



Order-Dependent Residual Stiffness in Collagenous Soft Tissue:

A Testable Framework for Sequence-Sensitive Mechanics

Douglas Chapman

Unwindology Institute

Correspondence: doug@unwindology.com

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Abstract

Collagenous soft tissues are known to exhibit history-dependent mechanical behavior, including viscoelastic hysteresis and preconditioning effects. However, a sharper question remains largely unexamined: does the order in which matched deformation components are applied produce measurably different residual mechanical states? This paper proposes a falsifiable framework for testing sequence-dependent residual mechanics in collagenous soft tissue.

The core hypothesis is that two matched deformation sequences, A-then-B and B-then-A, applied with identical total loading budgets, will produce different post-sequence residual stiffness states as measured by shear-wave elastography (SWE). A within-subject crossover protocol is specified, along with a hard falsification criterion: if AB and BA final states differ by less than the instrument precision threshold in 95% or more of healthy subjects, the proposed sequence-dependent mechanism is not supported at the accessible measurement scale.

The framework does not require commitment to any specific microscopic theory; it tests only whether order-dependent residual mechanics are empirically detectable. If supported, this result would have implications for soft tissue modeling, manual therapy sequencing, and rehabilitation protocol design.

Keywords: soft tissue mechanics, sequence dependence, residual stiffness, collagen, shear-wave elastography, path dependence, fascia, preconditioning, non-commutative mechanics

1. Introduction

Collagenous soft tissues exhibit complex mechanical behavior that has been extensively studied across biomechanics, tissue engineering, and clinical rehabilitation. Properties including viscoelasticity, hysteresis, stress relaxation, creep, and preconditioning are well documented in the literature (Fung, 1993; Fratzl, 2008). It is widely accepted that prior loading history influences subsequent mechanical response. This history dependence is typically modeled using viscoelastic constitutive frameworks, often with internal state variables that evolve under deformation (Holzapfel, 2000).

However, the majority of existing models describe history dependence in terms of cumulative exposure: how much deformation has occurred, over what duration, and at what magnitude. A more specific question has received comparatively little direct empirical attention: does the order in which deformation components are applied matter? That is, if two distinct deformation modes A and B are applied to a tissue region with identical total loading budgets but in reversed sequence (A–then–B versus B–then–A), do the resulting residual mechanical states converge, or do they diverge?

If the final state depends only on the cumulative loading parameters, then the system is sequence-commutative: AB and BA should converge to the same residual state. If, however, the internal fiber architecture retains information about the deformation path—not merely its aggregate magnitude—then the system may exhibit non-commutative sequence dependence: $AB \neq BA$.

This paper proposes a testable framework for investigating this question. It does not attempt to identify the microscopic origin of any such sequence dependence. It does not require commitment to any particular constitutive model or geometric formalism. It proposes only that the question is empirically answerable using current measurement technology, and it specifies a protocol and falsification criterion for doing so.

2. Background

2.1 History Dependence in Collagenous Tissue

Collagenous tissues including tendon, ligament, skin, and fascia display marked history dependence. Repeated cyclic loading produces preconditioning effects in which the stress–strain response shifts progressively before stabilizing (Fung, 1993). Hysteresis loops indicate energy dissipation that varies with loading history. Stress relaxation and creep behaviors further demonstrate that tissue mechanical state depends on prior deformation (Provenzano et al., 2001; Duenwald et al., 2009).

At the microstructural level, collagen fibrils exhibit crimp patterns that recruit progressively under tension. Fibril sliding, reorientation, and interfibrillar matrix reorganization all contribute to history-dependent behavior (Screen et al., 2004; Gupta et al., 2010). The fascial system in particular has been increasingly recognized as a continuous tensional network whose mechanical behavior depends on distributed loading patterns (Schleip et al., 2012; Langevin, 2006).

2.2 Limitations of Standard Descriptions

Standard viscoelastic models capture many aspects of tissue history dependence through internal variables, dashpot–spring assemblies, or quasi-linear viscoelastic (QLV) frameworks (Fung, 1993). These approaches are well-validated for cyclic loading and stress relaxation under controlled conditions.

However, most standard descriptions characterize history dependence in terms of scalar quantities: cumulative strain, peak stress, number of loading cycles, or total energy input. Fewer studies have isolated the specific contribution of deformation order as an independent variable. Where preconditioning studies apply repeated identical cycles, they do not typically test whether two different deformation modes applied in reversed order produce distinguishable final states.

This leaves an empirical gap. It is not yet well established whether matched multimodal loading sequences commute in practice—that is, whether the final

residual state is truly independent of loading order, or whether tissue architecture preserves enough path information to make sequence mechanically consequential.

2.3 The Specific Unresolved Question

The question this paper addresses can be stated precisely:

Given two controlled deformation modes A and B, applied to the same tissue region with identical total loading parameters (duration, magnitude, number of cycles) but in reversed order, do the resulting residual mechanical states converge or diverge?

Define:

- A = a controlled deformation in one principal direction (e.g., longitudinal indentation/mobilization)
- B = a controlled deformation in a different principal direction (e.g., transverse or rotational mobilization)
- AB = sequence A followed by B
- BA = sequence B followed by A
- Same total loading budget: matched duration, magnitude, and cycle count

The primary outcome measure is the residual stiffness state of the tissue region after each complete sequence, assessed via shear-wave elastography.

3. Core Hypothesis

3.1 Primary Hypothesis

Matched deformation sequences AB and BA, applied to collagenous soft tissue under controlled conditions, produce measurably different post-sequence residual stiffness states.

3.2 Null Hypothesis

AB and BA converge to the same final residual stiffness state within the precision limits of shear-wave elastography measurement.

3.3 Falsification Criterion

The sequence-dependent hypothesis is considered not supported at the accessible scale if: the mean absolute difference between post-AB and post-BA residual stiffness values falls below the established instrument precision threshold of the SWE system in 95% or more of subjects tested under the specified protocol.

This criterion is deliberately conservative. It defines a clear rejection condition rather than relying solely on statistical significance testing. If the effect is not detectable above measurement noise in nearly all subjects, the proposed mechanism either does not exist at the accessible scale or is too weak to be mechanically meaningful under these conditions.

4. Theoretical Motivation

Why might deformation order matter? Several established features of collagenous tissue provide plausible grounds for this possibility, without requiring commitment to any specific constitutive theory.

Anisotropic fiber architecture. Collagenous tissues are structurally anisotropic. Fiber populations are oriented in preferred directions, and their mechanical response varies with loading direction (Holzapfel et al., 2000; Lanir, 1983). If deformation mode A preferentially recruits one fiber population while mode B recruits a different population, then the order of recruitment may determine which population is conditioned first, potentially influencing the configuration available for the second deformation.

Progressive fibril recruitment. Under tension, collagen fibrils recruit from crimped to straightened states in a progressive, direction-dependent manner (Hansen et al., 2002). A deformation in direction A may alter the crimp geometry or interfibrillar spacing available for a subsequent deformation in direction B, and vice versa.

Matrix reorganization. The extrafibrillar matrix, including proteoglycans and water, reorganizes under loading (Screen et al., 2004). If this reorganization is directionally specific, then the order in which different deformation modes alter the matrix environment may affect the final equilibrium configuration.

Non-linear coupling. In any system with non-linear mechanical coupling between degrees of freedom, the order of activation generally matters. Soft tissue, with its non-linear stress–strain behavior and coupled fiber–matrix interactions, may satisfy this condition at clinically accessible scales.

The present paper does not require that any one of these mechanisms is the explanation. It requires only that the question is plausible enough to warrant a direct empirical test. The proposed protocol is designed to detect sequence-dependent residual mechanics regardless of their microscopic origin.

5. Proposed Experimental Design

5.1 Study Design

A within-subject crossover design is proposed. Each participant receives both the AB and BA sequences on the same tissue region in separate sessions, with an adequate washout period between sessions. This design controls for inter-subject variability in tissue composition, hydration, and baseline stiffness.

5.2 Participants

An initial study should recruit 20–30 healthy adult participants (age 25–55) with no history of connective tissue disorders, recent injury to the target region, or current anti-inflammatory medication use. Exclusion criteria should include systemic inflammatory conditions, recent surgical procedures in the measurement area, and conditions affecting tissue hydration or collagen metabolism.

5.3 Target Tissue

The thoracolumbar fascia is recommended as the primary target. This tissue is: (a) accessible to both controlled mechanical loading and SWE measurement; (b) well-characterized in the biomechanics literature; (c) sufficiently thick and organized to produce reliable elastographic signals; and (d) clinically relevant to manual therapy and rehabilitation contexts.

5.4 Operational Definition of Deformation Modes

The deformation modes must be mechanically standardized and reproducible. The following definitions are proposed:

Mode A — Longitudinal mobilization. A calibrated indentation device applies cyclical compression–release along the craniocaudal axis of the thoracolumbar fascia. Parameters: 10 N peak force, 0.5 Hz cycle rate, 3 minutes total duration (90 cycles).

Mode B — Transverse mobilization. The same device applies cyclical compression–release along the mediolateral axis of the same tissue region. Parameters: 10 N peak force, 0.5 Hz cycle rate, 3 minutes total duration (90 cycles).

Both modes use identical loading magnitudes, durations, and cycle counts. Only the direction of application differs. Operator variability is minimized by using a mechanical indentation system rather than manual application.

5.5 Protocol

Session 1 (AB sequence):

1. Participant positioned prone, standardized posture, target region marked.
2. Baseline SWE measurement (3 acquisitions, averaged).
3. Mode A applied (3 minutes).
4. 5-minute rest period.
5. Mode B applied (3 minutes).
6. Post-sequence SWE measurement (3 acquisitions, averaged), taken at 2, 5, and 10 minutes post-completion.

Session 2 (BA sequence):

Same protocol with reversed order: Mode B first, then Mode A.

Minimum 72-hour washout period between sessions to allow tissue recovery to baseline. Session order (AB-first vs BA-first) counterbalanced across participants.

5.6 Primary Outcome Measure

The primary outcome is the difference in residual shear-wave velocity (or derived Young's modulus) between the post-AB and post-BA states at the 5-minute post-completion time point. This measure is chosen because: (a) SWE is non-invasive, quantitative, and increasingly standardized; (b) shear-wave velocity is directly related to tissue stiffness; and (c) the 5-minute time point allows initial transient effects to dissipate while remaining close enough to capture residual mechanical differences.

5.7 Secondary Outcome Measures

Secondary outcomes include: (a) directional stiffness differences at each time point (2, 5, and 10 minutes); (b) recovery trajectory—whether the AB and BA states converge over the 10-minute post-sequence window or remain divergent; and (c) within-subject reproducibility across repeated sessions (if a subset of participants is tested twice).

5.8 Statistical Analysis

The primary comparison is a paired analysis of post-AB versus post-BA residual stiffness values across subjects. A paired t-test or Wilcoxon signed-rank test (depending on distribution normality) will assess whether the mean difference is significantly different from zero. Effect size (Cohen's d) will be reported. Additionally, the proportion of subjects showing an AB–BA difference exceeding the SWE instrument precision threshold will be calculated and compared against the 95% falsification criterion defined in Section 3.3.

6. Predicted Outcomes

6.1 If Sequence Dependence Is Supported

A consistent within-subject difference between post-AB and post-BA residual stiffness, exceeding instrument precision in a clear majority of subjects, would support the hypothesis that deformation order is mechanically consequential in collagenous soft tissue. This would suggest that the tissue's internal organization retains path-dependent information beyond what cumulative loading parameters alone predict.

6.2 If Sequence Dependence Is Not Supported

If the AB–BA difference falls below instrument precision in 95% or more of subjects, then order-dependent residual mechanics are not detectable at this scale and protocol. This would not rule out sequence effects at smaller scales, different tissue types, or under different loading regimes, but it would indicate that the proposed mechanism is not accessible under the specified conditions.

6.3 Secondary Predictions

If sequence dependence is observed, secondary analysis may reveal: (a) whether the effect is directionally asymmetric ($AB > BA$ or vice versa consistently); (b) whether the divergence persists, grows, or decays over the post-sequence recovery window; and (c) whether baseline stiffness or individual tissue characteristics predict the magnitude of the sequence effect.

7. Discussion

7.1 Interpretation

The framework proposed here does not attempt to establish a new theory of soft tissue mechanics. It proposes only that a specific, previously under-examined question—whether deformation order produces distinguishable residual states—is worth testing directly. The hypothesis is grounded in well-established properties of collagenous tissue, including anisotropy, progressive fiber recruitment, and non-linear mechanical coupling.

If supported, the result would not explain why order matters. It would establish that it does, at a specific scale and under defined conditions. Identifying the underlying mechanism would require subsequent investigation at the microstructural level.

7.2 Relation to Existing Literature

Preconditioning studies have long established that prior loading alters subsequent tissue response (Fung, 1993; Carew et al., 2004). However, most preconditioning protocols use repeated identical loading cycles rather than testing the interaction of different deformation modes in varying order. The present framework extends this body of work by isolating deformation sequence as an independent experimental variable.

Recent interest in non-Markov mechanical behavior and memory effects in biological materials (Bonfanti et al., 2020) provides additional theoretical context. If soft tissue exhibits order-dependent residual states, this may relate to broader work on materials with mechanical memory.

7.3 Clinical Relevance

If sequence-dependent residual mechanics are confirmed, the practical implications include: (a) manual therapy protocols may benefit from attention to intervention order, not only technique selection; (b) rehabilitation loading programs may need to consider deformation sequence as a design variable; and (c) tissue modeling for

surgical planning and prosthetic design may require richer state descriptions than cumulative loading parameters provide.

7.4 Future Directions

If the primary hypothesis is supported, natural extensions include: (a) testing whether local deformation in one region produces measurable stiffness changes at remote anatomical sites through continuous fascial planes; (b) investigating whether directional anisotropy in the residual effect reveals organized geometric structure in tissue deformation memory; and (c) developing more formal mathematical descriptions of the non-commutative mechanics observed.

8. Limitations

This framework has several important limitations that should be acknowledged explicitly.

First, the proposed protocol tests only one tissue region (thoracolumbar fascia) in healthy subjects. Results may not generalize to other collagenous tissues, pathological states, or different anatomical locations.

Second, the framework does not identify the microscopic origin of any observed sequence dependence. Confirmation of the $AB \neq BA$ effect would establish the phenomenon, not its mechanism.

Third, SWE measurement precision imposes a floor on detectability. Subtle sequence effects below the instrument threshold would not be captured.

Fourth, the use of mechanical indentation devices, while improving reproducibility, may not fully replicate the multimodal loading that occurs during manual therapeutic intervention.

Fifth, the 72-hour washout period is an estimate. Individual recovery rates may vary, and the adequacy of this interval would need to be validated in preliminary testing.

Sixth, this paper presents a framework and protocol proposal, not empirical data. The hypotheses require experimental testing before any conclusions can be drawn.

9. Conclusion

This paper proposes that collagenous soft tissue may exhibit order-dependent residual mechanics—that matched deformation sequences applied in different orders produce measurably different final stiffness states. A falsifiable protocol using within-subject crossover design and shear-wave elastography is specified, along with a conservative rejection criterion.

The question is simple, specific, and testable with current technology. It does not depend on any particular constitutive theory. It asks only whether deformation order is mechanically consequential in collagenous tissue at clinically accessible scales.

If supported, this finding would suggest that soft tissue mechanical models may benefit from richer state descriptions that account for loading sequence. If not supported, a clear empirical boundary will have been established. Either outcome advances the field.

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