A General Method for Computing an Average Curve and Statistical Response Corridors Using Biomechanical Monotonic and Load-Unload Data

Devon C. Hartlen, Duane S. Cronin

Abstract Computing an average curve and response corridors is critical for assessing biomechanical data and comparisons to other datasets and numerical models. However, extant methods are often case-specific and lack a strong statistical foundation. A general methodology using arc-length re-parameterisation and non-linear signal registration has been proposed to provide a feature-based assessment of average biomechanical responses and statistical variability with the key advantage of the applicability of a single method to a wide range of physical responses. In this study, the arc-length-based methodology was applied to two experimental datasets: the compressive behaviour of porcine brain tissue and the load-unload response of a human thorax. In both cases, the arc-length corridor method captured the underlying shape of material or subject responses without *a priori* assumptions of response behaviour, suitable to a wide range of biomechanical data from monotonic signals without a common termination point to highly variable, hysteretic responses, and did not distort the underlying shape or variability of the average response like common contemporary methods. The arc-length corridor method is distributed freely in the software package ARCGen, available for MATLAB and Python under a permissive, open-source license (https://github.com/IMMC-UWaterloo).

Keywords Arc-length re-parameterisation, average curve, biomechanical data, statistical response corridors, biomechanical data, statistical analysis.

I. INTRODUCTION

Biomechanical response data collected from tissues, volunteers, or post-mortem human subjects (PMHSs) is vital to assess the performance of physical and numerical human or tissue surrogates but is often highly variable [1]. Such assessments often require a single representative curve or mean response to compute curve-matching metrics such as the coefficient of determination (R^2) or more sophisticated metrics such as BioRank [2] or CORA [3]. Furthermore, the experimental variability of biomechanical data is often represented using response corridors. However, until recently, there has been no general method for computing an average response nor a general and statistically rigorous method of determining response corridors across the wide range of signal types common in biomechanical data.

Existing methodologies to compute average response and corridors can be broadly categorised into time-based and cross-variable approaches [4]. Time-based methods are by far the most common, given the prevalence of time-series data in the literature, but have some key limitations. These techniques rely on a pointwise calculation of average responses [4], necessitating all signals to have the same number of points and terminate at the same location. While widely used, these techniques can distort the underlying shape of experimental data if features shared across input signals are not aligned temporally. Various methodologies have been used to minimise distortion by aligning features, such as phase shifting to align to a single feature [5] or to maximise the correlation between signals [5]. However, these methodologies often still distort the underlying shape of experimental data if input signals contain more than one critical feature (such as multiple peaks or valleys in kinematic data) [6].

Pointwise averaging often fails for non-time-series data, such as force-displacement or stress-strain responses, as signals do not necessarily terminate at the same location. To that end, a range of methods have been proposed, such as assuming an analytical form [7], manual segmentation of signals into common features [8], or even manually estimating an *eye-ball average* [9]. However, these methods are often case-specific and are particularly

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poor at handling data which may be non-monotonic or hysteretic.

This paper uses a single, general arc-length-based methodology to redefine the average responses and response corridors for two literature datasets. The resulting average and corridors could be used as inputs to curve-matching metrics such as BioRank or CORA, although that work is not performed here. These exemplar datasets were selected as representative of common types of biomechanical responses for which no single averaging method is applicable. The first dataset, the compressive stress-strain response of porcine brain tissue, was predominantly monotonic, with signals that did not terminate at the x-value. The second dataset, load-unload responses of a human thorax under lateral impact, exhibited significant variability between subjects and a characteristic hysteresis that existing methods cannot accommodate without manual segmentation. The arc-length-based methodology is applied and compared to the reported literature results in both cases.

II. METHODS

Detailed coverage of the arc-length-based methodology can be found in [10]. The key advantage of the arc-length-based methodology over contemporary corridor methods is that it provides a feature-based statistical assessment of signals, capturing the average location and variability of shared features, such as peaks or valleys, in a set of signals in both axes simultaneously. Here, the methodology is summarised with the goal of building intuition into how the approach works rather than the precise technical and mathematical details. Two exemplar datasets, introduced below, were selected to demonstrate the efficacy and generality of the arc-length corridor method over contemporary methodologies.

Arc-Length-Based Average and Corridor Calculation

The arc-length-based methodology developed by [10] can be divided into three stages (Fig. 1): arc-length re-parametrisation, signal registration, and statistical analysis. The signals to be analysed do not need to be the same number of data points in length, terminate at the same location, or be of a specific shape. While it is recommended that noisy signals are filtered prior to applying the arc-length corridor method, this is not a requirement, and signal registration will often accommodate signals with a modest amount of noise, so long as the noise does not significantly alter the arc-length of the signal.

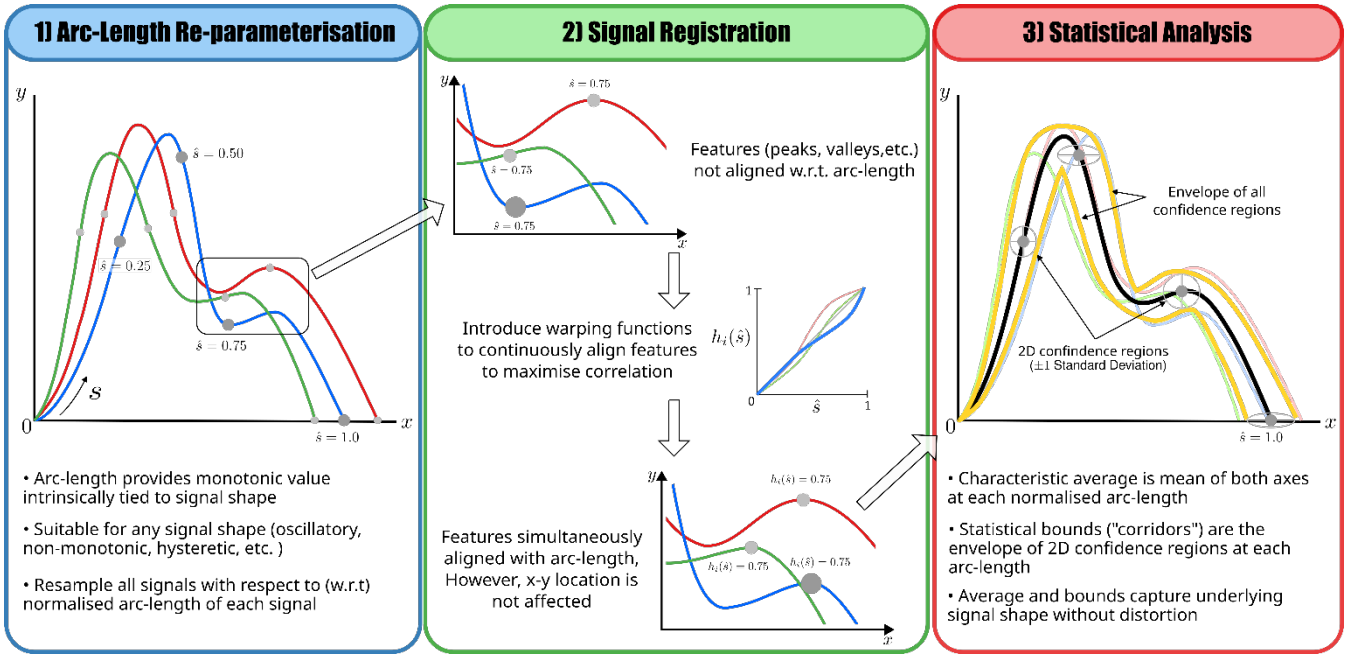


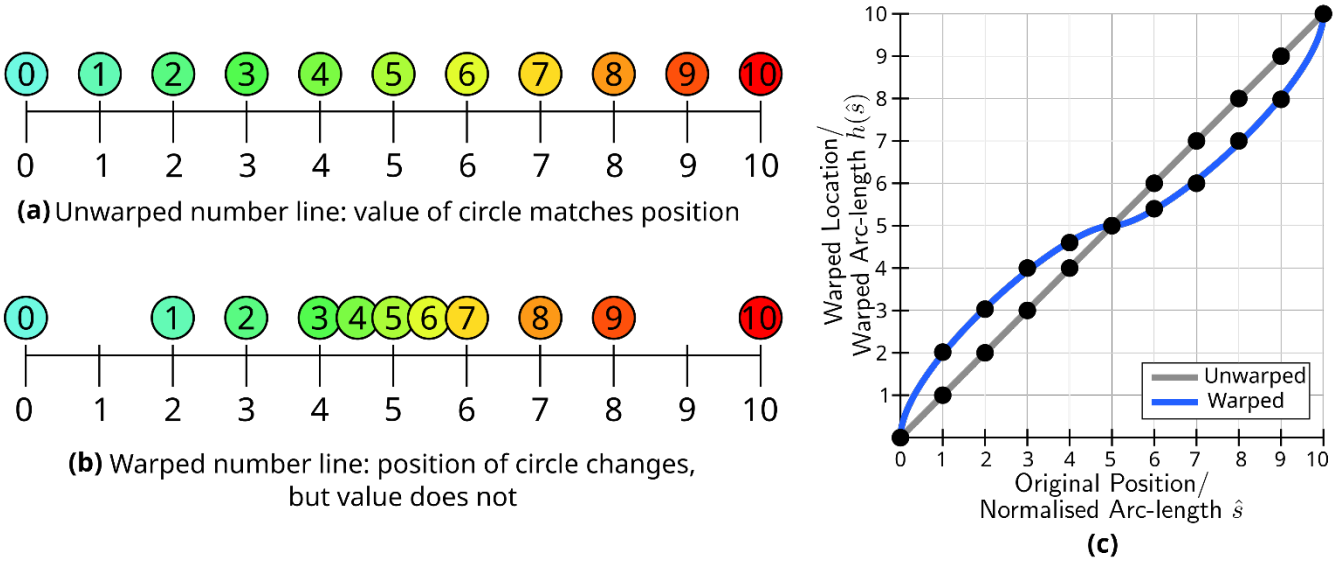
Fig. 1. A high-level graphical overview of the three stages of the arc-length corridor method. 1) Signals are re-parameterised with respect to normalised arc-length. 2) Re-parameterised signals are subject to signal registration to align critical features with respect to normalised arc-length. The physical location of features remains unchanged, only the arc-length assigned to the features. 3) Characteristic average and response corridors are computed using registered, re-parameterised signals.

The first stage of the arc-length-based method is, aptly enough, arc-length re-parameterisation. The purpose

of arc-length re-parametrisation is twofold. First, it provides a strictly monotonic sampling variable intrinsically linked to the underlying shape of the input signals, eliminating concerns about non-monotonic behaviour in either axis. Second, as arc-length is tied to the shape of the signal, features shared between input signals should occur at approximately the same normalised arc-length, laying the foundation for feature-based statistical analysis.

The arc-length of each signal was computed assuming linear behaviour between data points for simplicity. Next, arc-length was normalised by the length of each signal, such that all signals have a normalised arc-length ranging from 0 to 1. This step accommodates differences in arc-length between input signals. Finally, each signal is uniformly resampled with respect to normalised arc-length, such that each signal has the same number of data points and is sampled at the same normalised arc-length.

An underlying assumption behind arc-length re-parameterisation is that shared features, such as peaks or valleys, occur at the same normalised arc-length in each signal. However, experimental noise and subject variability can misalign features somewhat, distorting or smearing the resulting average, similar to the pointwise approaches discussed earlier. To ameliorate this, non-linear signal registration was utilised. From a technical perspective, this involves introducing a strictly monotonic warping function to each signal. These warping functions, in this case piecewise cubic Hermite splines (MATLAB command `pchip()` [11]), continuously adjust the arc-length of each signal to maximise cross-correlation between all input signals and align key features with respect to warped arc-length. Optimisation was performed with MATLAB command `fmincon()`. As this process can be conceptually difficult, consider the number line in Fig. 2a, where each numbered circle is located at the corresponding position on the number line. The warping function for this situation would be the straight grey line in Fig. 2c, describing a linear mapping between the original location of the circles and the position on the number line. Fig. 2b shows what happens when an arbitrary warping function is introduced. The location of the circles on the number line changes relative to their initial position, resulting in the non-linear mapping shown as the blue curve in Fig. 2c. While the position of the circles changes, the value of the circles does not, which enables the statistical analysis in the next step. While a single number line and an arbitrary warping function are shown here, signal registration introduces a unique warping function determined numerically using non-linear optimisation. A penalty factor, λ, was introduced during optimisation to prevent warping functions from skewing or otherwise altering the physical interpretation of the signals. A penalty factor of between 10^{-3} to 10^{-2} has been shown to provide effective alignment of critical features without disrupting the shape of the signals [10] and is recommended in most cases. If the penalty factor (10^{-1} to 10^{0}) is too high, no feature alignment is performed. However, if the penalty factor is too low (less than 10^{-3} and approaching 0), the resulting average can be unrealistic as signal points are clustered to a single feature. Strategies for selecting an appropriate penalty factor are provided in [10].



(a) Unwarped number line: value of circle matches position

(b) Warped number line: position of circle changes, but value does not

(c)

Fig. 2. A graphical explanation of how warping functions are used during signal registration. Consider an ordered number line (a), where the value of each circle matches their initial position. During registration, the position of the circles shifts (b), such that the original location of each circle maps onto a new, warped location (c). During this process, the location of each circle is changed, but the value is not.

Following the signal registration process, all inputted signals have key features aligned with respect to their warped, normalised arc-length. The statistical analysis stage commences by calculating the characteristic average pointwise using the mean value of both axes at each warped, normalised arc-length. The standard deviation for both axes is also calculated at each point. Then, using the mean and standard deviation and assuming an uncorrelated two-dimensional normal distribution, an ellipsoidal confidence region can be defined at each point of the characteristic average. Ellipsoidal confidence intervals enable the capture of the variability of features in both axes, despite the warping functions introduced during signal registration. This step results in a series of overlapping ellipsoidal confidence regions at each point of the characteristic average. The response corridors are defined as the envelope of these ellipses and were extracted numerically using a marching-squares algorithm [12] before being split into inner and outer corridors.

Dataset Selection for Demonstration

Two datasets were selected to demonstrate the capability of the arc-length-based methodology. These datasets were selected to augment the datasets used to demonstrate the effectiveness of the arc-length-based methodology in [10], which included monotonic signals but contained significant variability, highly oscillatory signals yet had low run-to-run variability, and load-unload signals which exhibited non-monotonic behaviour in both axes. The datasets used in this work were selected, in part, because the average response and corridors calculated in the published literature lacked a strong statistical foundation.

The first dataset comprised compressive stress-strain responses for porcine brain tissue under several test conditions (Fig. 3) [7]. This dataset demonstrates predominately monotonic behaviour with variability between test specimens that do not share a common endpoint. Porcine brain tissue samples were loaded in compression until the specimen failed. Stress-strain curves were reproduced from the original experimental data provided by the authors. Three test conditions have been examined in this work: fresh tissue, tissue stored frozen for 24 hours, tissue stored frozen for 48 hours, tissue stored at room temperature for 24 hours, and tissue stored at room temperature for 48 hours. In addition to different termination points, the number of specimens varied between each test condition.

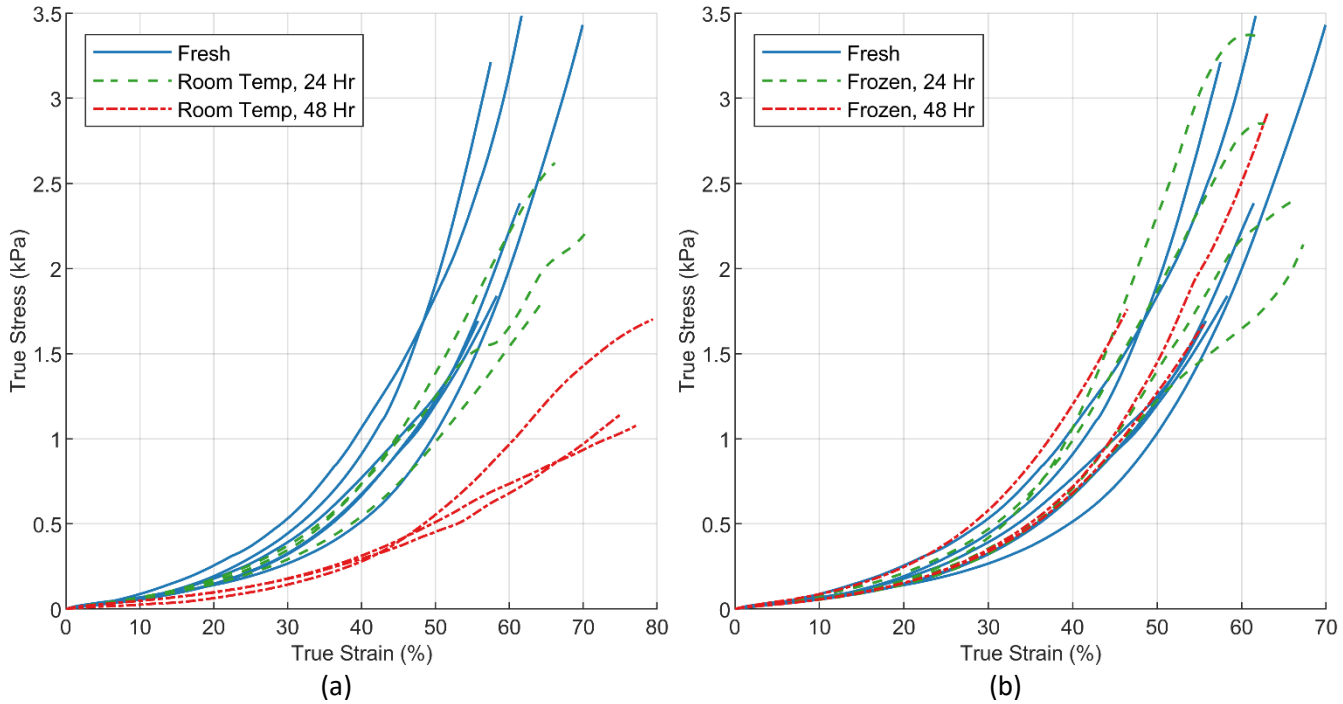


Fig. 3. Compressive stress-strain responses of porcine brain tissue tested after various storage conditions. (a) Tested fresh and after being stored at room temperature for 24 and 48 hours. (b) Tested fresh and after being frozen for 24 and 48 hours.

The second dataset selected for this work was the force-displacement responses of a human thorax under lateral loading (Fig. 4) [13]. Data was collected from PMHSs impacted laterally with a pendulum at three velocities. The hysteretic load-unload nature of this dataset precluded the usage of traditional averaging techniques without

resorting to manual data segmentation. Input signals analysed here were digitised from the best available version of the original publication with no additional processing. In addition to the defining hysteretic shape, there was significant variation between signals in the same test condition.

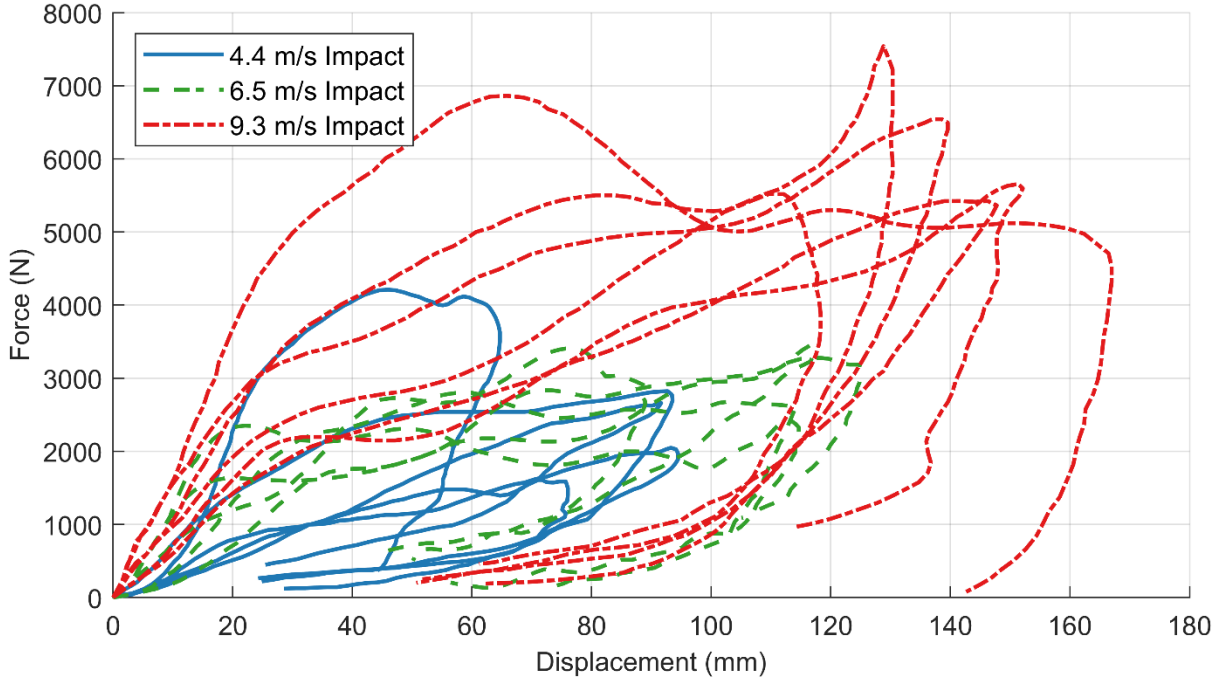


Fig. 4. Force-displacement responses of PMHS thorax subject to lateral impact at three different impactor velocities.

III. RESULTS

Porcine Brain Tissue

The arc-length-based methodology was applied to each of the five test conditions (Fig. 5). Given the monotonic nature of the signals, no signal registration was necessary. For each test condition, the average response captured the expected trend of the brain tissue well, specifically a period of low stiffness, with stiffness increasing significantly at large strains. The response corridors, defined to be ± 1 standard deviation in size, exhibit increasing variability with increasing strain and variation in the termination point of each signal.

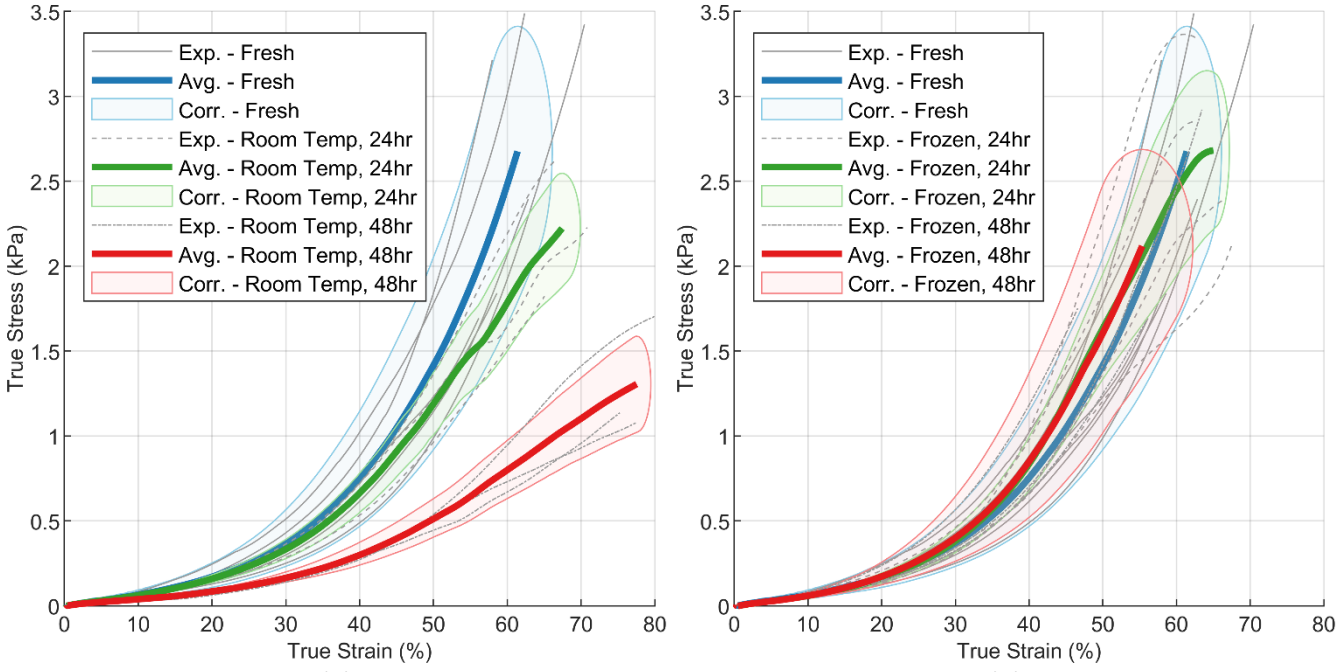


Fig. 5. Average and ± 1 standard deviation response corridors for porcine brain tissue tested after (a) storage at room temperature and (b) thawed from frozen.

Lateral Thoracic Impact

The non-monotonic nature of the Viano thoracic dataset necessitated the use of signal registration to align key features in both axes simultaneously. Three control points with a penalty factor of $\lambda = 10^{-2}$ were used in this work to align shared features. In all test conditions, the characteristic average captured the characteristic shape of the initial ramp, plateau and unload responses observed in the experimental data. Unlike other methods reported for hysteretic cross-variable data [8], the arc-length-based methodology was applied uniformly across the range of behaviour reported without requiring segmentation or manual processing of each signal.

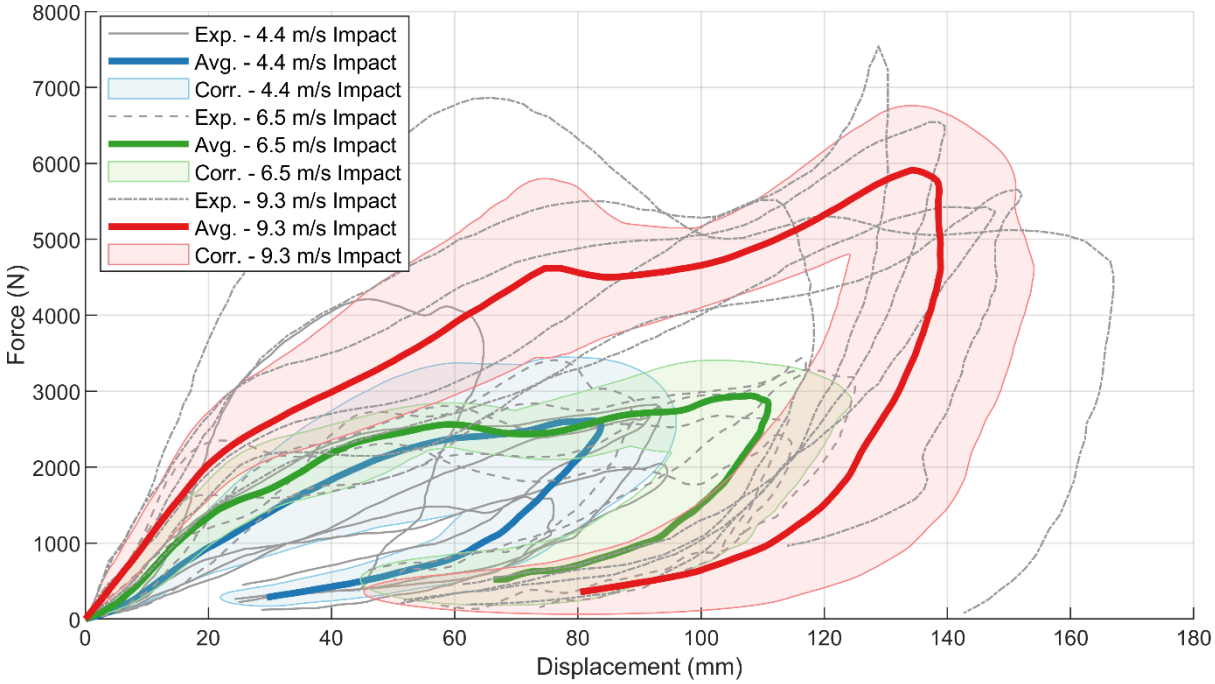


Fig. 6. Average force-displacement responses and ± 1 standard deviation response corridors for the lateral thoracic impact of PMHSs to different impact velocities. Signal registration was applied with three control points and a penalty factor of $\lambda = 10^{-2}$.

IV. DISCUSSION

The porcine brain tissue exhibited both variability and the lack of a common termination point that would have made pointwise statistics inapplicable without scaling of either axis, which has been shown to affect the characteristic shape of the input signals [14]. In the original publication [7], data was cropped to a common strain of 50% and fitted to an Ogden hyperelastic model to perform statistical hypothesis testing. While this approach was effective for developing an average response suitable for numerical modelling, it required assuming the shape of the material response and arbitrarily cropping material data. However, the reported average and corridors were computed with a pointwise approach with respect to displacement (Fig. 7 and Appendix A, Fig. A-1-A-3) rather than mean Ogden parameters. In this work, no assumptions of signal shape were made. Despite this, the resulting average agreed with the expected hyperelastic response of brain tissue. Furthermore, the ability of the arc-length-based methodology to incorporate signals with different termination points allowed for the resulting average and corridors to capture the variation of stress and strain at failure within the response corridors. In contrast, handling this task was separate from corridor generation from cropped data in [7]. In comparison to the pointwise corridors, the arc-length-based approach produced generally broader corridors, owing to the variation in displacement being accounted for. This displacement variation directly results from differences in material stiffness, given the expected hyperelastic response of brain tissue and strains at failure.

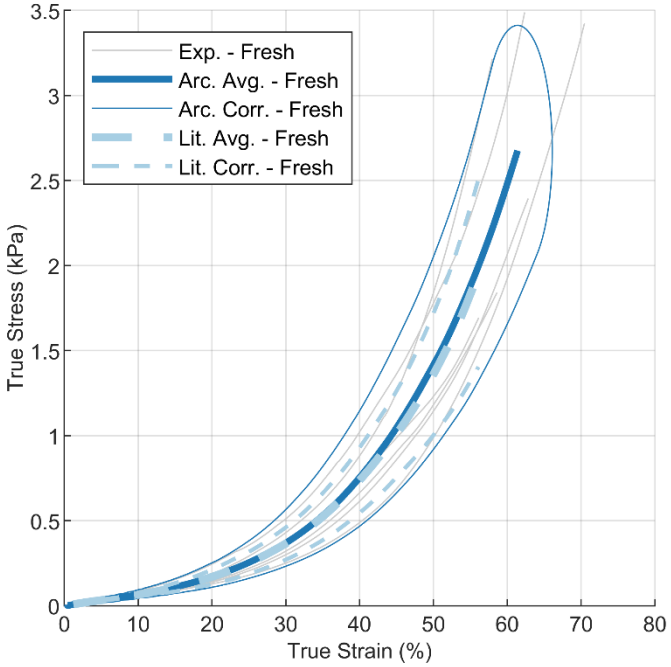


Fig. 7. The average and corridors computed with the arc-length-based method (dark blue) compared with the pointwise average and corridors computed by [7] overlaid on the original experimental signals for fresh tissue. A comparison of corridors for all other conditions is presented in Appendix A.

Further, unlike the methodology of reference [7], the arc-length-based approach produced statistical response corridors directly. However, while [7] were able to perform statistical hypothesis testing to determine if there were statistical differences between test conditions, no existing framework can easily accommodate the arc-length-based corridors computed here. That said, qualitative assessments of the corridors can be used to visualise any differences. The hypothesis testing by [7] showed that while there was no significant difference between brain tissue tested fresh and after being stored for 24 hours at room temperature, there was a significant change in response after 48 hours of room temperature storage. Visually, the corridors produced with the arc-length-based methodology agree with these statistical inferences (Fig 5a), as average responses diverged and corridors did not overlap. Similarly, [7] found no difference between testing fresh tissue and testing after being frozen for 24 and 48 hours, which the corridors produced with the arc-length-based methodology agreed with qualitatively (Fig. 5b) given the overlapping corridors.

While the corridors produced for porcine brain tissue may not be directly used for statistical hypothesis testing, they present some interesting opportunities. Consider that the main purpose of characterising the compressive behaviour of these tissues is for parameterisation of constitutive models and subsequent use in larger, more complex numerical models. While the average response is typically used for this purpose, the ± 1 standard deviation corridors produced with the arc-length-based methodology could also be used to parameterise constitutive models, enabling researchers to understand how variation in material properties would influence the behaviour of larger models.

The lateral thoracic impact data is a particularly influential dataset in assessing occupant safety. Despite this, the corridors proposed by [13] were quite simplistic, being the maximum and minimum extent of the force-displacement response, with only corridors for the 6.5 m/s impact being reported (Fig 8). While effective, this approach lacks a statistical foundation and does not produce an average response. In related work on thoracic impact, Reference [9] proposed an average response for hysteretic data based on a so-called *eye-ball average*, which lacked any statistical foundation. While the force-displacement responses published by [13] also include limited force-time and displacement-time signals, work has shown that combining the averages and corridors of two time-series responses into a single cross-variable response can lead to skewed behaviour for complex signal shapes [4]. Furthermore, it may be the case that the original time-series data may no longer be available, forcing one to operate directly on the reported cross-variable responses.

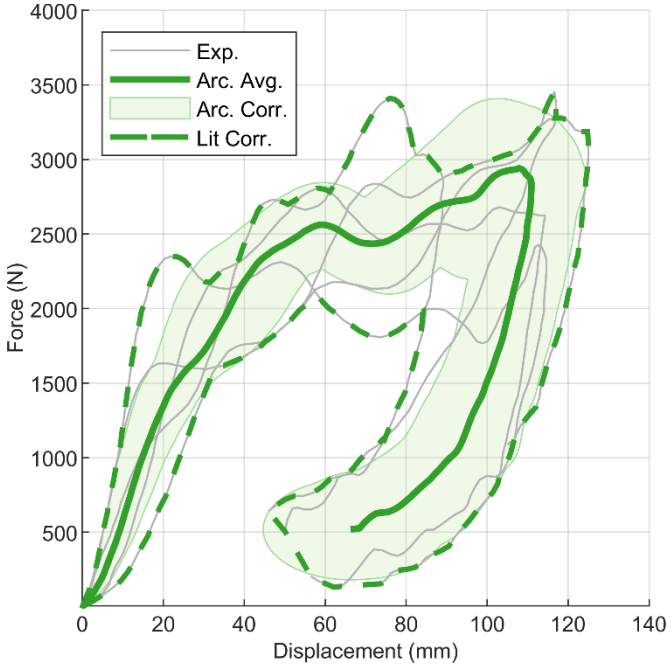


Fig. 8. The average and corridors computed with the arc-length-based method (dark green) compared with the corridors presented by [13] overlaid on the original experimental signals for the 6.5 m/s impact. Comparisons of the arc-length-based methodology and the method of [13] are given for each impact velocity in Appendix A.

The arc-length-based methodology directly operated on the thoracic force-displacement responses without manual pre-processing or segmentation. In addition, the inclusion of signal registration enabled a feature-based assessment of average behaviour and uncertainty despite the variability between signals. In particular, the 4.4 m/s impact test case (Fig. 4, blue curves) had one signal with a substantially higher peak force than the other signals. With signal registration, the shared shape of the test condition (specifically an initial rise, plateau, and unload in force and displacement simultaneously) was captured faithfully, while the impact of the outlying signal resulted in the increased width of the resulting corridors (Fig. 6 and Fig A-4).

As noted, signal registration enabled the feature-based assessment of average behaviour and variability using warping functions. While this granted a significant advantage over existing methodologies, it did require the user to define the number of interior warping control points. Reference [10] has suggested using the number of prominent inflection points (changes in concavity) present in the underlying signal shape. Alternatively, one could also set the number of control points equal to the number of critical features (such as peaks and signal reversals) present in the signals, although this approach lacks a certain degree of rigour. The thoracic impact response corridors in this work were computed with three warping control points, corresponding to the start and end of the plateau in force behaviour and the point where displacement begins to decrease. In general, however, there is a limited effect when using more than the recommended number of warping points, although a process akin to overfitting can occur at an unrealistically large number of warping points. Selecting the number of warping points is an important consideration when using this approach, and readers are directed to [10] for more detailed coverage of this topic. Critically, researchers who use this technique to produce characteristic averages and response corridors are advised to report the number of warping control points and penalty factor used.

One of the key advantages of the arc-length-based methodology is that it can be applied to an extremely wide range of data, regardless of the physical context of that data. For example, it is common to normalise and scale data collected from human volunteers or PMHS to account for variation in anthropometrics and age between subjects. While no scaling was performed on the thoracic data used in this work, this does not preclude its use. Incorporation of normalisation and scaling of force, displacement, or other measured responses should be performed on experimental data prior to computing an average and corridors using the arc-length-based methodology or on the computed responses.

While the arc-length-based methodology can accept signals with different lengths or sampling rates, the signals must be sufficiently sampled to define shared features well. If signals are sampled too sparsely, arc-length calculations, which are based on linear interpolation between points, can incorrectly capture the underlying

shape of the signal and can distort sparsely sampled critical features. It is recommended that signals be sampled in sufficient detail to resolve critical features well.

As noted earlier, while the arc-length-based methodology produces statistically rigorous response corridors, these corridors cannot be directly used for hypothesis testing. One of the key limitations is the insufficient framework for handling hypothesis testing on continuous data compared to traditional hypothesis testing. However, future work will explore this space to provide undirected hypothesis testing between two sets of signals capable of detecting statistically significant differences in the same feature-based paradigm used herein.

V. CONCLUSIONS

The average response and response corridors for two literature biomechanical datasets were redefined using a single methodology based on arc-length re-parameterisation and non-linear signal registration. These averages and corridors capture the shape, trends, and variability of the experimental data well, despite significant differences in signal type and shape between the datasets. This work demonstrates that the arc-length-based methodology has no issues handling the very different characteristics of each dataset, be it signals that do not share a common termination point or those that are highly variable and hysteretic. Further, when assessed in the context of existing work, the arc-length corridor method produced average responses that agreed well with published data without *a priori* knowledge of the underlying shape of the signals.

The arc-length-based methodology used here is freely available as ARCGen, an open-sourced software available for both MATLAB and Python under a permissive, open-source license (https://github.com/IMMC-UWaterloo).

VI. ACKNOWLEDGEMENT

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VIII. Appendix A – Comparison of Arc-length-based Methodology to Literature

Porcine Brain Tissue

Average and ± 1 standard deviation corridors computed with the arc-length-based methodology are compared with those reported in the original publication [7] for each of the five test conditions reported in the main body of this manuscript. The average response and corridors published in [7] were computed by a pointwise approach with respect to displacement.

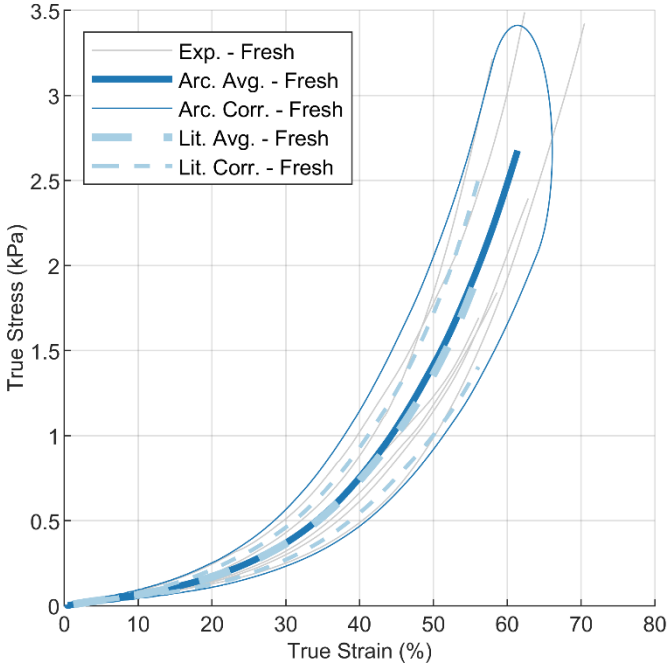

Fig. A-1. Average and ± 1 standard deviation response corridors computed with both the arc-length-based methodology and literature method for porcine brain tissue tested fresh at room temperature.

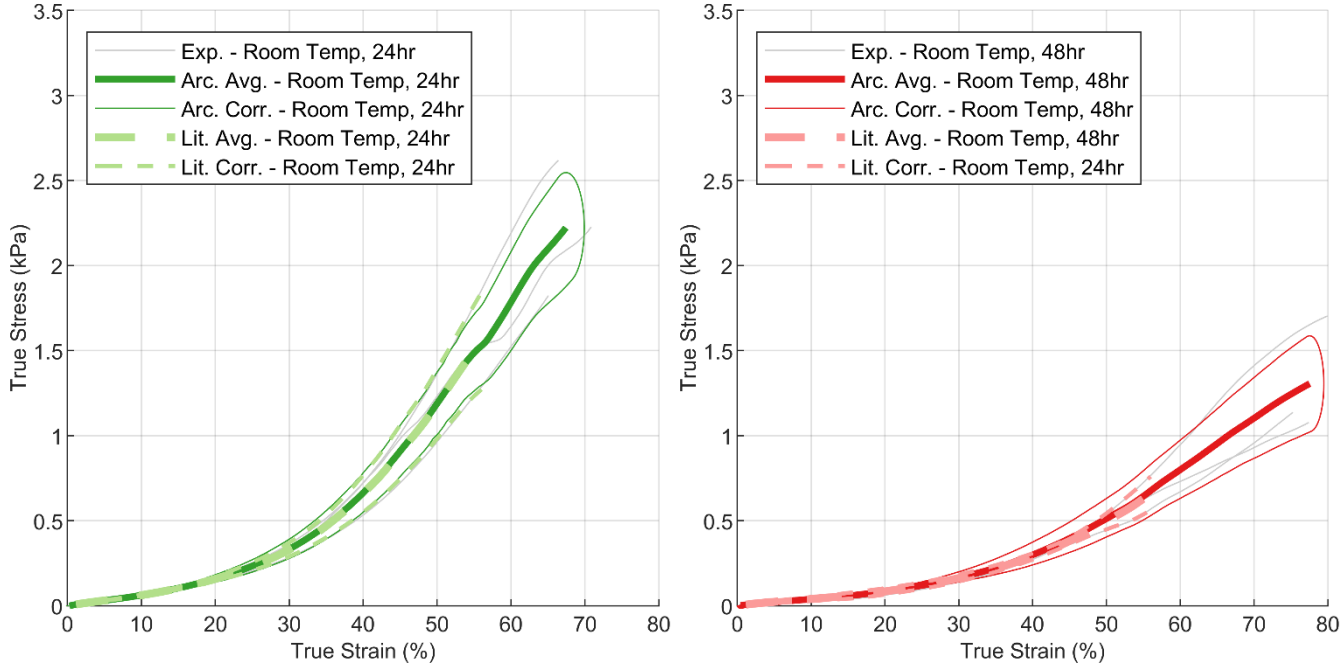

Fig. A-2. Average and ± 1 standard deviation response corridors computed with both the arc-length-based methodology and literature method for porcine brain tissue tested after (a) storage at room temperature for 24 hours and (b) stored at room temperature for 48 hours.

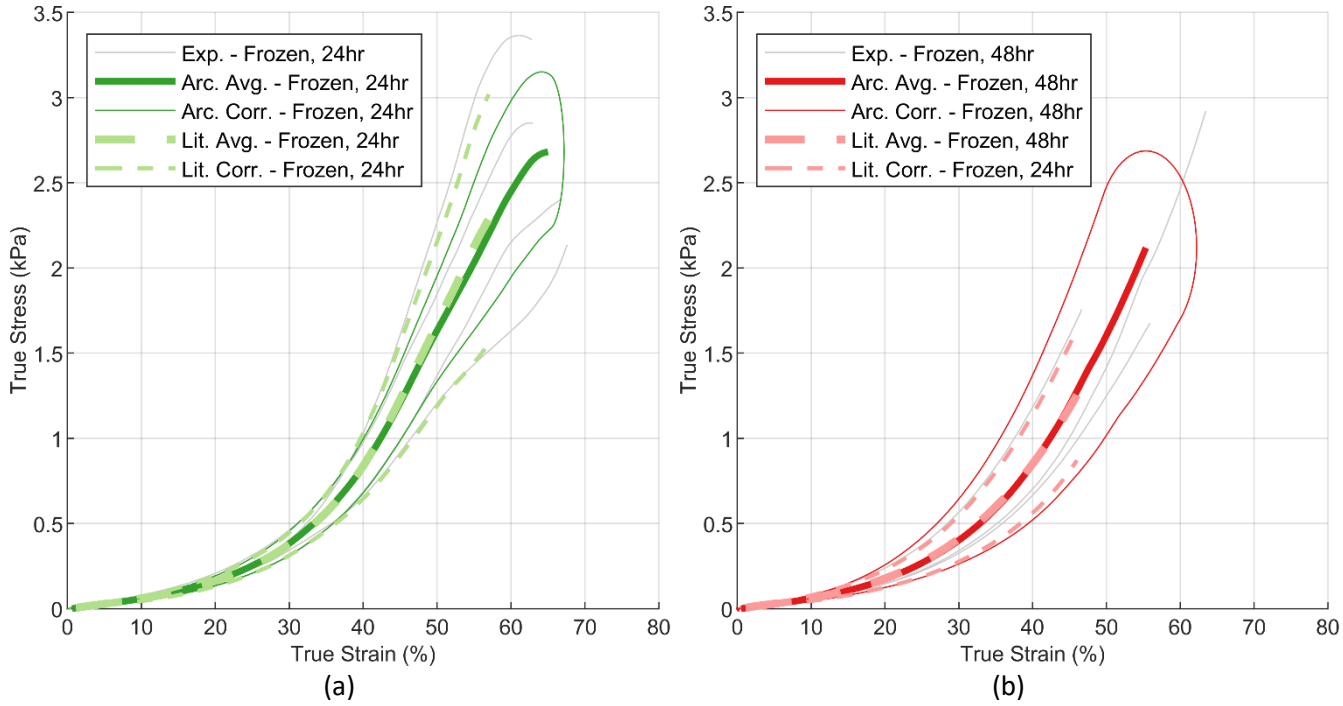

Fig. A-3. Average and ± 1 standard deviation response corridors computed with both the arc-length-based methodology and literature method for porcine brain tissue tested after (a) thawed from frozen after 24 hours and (b) thawed from frozen after 48 hours

Lateral Thoracic Impact

Average and ± 1 standard deviation corridors computed with the arc-length-based methodology are compared with those reported in the original publication [13] for each of the five test conditions reported in the main body of this manuscript. Corridors were only published in [13] for the 6.5 m/s impact and were defined as the extreme extents of force and displacement across all signals. No average response was calculated in [12]. Corridors computed with the arc-length-based method used three warping control points and a penalty factor of 10^{-2}.

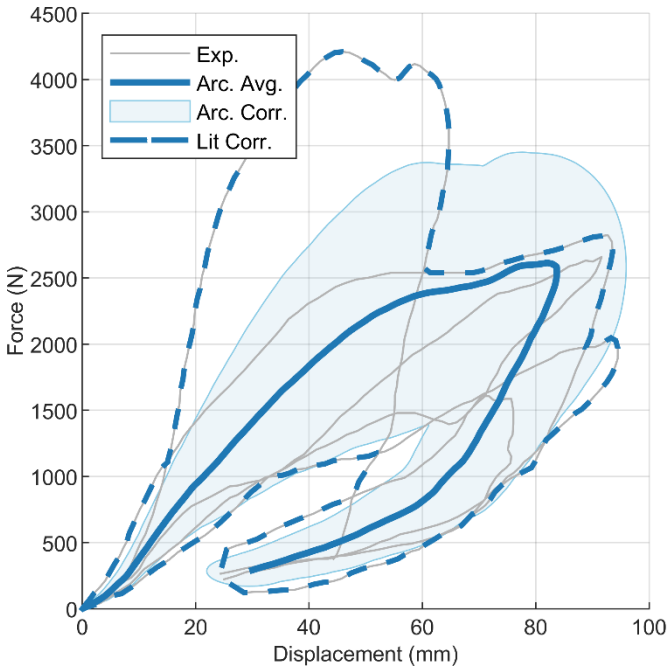

Fig. A-4. Average and ± 1 standard deviation corridor computed with the arc-length-based methodology compared to the corridor method published by [13] for the force-displacement response of PMHS thorax subject to a 4.4 m/s impact.

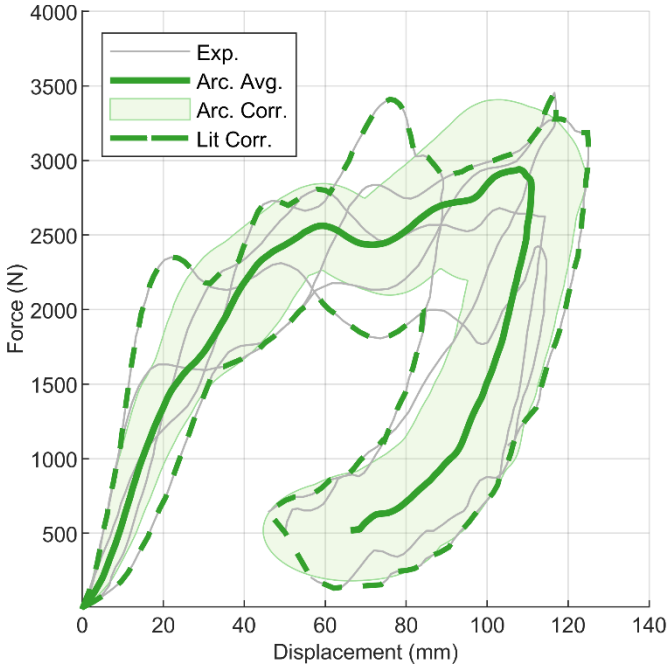

Fig. A-5. Average and ± 1 standard deviation corridor computed with the arc-length-based methodology compared to the corridor method published by [13] for the force-displacement response of PMHS thorax subject to a 6.5 m/s impact.

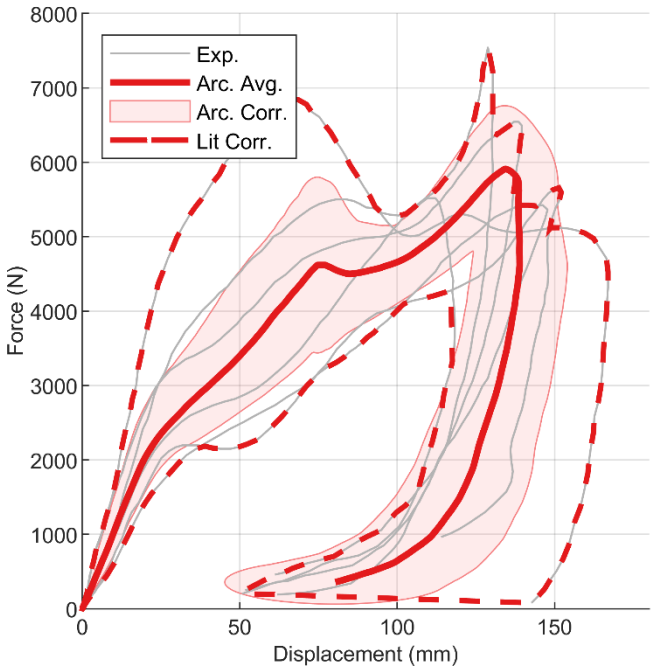

Fig. A-6. Average and ± 1 standard deviation corridor computed with the arc-length-based methodology compared to the corridor method published by [13] for the force-displacement response of PMHS thorax subject to a 9.3 m/s impact.