1. Dynamic Neuromuscular Models

Early NMS models laid the groundwork for dynamic neuromuscular simulations, focusing on reflex responses and intrinsic muscle properties during limb motion. He et al. (1997) [19] developed

 doi:10.20944/preprints202508.1608.v1

one of the first models to incorporate reflex thresholds and gain parameters in pendulum test simulations, capturing the abnormal oscillations characteristic of spastic limbs. These early efforts demonstrated the feasibility of combining biomechanics with neural feedback in a closed-loop system, setting the stage for more sophisticated models.

Subsequent advancements by Fee and Foulds (2004) [15] introduced velocity-dependent feedback mechanisms to simulate muscle responses to rapid stretch, a defining feature of spasticity. These models replicated the dynamic behavior of spastic muscles during clinical assessments, such as the sudden "catch" observed in the Tardieu Scale. More recent work by Koo and Mak (2006) [21] and Falisse et al. (2018) [35] expanded this architecture to include proprioceptive inputs from muscle spindles and Golgi tendon organs, enabling simulations of both excitatory and inhibitory influences on muscle activation. These additions improved the realism of simulated behaviors, allowing models to reproduce nuanced spastic responses under varying movement speeds and joint configurations.

Modern dynamic neuromuscular models emphasize personalization, incorporating subject-specific muscle geometry, activation profiles, and reflex characteristics. For example, a personalized model for a stroke survivor might simulate how heightened reflex sensitivity in the biceps affects elbow flexion during reaching tasks, guiding targeted interventions like botulinum toxin injections. By embedding reflex pathways within the context of muscle-tendon mechanics and segmental inertia, these models achieve greater anatomical and physiological fidelity. This integration is critical, as reflex responses depend not only on neural thresholds but also on the instantaneous length and velocity of the muscle-tendon unit, which are influenced by joint kinematics, external forces, and the muscle's own force-length-velocity properties, and potentially its force-generating state, as recent evidence suggests muscle spindle firing can be strongly correlated with muscle force (e.g., [36]).

The clinical relevance of dynamic neuromuscular models lies in their ability to bridge theoretical constructs and practical applications. These models support diagnostics by quantifying reflex hyperexcitability, aid treatment planning by predicting intervention outcomes, and facilitate outcome prediction by simulating functional improvements. For instance, a model might predict how reducing reflex gain through pharmacological intervention affects gait symmetry in CP, informing dosage adjustments. As personalization techniques advance, these models are becoming indispensable tools for personalized rehabilitation, offering tailored insights into spasticity assessment and management across diverse patient populations.

2.2. Physics-Based Simulations

Physics-based simulations have significantly enhanced the fidelity of NMS modeling, enabling accurate representations of muscle and joint behavior under physiological conditions. These models leverage fundamental principles, such as Newton-Euler equations of motion, muscle activation-contraction dynamics, tissue constitutive laws, force balance, torque generation, and material deformation, to simulate spastic responses across a range of joint configurations, movement speeds, and loading conditions. Unlike empirical or heuristic models, physics-based approaches are inherently adaptable, making them ideal for simulating complex functional tasks like walking, reaching, or postural transitions.

Falisse et al. (2020) [23] utilized personalized physics-based models to simulate crouch gait in children with CP, revealing that altered muscle-tendon properties, such as reduced compliance or excessive passive stiffness, often contribute more to functional impairments than spasticity alone. These insights help clinicians differentiate neural and mechanical contributors to abnormal movement, guiding decisions about interventions like tendon lengthening or orthotic support. Van der Krogt et al. (2016) [34] employed subject-specific neuromusculoskeletal simulations of instrumented hamstring stretch tests in children with CP, enabling the separation of neural contributions (spasticity) from mechanical factors (contracture-related stiffness) in torque responses.

A cornerstone of physics-based NMS modeling is the ability to quantify joint impedance, which encompasses stiffness (resistance to displacement) and damping (resistance to velocity). These metrics provide objective measures of spasticity's mechanical impact, surpassing the subjectivity of

 doi:10.20944/preprints202508.1608.v1

clinical scales like MAS. Joint stiffness and damping are calculated using partial derivatives of muscle force in relation to muscle length and velocity, respectively, offering precise insights into mechanical behavior. These are often referred to as "true" stiffness and damping, as they are derived from first principles, isolating mechanical contributions from neural activation. Specifically, 'true' stiffness and damping, obtained from the partial derivatives of muscle force concerning muscle-tendon unit (MTU) length and velocity at a given level of muscle activation, capture the intrinsic mechanical properties and their contribution to joint torque. In contrast, "quasi-stiffness" and "quasi-damping" are empirical approximations derived from joint angle-torque relationships during movement, which may conflate neural and mechanical effects, reducing specificity. For example, quasi-stiffness might overestimate resistance by including reflex-driven torque, while true stiffness focuses solely on passive and active intrinsic muscle-tendon properties at a specific activation state.

Joint Stiffness

Joint stiffness and damping quantify the resistance of spastic muscles to stretch and movement, critical for understanding dynamic impairments. Stiffness reflects resistance to displacement (e.g., muscle lengthening), while damping reflects resistance to velocity (e.g., rapid joint motion). These metrics, derived from muscle-tendon forces and joint kinematics, provide objective measures of spasticity's mechanical impact, surpassing subjective scales like MAS.

$$k_j = -\frac{\partial M_j}{\partial \theta_j} \text{ where } M_j = \sum_{i=1}^{n} r_{ij} F_i^T \qquad (1)$$

Carrying out the partial derivative and employing the chain rule for differentiation leads to

$$k_j = -\sum_{i=1}^{n} \left(\frac{\partial r_{ij}}{\partial \theta_j} F_i^{MT} + r_{ij} k_i^{MT} \frac{\partial \ell_i^{MT}}{\partial \theta_j} \right) \qquad (2)$$

Recalling that $r_{ij} = -\frac{\partial \ell_i^{MT}}{\partial \theta_j}$, Equation (2) simplifies further to

$$k_j = -\sum_{i=1}^{n} \left(\frac{\partial r_{ij}}{\partial \theta_j} F_i^{MT} - r_{ij}^2 k_i^{MT} \right) (3)$$

$$k_i^{MT} = -\frac{\partial F_i^{MT}}{\partial \ell_i^{MT}} (4)$$

On the other hand, assuming a serial elasticity between tendon and muscle,

$$k_i^{MT} = \left(\frac{1}{k_i^M} + \frac{1}{k_i^T} \right)^{-1} (5)$$

$$\text{Where } k_i^M = -\frac{\partial F_i^M}{\partial \ell_i^M} \text{ and } k_i^T = -\frac{\partial F_i^T}{\partial \ell_i^T} (6)$$

if the muscle model is assumed to have noncompliant tendon [37–39], tendon stiffness approaches infinity, and MT stiffness will become equal to the muscle stiffness, $k_i^{MT} = k_i^M$, in which case it can be formed analytically [40]. Assuming a noncompliant tendon (infinite stiffness) simplifies calculations, though in spasticity, tendon compliance may contribute significantly to joint resistance. In the above equations, k_j is stiffness of joint j, M is joint moment, θ is joint angle, r is the moment arm of muscle-tendon (MT) unit i about joint j, F^{MT} is force of the muscle-tendon unit.

Joint Damping

$$c_j = -\frac{\partial M_j}{\partial \dot{\theta}_j} \text{ where } M_j = \sum_{i=1}^{n} r_{ij} F_i^{MT} \qquad (7)$$

 doi:10.20944/preprints202508.1608.v1

$$c_j = -\sum_{i=1}^{n}\left(\frac{\partial r_{ij}}{\partial \dot{\theta}_j}F_i^{MT} + r_{ij}\frac{\partial F_i^{MT}}{\partial \dot{\theta}_j}\right) \quad (8)$$

Note that moment arm r_{ij} does not depend on joint velocity $\dot{\theta}_j$, so $\frac{\partial r_{ij}}{\partial \dot{\theta}_j} = 0$; therefore,

$$c_j = -\sum_{i=1}^{n}\left(r_{ij}\frac{\partial F_i^{MT}}{\partial v_i^{MT}}\frac{\partial v_i^{MT}}{\partial \dot{\theta}_j}\right) \quad (9)$$

where c_j is joint damping, v is MT velocity, $\dot{\theta}$ is joint angular velocity. The term $c_i^{MT} = -\frac{\partial F_i^{MT}}{\partial v_i^{MT}}$, representing the damping of the muscle-tendon unit, can be calculated analytically, similar to the stiffness case, if the tendon is assumed to be noncompliant.

Quasi-Stiffness and Damping

$$k_{j,quasi} = -\frac{dM_j}{d\theta_j} \quad (10)$$

$$c_{j,quasi} = -\frac{dM_j}{d\dot{\theta}_j} \quad (11)$$

These equations enable dynamic estimation of joint impedance across tasks, speeds, and muscle activation states, capturing spasticity's variable presentation. For instance, a model might quantify increased knee stiffness in a CP patient during stair climbing, informing orthotic adjustments. Complementing these mechanical metrics, neural metrics like TSRT and DSRT, introduced earlier as measures of reflex thresholds, quantify the joint angle and velocity at which stretch-induced muscle activation occurs. TSRT represents the tonic threshold for reflex activation during slow stretches, while DSRT captures dynamic thresholds during rapid movements, both critical for understanding spasticity's neural drivers. By integrating TSRT and DSRT with these biomechanically derived impedance metrics, NMS models provide a comprehensive simulation of spasticity, accounting for both intrinsic mechanical changes (e.g., increased passive muscle fiber stiffness, altered tendon properties) and neurophysiological (reflex thresholds) contributors.

2.3. Clinical Applications

Translation of NMS modeling into clinical practice is an emerging area with growing interest and early-stage implementation. Personalized simulations are increasingly supporting assessment, intervention planning, and treatment monitoring, particularly in research settings and pilot clinical applications (e.g., [17,35]). These models offer objective, quantitative measures of spasticity-related impairments, surpassing the limitations of subjective scales like MAS and providing clinicians with actionable insights.

Ang et al. (2018) [17] developed an upper limb model that combined motion capture data with surface electromyography (sEMG) to estimate muscle activation patterns in stroke survivors. By comparing simulated results with clinical spasticity scores, they demonstrated that NMS modeling could produce precise motor dysfunction measures, such as abnormal co-contraction during reaching, that align with but exceed traditional scales' diagnostic resolution. sEMG has proven particularly valuable for validating reflex thresholds like the Tonic Stretch Reflex Threshold (TSRT) and Dynamic Stretch Reflex Threshold (DSRT), which were originally conceptualized by Levin and Feldman (1994) [24] and further developed in later methodological and clinical studies ([25,41,42]). These approaches quantify the joint angle and velocity at which reflex activity is triggered, offering an objective means of assessing neural hyperexcitability beyond traditional scales. For example,

 doi:10.20944/preprints202508.1608.v1

sEMG can detect the onset of reflex activity in the quadriceps during a knee extension test, guiding targeted interventions.

Other laboratory measurements enhance the objectivity of NMS models. Kinematic data from inertial measurement units (IMUs) and electrogoniometers capture joint motion in real time, while torque measurements from dynamometers quantify resistance during both passive and active movements ([28]). Advanced imaging techniques, such as magnetic resonance imaging (MRI) and ultrasound elastography, provide detailed insights into muscle stiffness, cross-sectional area, and tissue composition. For example, Barber et al. (2011) [43] combined ultrasound and dynamometer assessments to show that young adults with spastic cerebral palsy exhibit significantly increased ankle joint stiffness, reduced gastrocnemius fascicle strain, and smaller muscle cross-sectional area compared to typically developing individuals. Similarly, Lacourpaille et al. (2014) [44] demonstrated the potential of ultrasound shear-wave elastography to quantify in vivo muscle stiffness, establishing its clinical applicability for neuromuscular disorders and providing a methodological foundation for its later use in conditions such as cerebral palsy. These objective data sources reduce reliance on subjective clinical scales, enhance diagnostic accuracy, and support more personalized and effective treatment planning.

NMS simulations also play a critical role in predicting intervention outcomes. Personalized models have been used to evaluate the effects of orthopedic surgeries (e.g., tendon lengthening or transfers) ([23]), pharmacological treatments (e.g., botulinum toxin injections) ([45]), and rehabilitative strategies (e.g., robotic-assisted therapy) ([46,47]). For example, a model might predict how reducing spasticity in the hamstrings affects knee extension during gait, informing decisions about whether to pursue surgical options or alternative interventions. Indeed, quantitative metrics derived from such models, like estimated changes in muscle viscosity or reflex thresholds (DSRT), have been used to objectively track the efficacy of treatments like botulinum toxin, sometimes revealing improvements not captured by subjective clinical scales ([16,27]). These simulations help clinicians identify interventions likely to yield functional gains while avoiding those that may exacerbate impairments due to individual biomechanical constraints, such as excessive passive stiffness.

Spasticity manifests differently across neurological conditions, and neuromuscular simulation models can capture these condition-specific profiles [34,48]. In stroke, increased stiffness can be accompanied by reduced damping, leading to joint instability and exaggerated oscillations during movement [49–51]. In contrast, cerebral palsy (CP) may involve abnormal co-contraction patterns and excessive reflex gain, resulting in stiff, uncoordinated movements [52,53]. By modeling these profiles accurately, clinicians can design targeted therapies that address the underlying causes of motor dysfunction [23]. For instance, a model for a CP patient might recommend selective dorsal rhizotomy to reduce reflex hyperexcitability [54], while a stroke model might prioritize botulinum toxin to address reflex-mediated activity and intrinsic stiffness [55].

Wearable technologies and real-time feedback systems are further expanding the clinical applications of NMS modeling. Closed-loop therapy environments integrate models with sensor data (e.g., sEMG, kinematics, forces) to track spastic muscle behavior and provide clinicians or robotic devices with actionable feedback. For example, a wearable system might update a model in real time during a gait training session, adjusting robotic assistance to optimize muscle activation patterns using frameworks such as CEINMS-RT [13]. While still largely in the research phase, this level of personalization shows promise for accelerating rehabilitation, reducing clinician workload, and enhancing patient engagement by providing immediate, task-specific feedback.

Emerging joint impedance formulations, derived from personalized simulations, offer clinicians a new class of quantitative biomarkers. These metrics, dynamic stiffness and damping estimates, supplement qualitative assessments like MAS, providing continuous, task-relevant measures of spasticity that reflect both neural and mechanical contributions. For instance, impedance metrics can quantify how spasticity affects elbow flexion during a reaching task, guiding the design of assistive devices or therapy protocols. By embedding these formulations within NMS frameworks, clinicians

 doi:10.20944/preprints202508.1608.v1

gain access to high-resolution, interpretable metrics that support real-time decision-making and long-term treatment planning, ultimately improving patient outcomes.

Section 3: Comparing and Evaluating Models

As spasticity models grow in complexity and diversity, a rigorous framework for comparison and evaluation is essential to assess their utility and guide future development. Models range from simple mechanical analogs to sophisticated, personalized NMS simulations, each judged by their fidelity to real-world phenomena, predictive accuracy, clinical usability, and scalability across populations. This section reviews the primary criteria for evaluating spasticity models, explores how NMS models address these benchmarks, and discusses the implications of current limitations for patient care. A summary comparison table (Table 3) is provided to highlight key characteristics, strengths, and limitations of each modeling approach.

Table 3. Summary Comparison of Spasticity Modeling Approaches.

Model Type	Key Features	Strengths	Limitations	Clinical Applicability	Example Applications
Mechanical	Spring-damper analogs, passive tissue modeling	Simple to implement; effective for capturing passive stiffness	Does not model neural dynamics; limited to low-velocity tasks	Passive assessments, e.g., pendulum tests	Pendulum tests for elbow stiffness
Neurological	Reflex pathways, neural gain, feedback delays	Simulates neural contributions; useful for studying reflexes	Lacks biomechanical realism; often population-averaged parameters	Understanding reflex hyperexcitability	Identifying reflex triggers in stroke
Threshold Control	TSRT/DSRT reflex thresholds based on joint angle/velocity	Quantifies reflex triggers; applicable during passive movements	Requires biomechanical integration for task-level simulation	Botulinum toxin targeting; spasticity quantification	Optimizing injection sites in CP
Hybrid	Combines neural and mechanical elements	Simulates reflex-mechanical interactions	Often low-dimensional; not fully personalized	Simulated resistance during clinical tasks	Modeling elbow catch in stroke
Personalized NMS	Patient-specific anatomy, EMG, multiscale modeling	High anatomical fidelity; predicts functional outcomes	Computationally intensive; requires technical expertise	Diagnosis, treatment planning, outcome prediction	Gait optimization in CP

3.1. Metrics for Evaluation

The primary goal of spasticity models is to accurately replicate clinical and experimental observations, encompassing passive stretch responses, joint stiffness profiles, and complex dynamic behaviors like gait deviations, co-contractions, and clonus. A key benchmark is the correlation between model outputs and experimental data, particularly EMG activity, joint torques, and kinematic trajectories. Falisse et al. (2018, 2020) [23,35] demonstrated strong concordance between simulated and observed EMG patterns in CP patients during passive limb movement and gait, highlighting the importance of neural feedback mechanisms in achieving realistic activation timing.

 doi:10.20944/preprints202508.1608.v1

Similarly, torque measurements from dynamometers and kinematic data from IMUs validate model accuracy, ensuring simulations reflect real-world spastic responses across tasks like walking or reaching.

Given the significant inter-individual variability in spasticity presentation, parameter sensitivity and robustness are crucial for clinical applicability. Factors such as lesion location, severity, age, muscle tone, and activity levels influence spastic behavior, requiring models to handle variations in reflex gain, passive muscle stiffness, tendon slack length, and activation thresholds. Sensitivity analyses, such as those by Kamper et al. (2001) [30], reveal how small changes in input parameters can significantly affect model outputs, underscoring the need for accurate, individualized calibration. For example, a model for a pediatric CP patient must account for developmental changes in muscle architecture, while a stroke model must reflect age-related declines in neural control.

Scalability and generalizability pose additional challenges, particularly for early models focusing on single joints or limbs. Modern NMS models have progressed in scaling up to simulate full-body movement across diverse tasks, such as sit-to-stand transitions or stair climbing. However, generalizability depends on diverse anatomical datasets and normative biomechanical parameters. Population-specific differences, in muscle architecture (e.g., fiber lengths, pennation angles, physiological cross-sectional areas), spasticity patterns, or neural compensation strategies, must be accounted for to ensure clinical utility across pediatric and adult cohorts, and different neurological diagnoses. Personalized NMS models, built around patient-specific data from motion capture, EMG, and MRI, offer a promising solution, providing faithful representations of individual spastic behavior and intervention responses.

3.2. Integration of Neural and Biomechanical Components

The most effective spasticity models integrate neural dynamics and biomechanical properties into a cohesive framework, reflecting the physiological reality of spastic movement. On the neural side, features like TSRT, DSRT, feedback delays, and excitatory/inhibitory balance are essential for simulating velocity-dependent behaviors. For instance, Falisse et al. (2018) [35] showed that incorporating proprioceptive feedback improves the reproduction of clinically observed EMG activation patterns, particularly for exaggerated stretch reflexes and clonus in spastic muscles. These neural elements capture the dynamic interplay of reflex pathways and motor control, which is critical for understanding spasticity's neural origins.

An accurate representation of muscle-tendon stiffness (both active and passive components), joint damping, and passive resistance is equally important biomechanically. Advances in personalized simulation enable subject-specific estimation of these properties, moving beyond generic approximations to clinically meaningful biomarkers. Impedance modeling, which defines joint stiffness and damping as context-sensitive, time-varying quantities, has emerged as a powerful method for quantifying spastic behavior during dynamic tasks. Unlike traditional quasi-stiffness metrics, NMS-based formulations isolate mechanical contributions from neural activation, providing interpretable measures of intrinsic muscle and joint properties.

Reflex threshold metrics, such as TSRT and DSRT complement these biomechanical measures, offering a neural perspective on spasticity. Derived from EMG and kinematic data during passive movement, these thresholds quantify the onset of reflex activity, providing insights into altered neural control strategies. When integrated into NMS models, they enhance simulation fidelity, enabling accurate predictions of how spasticity interacts with joint position, speed, and mechanical loading. For instance, a model incorporating TSRT might simulate how reflex hyperexcitability affects ankle dorsiflexion in a person with CP, guiding surgical or pharmacological interventions.

Integrating neural and biomechanical components in personalized NMS models represents a significant advancement, enabling high-fidelity simulations that reflect the full spectrum of physiological processes underlying spasticity. These models support a multidimensional understanding of spastic behavior, facilitating precise diagnosis and tailored treatment planning across diverse clinical scenarios.

 doi:10.20944/preprints202508.1608.v1

3.3. Limitations and Validation Challenges

Despite their promise, spasticity models face several limitations that constrain their widespread adoption, particularly in clinical settings. These shortcomings directly impact patient care, diagnosis, and treatment, perpetuating reliance on subjective assessments and limiting therapeutic efficacy.

Computational complexity is a major barrier to real-time applications. High-fidelity NMS models, incorporating multiscale muscle properties (e.g., Hill-type models with detailed force-length-velocity characteristics, or even fiber-level models), neural dynamics, and finite element representations, are resource-intensive, requiring significant computational power and time. This computational demand limits their use in fast-paced clinical environments, where timely decision-making is critical. In the absence of accessible real-time tools, clinicians must often rely on coarse, subjective measures like the MAS, which may not accurately differentiate between neural and mechanical contributors to spasticity. For example, two patients may receive similar MAS scores despite having different underlying impairments, such as reflex hyperexcitability in one and increased passive stiffness in the other, leading to mismatched interventions, such as suboptimal botulinum toxin targeting. Surrogate modeling and model-order reduction techniques are being explored to approximate key model outputs more efficiently, but further refinement and validation are necessary before these approaches can support real-time clinical decision-making.

Limited sample diversity in validation studies restricts model generalizability. Many simulations are based on small, homogeneous datasets from single clinical centers or specific subpopulations, limiting applicability across broader demographics. This lack of diversity can result in models that fail to account for variations in spasticity presentation or underlying biomechanical differences due to age, sex, or pathology, potentially leading to inaccurate characterization of impairments or suboptimal treatment choices for underrepresented groups, such as pediatric patients or those with atypical etiologies like SCI. Multicenter collaborations and open-access repositories are essential to expand validation efforts, ensuring robust and inclusive models across age, sex, and condition.

The usability gap between research-grade models and clinical practice is another significant hurdle. While NMS modeling platforms are becoming more sophisticated, they often require technical expertise in coding, musculoskeletal anatomy, and numerical optimization, making them inaccessible to most clinicians. This gap prevents the adoption of objective, quantitative measures, limiting the accuracy and consistency of clinical assessments and treatment decisions. For instance, without user-friendly tools, clinicians cannot leverage NMS models to predict surgical outcomes or tailor botulinum toxin injections, potentially exacerbating motor impairments. Developing intuitive interfaces, automated data integration pipelines, and seamless sensor integration is critical to bridging this gap and enhancing clinical utility.

Regulatory and standardization issues further complicate clinical adoption. For computational models to be accepted as medical decision-support tools, they must undergo rigorous validation against gold-standard clinical measures and comply with regulatory guidelines. The lack of standardized benchmarks hinders model comparison and clinical trust, delaying integration into practice. This regulatory gap perpetuates reliance on subjective scales, reducing treatment effectiveness. For example, without standardized evaluation criteria, models cannot reliably predict functional outcomes, limiting their use in treatment planning. Establishing benchmarks, such as agreement with MAS or Tardieu scores, task-specific functional outcomes, and sensitivity to therapeutic change, is essential for regulatory approval and clinical acceptance.

These limitations collectively impact patient care by hindering the adoption of objective, simulation-informed tools. Subjective assessments like MAS fail to distinguish between neural and biomechanical factors, leading to suboptimal treatment decisions, such as inappropriate surgical timing or orthotic misdesign, which can reduce therapeutic effectiveness and quality of life. Similarly, gaps in computational efficiency, validation diversity, usability, and standardization hinder precise diagnosis and targeted treatment, delaying recovery and exacerbating motor impairments. Addressing these challenges requires interdisciplinary collaboration, technological innovation, and

 doi:10.20944/preprints202508.1608.v1

large-scale validation efforts to translate NMS models into essential components of modern spasticity care.

Section 4: Gaps and Future Directions

Despite advancements, several critical gaps in spasticity modeling remain and must be addressed to fully realize its clinical and research potential. Personalized NMS modeling has made meaningful progress in simulating spasticity and supporting early-stage clinical assessments. However, its broader adoption as a routine clinical tool will require further improvements in model fidelity, data acquisition workflows, computational efficiency, interdisciplinary collaboration, and regulatory validation. This section identifies the most pressing limitations, examines their implications for diagnosis and treatment, and proposes a roadmap to advance the field toward broader clinical impact.

4.1. Personalized Modeling

Personalized NMS modeling represents a transformative approach that tailors simulations to individual neuromechanical characteristics, thereby improving assessment accuracy and intervention outcomes. A key priority is integrating advanced imaging data, such as MRI, diffusion tensor imaging (DTI), and ultrasound elastography, to inform anatomical and physiological parameters. These techniques provide high-resolution insights into muscle architecture (e.g., volumes, optimal fiber lengths, pennation angles), tissue composition (e.g., fat infiltration, fibrosis), passive mechanical properties (stiffness from elastography), and neural tract integrity, enabling precise calibration of variables like muscle-tendon length, cross-sectional area, and stiffness. For example, DTI can map neural connectivity in stroke patients, refining models of reflex hyperexcitability, while ultrasound elastography quantifies muscle stiffness in CP, validating impedance parameters and informing passive force components of muscle models.

Real-time integration of wearable sensor data is another critical area. Wearable technologies that capture sEMG, joint kinematics, and ground reaction forces enable dynamic model updates that support adaptive rehabilitation strategies. For instance, a wearable system might track sEMG signals during gait training, updating a model to optimize robotic assistance in real time. Machine learning algorithms can enhance this process by identifying trends in sensor data, predicting spasticity flare-ups, or suggesting therapy adjustments. These capabilities are essential for continuous monitoring and personalized intervention. However, gaps in sensor integration and data processing risk incomplete personalization, leading to suboptimal outcomes, such as ineffective orthotic adjustments or pharmacological dosing.

Reflex threshold-based modeling, such as TSRT and DSRT, further enriches personalization by quantifying patient-specific reflex dynamics. These thresholds, derived from EMG and kinematic data, define the onset of stretch reflexes on a per-muscle basis, enabling simulations that reflect individual neural profiles. Embedding these thresholds within NMS models enhances fidelity, supporting multidimensional spasticity assessments. Investigating these thresholds during both passive and active movements can reveal crucial differences, as volitional effort can modulate reflex sensitivity and the functional range of motion. For example, a model incorporating DSRT might simulate how reflex hyperexcitability affects wrist extension in a stroke patient, guiding targeted botulinum toxin injections. Furthermore, model refinements could also explicitly account for the influence of the initial stretch level or joint position at the onset of movement, as this has been shown to modulate spastic reflex responses but is not always incorporated into current models. Addressing gaps in imaging, sensor integration, and comprehensive reflex characterization is crucial to ensure accurate diagnosis and tailored treatments, maximizing therapeutic effectiveness.

 doi:10.20944/preprints202508.1608.v1

4.2. Bridging Research and Clinical Practice

The usability gap between research-grade NMS models and clinical practice limits their impact on patient care. These models have the potential to revolutionize spasticity management by improving diagnostic accuracy, predicting intervention outcomes, and tracking therapeutic progress. For instance, NMS models can differentiate neural and biomechanical contributions to spasticity, enabling precise diagnoses that prevent the misclassification of contractures (a primarily mechanical limitation) as spasticity (a neural-driven phenomenon with mechanical consequences). They can also predict the outcomes of interventions like tendon lengthening or botulinum toxin injections, ensuring treatments are tailored to individual needs. Additionally, quantitative metrics from models can objectively monitor changes in spasticity severity, guiding therapy adjustments and enhancing long-term outcomes.

However, current shortcomings, reliance on subjective scales like MAS, computational complexity, and limited clinical usability, hinder these benefits. Without objective tools, clinicians may struggle to distinguish reflex-driven hyperactivity from passive stiffness, risking inappropriate treatments such as mistargeted botulinum toxin injections or ineffective orthotic prescriptions. These errors can exacerbate motor impairments, delay recovery, and diminish quality of life. Similarly, complex models requiring technical expertise limit clinicians' ability to utilize objective tools, perpetuating reliance on less precise methods.

To enhance the clinical utility of NMS models, it is critical to balance their technical complexity with accessibility for clinicians who may lack expertise in computational modeling or biomechanics. The current technical focus of NMS models, while essential for researchers, risks alienating clinicians, limiting adoption in routine practice. Incorporating clinical examples and case studies can illustrate how models translate to actionable insights, making their value tangible. For instance, a personalized NMS model for a 10-year-old with cerebral palsy (CP) might reveal that heightened gastrocnemius reflex sensitivity contributes to crouch gait. By simulating the effects of botulinum toxin injections, the model could predict optimal injection sites and dosages, reducing knee flexion by 15° and improving gait symmetry, outcomes not discernible from subjective scales like the Modified Ashworth Scale (MAS) alone. Such vignettes demonstrate how NMS models can guide precise interventions, enhancing clinician confidence in their application.

Addressing computational complexity and usability also requires practical solutions, such as developing user-friendly platforms or prototypes tailored to clinical workflows. Existing tools, like simplified interfaces in OpenSim or prototype dashboards for the CEINMS-RT framework, offer promising starting points. These platforms could integrate automated data processing (e.g., EMG, motion capture) and provide intuitive visualizations, such as predicted joint torque profiles or reflex threshold maps, to support real-time decision-making. For example, a clinician-facing dashboard might display simulated outcomes of botulinum toxin injections, highlighting target muscles and expected functional gains, while also suggesting complementary therapy strategies to maximize effectiveness. By prioritizing intuitive design and automated workflows, these tools can reduce the technical barrier, enabling clinicians to leverage NMS models for precise diagnosis, intervention planning, and treatment monitoring.

Simplified computational frameworks are needed to retain predictive power while reducing computational demands. Surrogate modeling offers a viable solution, where reduced-order models are trained on outputs from complex simulations. These models approximate key biomechanical and neural parameters with lower computational requirements, making them suitable for integrating wearable devices or low-latency clinical systems. Machine learning techniques, such as supervised regression and neural networks, can further enhance surrogate models by refining predictions based on real-time sensor data, enabling adaptive treatment adjustments.

User interface design is equally critical. Current modeling tools require expertise in coding and biomechanics, which limits their use in routine clinical care. Developing intuitive, clinician-facing applications, with simplified data entry, automated integration of patient-specific data (e.g., EMG, motion capture, imaging), interactive visualization dashboards, and decision-support modules, will

 doi:10.20944/preprints202508.1608.v1

lower adoption barriers. For example, a dashboard might display simulated outcomes of botulinum toxin injections, helping clinicians not only select optimal muscles for injection but also personalize accompanying therapy strategies. Since the effectiveness of botulinum toxin depends heavily on the frequency, timing, and type of rehabilitation that follows [56–62], future extensions of NMS modeling could support more integrated planning by incorporating therapy parameters alongside pharmacological interventions. Interdisciplinary collaboration among engineers, clinicians, neuroscientists, and data scientists is essential to define use cases, establish performance benchmarks, and co-develop tools that meet clinical needs to ensure usability and sustainability in real-world workflows.

4.3. Emerging Technologies

Emerging technologies are poised to reshape spasticity modeling, enhancing accuracy, responsiveness, and scalability of personalized NMS approaches. Machine learning and AI offer powerful tools for personalization and automation. Supervised learning models can estimate parameters from sparse datasets, while reinforcement learning can optimize intervention strategies in silico before clinical application. For example, a predictive model trained on longitudinal patient data might anticipate spasticity changes, enabling proactive therapy adjustments to prevent functional decline.

Multiscale modeling represents another frontier, bridging microscopic processes (e.g., sarcomere dynamics, cross-bridge cycling, neural firing patterns) and macroscopic outcomes (e.g., joint movement, gait). These models capture interactions across biological scales, providing insights into how cellular abnormalities propagate to affect motor function. For instance, a multiscale model might simulate how altered neural firing in CP contributes to muscle co-contraction, informing targeted pharmacological therapies. While computationally complex, multiscale approaches enhance the biological realism of NMS models, supporting precision medicine.

Augmented Reality (AR) and Virtual Reality (VR) technologies complement NMS modeling by delivering immersive, context-specific motor tasks. Combined with personalized models, AR/VR environments can simulate patient-specific movement challenges, offering therapists real-time insights into motor deficits and adaptive strategies. For example, a VR system might simulate a CP patient's gait, allowing therapists to test orthotic adjustments virtually. These technologies are particularly valuable in pediatric and post-stroke rehabilitation, where engagement and task realism are critical to therapy success.

4.4. Validation and Standardization Efforts

Validation and standardization are critical for clinical adoption, ensuring models are robust, reliable, and trusted by clinicians and regulators. Limited validation diversity raises the risk of inaccurate characterizations and poorly tailored interventions for underrepresented groups, such as pediatric patients or those with SCI. Large-scale validation studies, testing NMS models across diverse populations with varying etiologies, functional levels, and demographics, are essential. Open-access datasets and multicenter collaborations will facilitate the sample sizes and heterogeneity needed for robust validation.

Standardized benchmarks must be established to evaluate model performance, including agreement with clinical scales (e.g., MAS, Tardieu), task-specific functional outcomes (e.g., changes in gait speed, joint range of motion, or work done at a joint), responsiveness to intervention, and computational efficiency. Standardized movement tasks, such as instrumented gait, reaching, or sit-to-stand trials, can enable cross-study comparisons and inform best practices. For example, a benchmark might require models to predict changes in gait symmetry post-intervention, ensuring clinical relevance.

Regulatory compliance is equally crucial as computational models progress toward classification as medical devices or decision-support systems. Adherence to Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidelines mandates transparent

 doi:10.20944/preprints202508.1608.v1

reporting of model assumptions, parameter ranges, validation procedures, and limitations. The lack of regulatory validation impedes the integration of objective tools, obstructing accurate diagnosis and targeted treatment. Coordinated efforts among developers, clinicians, and regulators are essential to expedite the pathway from simulation to clinical impact, ensuring models promote equitable care across diverse populations.

4.5. Key Clinical Takeaways

Neuromusculoskeletal modeling offers transformative potential for spasticity management by providing objective, quantitative tools to enhance diagnostic accuracy, optimize interventions, and improve patient outcomes. Below are key takeaways for clinicians:

Enhanced Diagnostic Precision: NMS models integrate patient-specific data (e.g., EMG, kinematics, imaging) to differentiate neural (e.g., reflex hyperexcitability) from biomechanical (e.g., passive muscle stiffness) contributions to spasticity. This enables precise identification of impairment mechanisms, reducing misdiagnoses, such as mistaking contractures for spasticity, compared to subjective scales like the Modified Ashworth Scale (MAS).

Personalized Intervention Planning: Simulations predict individual responses to treatments such as orthotic adjustments, botulinum toxin injections, or orthopedic surgeries. For example, a model might identify optimal adjustments in gastrocnemius muscle–tendon properties to reduce crouch gait in cerebral palsy (CP), leading to a more upright posture and measurable improvements in knee extension, thereby guiding targeted therapy and minimizing ineffective interventions [23].

Objective Outcome Monitoring: Quantitative biomarkers, such as joint impedance (stiffness and damping) or reflex thresholds (TSRT, DSRT), enable continuous, task-specific assessment of spasticity severity and treatment efficacy. These metrics surpass the granularity of traditional scales, supporting data-driven adjustments to pharmacological or rehabilitative strategies.

Reduced Healthcare Burden: By optimizing interventions and preventing mistargeted treatments, NMS modeling can reduce complications (e.g., contractures, falls), lower healthcare utilization, and enhance patient quality of life through improved mobility and independence.

Future Accessibility: Emerging clinician-friendly platforms, integrating automated data processing and intuitive dashboards, promise to make NMS modeling accessible in routine practice. These tools will provide real-time insights, such as predicted functional gains from interventions, empowering clinicians to make informed decisions without requiring computational expertise.

By adopting NMS modeling, clinicians can transition from subjective assessments to simulation-informed, patient-centered care, ultimately improving therapeutic precision and outcomes across conditions like CP, stroke, and spinal cord injury.

Conclusions

Spasticity modeling has undergone a remarkable evolution, progressing from simplified representations of passive resistance to sophisticated, integrative NMS frameworks that simulate the dynamic interplay of neural control, muscle-tendon mechanics, and joint behavior. Personalized NMS models represent a pinnacle of this evolution, capturing the multifactorial nature of spasticity and supporting a paradigm shift toward objective, simulation-informed clinical decision-making. These models enable detailed investigations into reflex thresholds, muscle stiffness, joint damping, and proprioceptive feedback, facilitating precise diagnoses and tailored interventions across conditions like CP, brain injury, stroke, and SCI.

The potential of personalized NMS modeling is vast, offering predictive simulations that guide intervention outcomes, such as orthotic adjustments, botulinum toxin injections, or tendon surgeries. Integrated with real-time data from wearable sensors and imaging systems, these models support adaptive rehabilitation strategies that respond dynamically to changes in a patient's condition, enhancing therapeutic effectiveness. By providing quantitative biomarkers, such as impedance-based stiffness and damping or estimates of individual muscle contributions to pathological movement,

 doi:10.20944/preprints202508.1608.v1

NMS models surpass the limitations of subjective scales like MAS, offering clinicians high-resolution, task-specific metrics for real-time decision-making and long-term planning.

Despite these advances, significant challenges remain. High computational demands continue to hinder real-time use, delaying the development of scalable diagnostic tools. Inadequate validation across diverse populations limits generalizability, increasing the risk of overlooking condition-specific or demographic nuances. The disconnect between research-grade tools and clinical workflows slows adoption, while the absence of standardized benchmarks and regulatory validation impedes formal integration. As a result, clinicians remain dependent on coarse, subjective assessments, which can obscure root impairments, delay effective intervention, and ultimately diminish patient quality of life.

The future of spasticity modeling lies in scalable, clinically accessible, and biologically grounded frameworks. Emerging technologies, machine learning, multiscale modeling, and AR/VR environments, promise to expand model reach while reducing barriers to adoption. Open-source tools, shared datasets, and standardized benchmarks will foster trust among clinicians and regulators, ensuring models are robust and inclusive. Interdisciplinary collaboration among engineers, clinicians, neuroscientists, and data scientists is essential to translate these advancements into practice, ensuring tools meet clinical needs and regulatory standards.

In summary, personalized NMS modeling has the potential to fundamentally reshape spasticity management by uniting biomechanics, neuroscience, and computational modeling to deliver precise, patient-centered care. By addressing current gaps and leveraging emerging technologies, the field can advance toward a future where objective, simulation-informed tools are standard in clinical practice, thereby improving diagnostic accuracy, therapeutic precision, and quality of life for individuals with spastic motor impairments. Continued INNOVATION, collaboration, and commitment to inclusivity will be critical to realizing this transformative vision.

Author Contributions: Conceptualization, MS; methodology, MS; formal analysis, MS; investigation, MS; writing original draft preparation, MS; writing review and editing, MS, AS, SC, RK, and GF; visualization, MS; project administration, MS. AS, RK, and GF edited the manuscript, added references, and contributed ideas that shaped the perspective of the review. SC edited the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

NMS	**Neuromusculoskeletal**
MAS	Modified Ashworth Scale
TSRT	Tonic Stretch Reflex Threshold
DSRT	Dynamic Stretch Reflex Threshold
EMG	Electromyography
IMU	Inertial Measurement Unit
MRI	Magnetic Resonance Imaging
DTI	Diffusion Tensor Imaging
AI	Artificial Intelligence
AR	Augmented Reality
VR	Virtual Reality
CP	Cerebral Palsy
SCI	Spinal Cord Injury
MS	Multiple Sclerosis

 doi:10.20944/preprints202508.1608.v1

References

1. S. Li, G. E. Francisco, and W. Z. Rymer, "A new definition of poststroke spasticity and the interference of spasticity with motor recovery from acute to chronic stages," *Neurorehabil. Neural Repair*, vol. 35, no. 7, pp. 601–610, 2021.
2. A. Stampas et al., "Evidence of treating spasticity before it develops: a systematic review of spasticity outcomes in acute spinal cord injury interventional trials," *Ther. Adv. Neurol. Disord.*, vol. 15, p. 17562864211070656, 2022.
3. D. Dressler et al., "Consensus guidelines for botulinum toxin therapy: general algorithms and dosing tables for dystonia and spasticity," *J. Neural Transm.*, vol. 128, no. 3, pp. 321–335, 2021.
4. J. Wissel, L. D. Schelosky, J. Scott, W. Christe, J. H. Faiss, and J. Mueller, "Early development of spasticity following stroke: a prospective, observational trial," *J. Neurol.*, vol. 257, no. 7, pp. 1067–1072, 2010.
5. M. A. Rizzo, O. C. Hadjimichael, J. Preiningerova, and T. L. Vollmer, "Prevalence and treatment of spasticity reported by multiple sclerosis patients," *Mult. Scler. J.*, vol. 10, no. 5, pp. 589–595, 2004.
6. M. M. Adams and A. L. Hicks, "Spasticity after spinal cord injury," *Spinal Cord*, vol. 43, no. 10, pp. 577–586, 2005.
7. S. L. Delp et al., "OpenSim: open-source software to create and analyze dynamic simulations of movement.," *IEEE Trans. Biomed. Eng.*, vol. 54, no. 11, pp. 1940–1950, Nov. 2007.
8. A. Seth et al., "OpenSim: Simulating musculoskeletal dynamics and neuromuscular control to study human and animal movement," *PLoS Comput. Biol.*, vol. 14, no. 7, p. e1006223, Jul. 2018.
9. M. Damsgaard Rasmussen, J., Christensen, S. T., Surma, E., & de Zee, M., "Analysis of musculoskeletal systems in the AnyBody Modeling System," *Simul. Model. Pract. Theory*, vol. 14, no. 8, pp. 1100–1111, 2006.
10. C. L. Dembia, N. A. Bianco, A. Falisse, J. L. Hicks, and S. L. Delp, "Opensim moco: Musculoskeletal optimal control," *PLOS Comput. Biol.*, vol. 16, no. 12, p. e1008493, 2020.
11. T. Geijtenbeek, "Scone: Open source software for predictive simulation of biological motion," *J. Open Source Softw.*, vol. 4, no. 38, p. 1421, 2019.
12. C. Pizzolato et al., "CEINMS: A toolbox to investigate the influence of different neural control solutions on the prediction of muscle excitation and joint moments during dynamic motor tasks," *J. Biomech.*, vol. 48, no. 14, pp. 3929–3936, 2015.
13. M. Sartori et al., "Ceinms-rt: An open-source framework for the continuous neuro-mechanical model-based control of wearable robots," 2025.
14. J. He, W. S. Levine, G. E. Loeb, B. J. He, W. S. Levine, and G. E. Loeb, "Feedback gains for correcting small perturbations to standing posture," *IEEE Trans. Automat. Contr.*, vol. 36, no. 3, pp. 322–332, 1991.
15. J. W. Fee and R. A. Foulds, "Neuromuscular modeling of spasticity in cerebral palsy," *IEEE Trans. neural Syst. Rehabil. Eng.*, vol. 12, no. 1, pp. 55–64, 2004.
16. L. Alibiglou, W. Z. Rymer, R. L. Harvey, and M. M. Mirbagheri, "The relation between Ashworth scores and neuromechanical measurements of spasticity following stroke," *J. Neuroeng. Rehabil.*, vol. 5, pp. 1–14, 2008.
17. W. S. Ang, H. Geyer, I.-M. Chen, and W. T. Ang, "Objective assessment of spasticity with a method based on a human upper limb model," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 26, no. 7, pp. 1414–1423, 2018.
18. P. Le Cavorzin et al., "A computed model of the pendulum test of the leg for routine assessment of spasticity in man," *Itbm-Rbm*, vol. 22, no. 3, pp. 170–177, 2001.
19. J. He, W. R. Norling, and Y. Wang, "A dynamic neuromuscular model for describing the pendulum test of spasticity," *IEEE Trans. Biomed. Eng.*, vol. 44, no. 3, pp. 175–184, 1997.
20. Y. Cha and A. Arami, "Quantitative modeling of spasticity for clinical assessment, treatment and rehabilitation," *Sensors*, vol. 20, no. 18, p. 5046, 2020.
21. T. K. K. Koo and A. F. T. Mak, "Feasibility of using EMG driven neuromusculoskeletal model for prediction of dynamic movement of the elbow," *J. Electromyogr. Kinesiol.*, vol. 15, pp. 12–26, 2005.
22. E. De Vlugt, J. H. De Groot, K. E. Schenkeveld, Jh. Arendzen, F. C. T. van Der Helm, and C. G. M. Meskers, "The relation between neuromechanical parameters and Ashworth score in stroke patients," *J. Neuroeng. Rehabil.*, vol. 7, no. 1, p. 35, 2010.

 doi:10.20944/preprints202508.1608.v1

23. A. Falisse et al., "Physics-based simulations to predict the differential effects of motor control and musculoskeletal deficits on gait dysfunction in cerebral palsy: a retrospective case study," *Front. Hum. Neurosci.*, vol. 14, p. 40, 2020.
24. M. F. Levin and A. G. Feldman, "The role of stretch reflex threshold regulation in normal and impaired motor control," *Brain Res.*, vol. 657, no. 1–2, pp. 23–30, 1994.
25. A. Calota, A. G. Feldman, and M. F. Levin, "Spasticity measurement based on tonic stretch reflex threshold in stroke using a portable device," *Clin. Neurophysiol.*, vol. 119, no. 10, pp. 2329–2337, 2008.
26. L. Bar-On et al., "A clinical measurement to quantify spasticity in children with cerebral palsy by integration of multidimensional signals," *Gait Posture*, vol. 38, no. 1, pp. 141–147, 2013.
27. A. K. Blanchette, A. A. Mullick, K. Mo\"\in-Darbari, and M. F. Levin, "Tonic stretch reflex threshold as a measure of ankle plantar-flexor spasticity after stroke," *Phys. Ther.*, vol. 96, no. 5, pp. 687–695, 2016.
28. M. Germanotta et al., "Spasticity measurement based on tonic stretch reflex threshold in children with cerebral palsy using the PediAnklebot," *Front. Hum. Neurosci.*, vol. 11, p. 277, 2017.
29. N. A. Turpin, A. G. Feldman, and M. F. Levin, "Stretch-reflex threshold modulation during active elbow movements in post-stroke survivors with spasticity," *Clin. Neurophysiol.*, vol. 128, no. 10, pp. 1891–1897, 2017.
30. D. G. Kamper, B. D. Schmit, and W. Z. Rymer, "Effect of muscle biomechanics on the quantification of spasticity," *Ann. Biomed. Eng.*, vol. 29, pp. 1122–1134, 2001.
31. B. J. Fregly, "A Conceptual Blueprint for Making Neuromusculoskeletal Models Clinically Useful," *Appl. Sci.*, vol. 11, no. 5, p. 2037, 2021.
32. M. S. Shourijeh, N. Mehrabi, J. McPhee, and B. J. Fregly, "Advances in Musculoskeletal Modeling and their Application to Neurorehabilitation," *Front. Neurorobot.*, vol. 14, p. 65, 2020.
33. C. V Hammond et al., "The Neuromusculoskeletal Modeling Pipeline: MATLAB-based model personalization and treatment optimization functionality for OpenSim," *J. Neuroeng. Rehabil.*, vol. 22, no. 1, pp. 1–28, 2025.
34. M. M. van der Krogt, L. Bar-On, T. Kindt, K. Desloovere, and J. Harlaar, "Neuro-musculoskeletal simulation of instrumented contracture and spasticity assessment in children with cerebral palsy," *J. Neuroeng. Rehabil.*, vol. 13, no. 1, p. 64, 2016.
35. A. Falisse, L. Bar-On, K. Desloovere, I. Jonkers, and F. De Groote, "A spasticity model based on feedback from muscle force explains muscle activity during passive stretches and gait in children with cerebral palsy," *PLoS One*, vol. 13, no. 12, p. e0208811, 2018.
36. K. P. Blum, B. Lamotte D'Incamps, D. Zytnicki, and L. H. Ting, "Force encoding in muscle spindles during stretch of passive muscle," *PLoS Comput. Biol.*, vol. 13, no. 9, p. e1005767, 2017.
37. M. S. Shourijeh and J. McPhee, "Forward Dynamic Optimization of Human Gait Simulations: A Global Parameterization Approach," *ASME J. Comput. Nonlinear Dyn.*, vol. 9, no. 3, p. 31018, 2014.
38. A. J. Meyer and B. J. Fregly, "Muscle Synergies Facilitate Prediction of Subject-specific Walking Motions," 2016.
39. M. M. Vega et al., "Computational evaluation of psoas muscle influence on walking function following internal hemipelvectomy with reconstruction," *Front. Bioeng. Biotechnol.*, no. September, 2022.
40. M. S. Shourijeh and B. J. Fregly, "Muscle Synergies Modify Optimization Estimates of Joint Stiffness During Walking," *J. Biomech. Eng.*, vol. 142, no. 1, 2020.
41. M. F. Levin, D. Piscitelli, and J. Khayat, "Tonic stretch reflex threshold as a measure of disordered motor control and spasticity--A critical review," *Clin. Neurophysiol.*, vol. 165, pp. 138–150, 2024.
42. D. Piscitelli, J. Khayat, A. G. Feldman, and M. F. Levin, "Clinical Relevance of the Tonic Stretch Reflex Threshold and $μ$ as Measures of Upper Limb Spasticity and Motor Impairment After Stroke," *Neurorehabil. Neural Repair*, vol. 39, no. 5, pp. 386–399, 2025.
43. L. Barber, R. Barrett, and G. Lichtwark, "Passive muscle mechanical properties of the medial gastrocnemius in young adults with spastic cerebral palsy," *J. Biomech.*, vol. 44, no. 13, pp. 2496–2500, 2011.
44. L. Lacourpaille, A. Nordez, F. Hug, A. Couturier, C. Dibie, and G. Guilhem, "Time-course effect of exercise-induced muscle damage on localized muscle mechanical properties assessed using elastography," *Acta Physiol.*, vol. 211, no. 1, pp. 135–146, 2014.

 doi:10.20944/preprints202508.1608.v1

45. R. Wang, J. Gäverth, and P. A. Herman, "Changes in the neural and non-neural related properties of the spastic wrist flexors after treatment with botulinum toxin A in post-stroke subjects: an optimization study," *Front. Bioeng. Biotechnol.*, vol. 6, p. 73, 2018.
46. P. K. Artemiadis and K. J. Kyriakopoulos, "EMG-based control of a robot arm using low-dimensional embeddings," *IEEE Trans. Robot.*, vol. 26, no. 2, pp. 393–398, 2010.
47. G. Durandau, W. F. Rampeltshammer, H. van der Kooij, and M. Sartori, "Neuromechanical model-based adaptive control of bilateral ankle exoskeletons: Biological joint torque and electromyogram reduction across walking conditions," *IEEE Trans. Robot.*, vol. 38, no. 3, pp. 1380–1394, 2022.
48. J. W. Lance, "The control of muscle tone, reflexes, and movement: Robert Wartenbeg Lecture," *Neurology*, vol. 30, no. 12, p. 1303, 1980.
49. A. L. Shorter, J. K. Richardson, S. B. Finucane, V. Joshi, K. Gordon, and E. J. Rouse, "Characterization and clinical implications of ankle impedance during walking in chronic stroke," *Sci. Rep.*, vol. 11, no. 1, p. 16726, 2021.
50. N. J. O'dwyer, L. Ada, and P. D. Neilson, "Spasticity and muscle contracture following stroke," *Brain*, vol. 119, no. 5, pp. 1737–1749, 1996.
51. T. Sinkjær and I. Magnussen, "Passive, intrinsic and reflex-mediated stiffness in the ankle extensors of hemiparetic patients," *Brain*, vol. 117, no. 2, pp. 355–363, 1994.
52. T. D. Sanger, M. R. Delgado, D. Gaebler-Spira, M. Hallett, J. W. Mink, and T. F. on Childhood Motor Disorders, "Classification and definition of disorders causing hypertonia in childhood," *Pediatrics*, vol. 111, no. 1, pp. e89--e97, 2003.
53. L. Bar-On, E. Aertbeliën, G. Molenaers, and K. Desloovere, "Muscle activation patterns when passively stretching spastic lower limb muscles of children with cerebral palsy," *PLoS One*, vol. 9, no. 3, p. e91759, 2014.
54. P. Steinbok, "Selective dorsal rhizotomy for spastic cerebral palsy: a review," *Child's Nerv. Syst.*, vol. 23, no. 9, pp. 981–990, 2007.
55. A. Esquenazi et al., "Patient registry of outcomes in spasticity care," *Am. J. Phys. Med. Rehabil.*, vol. 91, no. 9, pp. 729–746, 2012.
56. G. E. Francisco and J. R. McGuire, "Poststroke spasticity management," *Stroke*, vol. 43, no. 11, pp. 3132–3136, 2012.
57. J. Wissel et al., "European consensus table on the use of botulinum toxin type A in adult spasticity.," 2009.
58. T. Maulet, S. Pouplin, D. Bensmail, R. Zory, N. Roche, and C. Bonnyaud, "Self-rehabilitation combined with botulinum toxin to improve arm function in people with chronic stroke. A randomized controlled trial," *Ann. Phys. Rehabil. Med.*, vol. 64, no. 4, p. 101450, 2021.
59. T. Hara, R. Momosaki, M. Niimi, N. Yamada, H. Hara, and M. Abo, "Botulinum toxin therapy combined with rehabilitation for stroke: a systematic review of effect on motor function," *Toxins (Basel).*, vol. 11, no. 12, p. 707, 2019.
60. P. B. Mills, H. Finlayson, M. Sudol, and R. O'Connor, "Systematic review of adjunct therapies to improve outcomes following botulinum toxin injection for treatment of limb spasticity," *Clin. Rehabil.*, vol. 30, no. 6, pp. 537–548, 2016.
61. N. A. Lannin et al., "Effect of additional rehabilitation after botulinum toxin-A on upper limb activity in chronic stroke," *Stroke*, 2020.
62. J.-H. Shin, G. Park, H. Kim, D. Y. Cho, and S. Kwon, "Combined effects and timing of robotic training and botulinum toxin on upper limb spasticity and motor function: a single-blinded randomized controlled pilot study," *J. Neuroeng. Rehabil.*, vol. 22, no. 1, p. 50, 2025.