Inter-Subject Variability in the Brain's Response to Rotational Loading

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I. INTRODUCTION

Biomechanical experiments using post-mortem human subjects (PMHSs) are often aimed at quantifying an average time-history response by combining data from subjects within a target anthropometry, often applying scaling procedures to group subjects. The average response can be used to validate the kinematics of population-average physical dummies or finite element (FE) models of the human body (e.g. 50th percentile male), and inform the inter-subject variability of the kinematic responses of the body. Evaluating the inter-subject variability of biomechanical responses of soft organs is a more difficult task, because organ anatomy can vary substantially, even within subjects of the same skeletal anthropometry, and scaling procedures for soft organs are not well established. The objective of this study was to develop methods to generate an average time-history response and inter-subject variability of multiple sets of dynamic brain motion data.

II. METHODS

For this effort, we leveraged a dataset of in situ brain displacement from six PMHSs, measured using sonomicrometry in 12 matching dynamic rotational loading conditions [1]. In combining this data, we identified methods to reduce the test variability to isolate the variability of inter-subject biomechanical responses. There were three main sources of variation that we attempted to minimise: 1) variation in head kinematics, 2) differences in head geometry, and 3) the averaging of spatially scattered sensors. The variations due to head kinematics and sensor position account for unintended differences during testing, while the variation in head geometry accounts for inherent neuroanatomical differences among the specimens. Several numerical and statistical methods were employed to account for these variations, and the harmonisation procedure was implemented in sequential order. After combining the harmonised response, we calculated average responses that included the inherent subject variability caused by population differences in brain biomechanics.

Step 1: The PMHS tests were designed have consistent loading conditions, but differences in head mass and inertia lead to slight variation in the input head kinematics. To account for this variation, linear state-space transfer functions (TF) were generated in MATLAB (Mathworks Inc., MA, USA) to adjust each sensor displacement time-history to common loading input. The TF was estimated by using each subject's head angular velocity as the input and the experimental brain displacement as the output, using a non-linear least square fitting with enforced stability. CORA [2] was used to assess each TF by comparing the experimental displacement and the predicted TF displacement. Once the transfer functions were calibrated, they were used to transform the brain displacements to a common set of head kinematics for all subjects. The common kinematic input was chosen to be the average input of the six subjects. The average kinematics were not drastically different than each subject's kinematics (6.26% ± 4.78% in the magnitude of the peak angular velocity), which maintained the TF validity.

Step 2: To account for differences in head geometry, a morphing technique was implemented to match the shape and intracranial volume of each subject to a common brain anthropometric space by registering the inner skull surfaces to the cranial geometry of the Global Human Body Model Consortium (GHBMC) M50 v4.4 brain model [3]. Briefly, the cranial surfaces were registered to the GHBMC model using an iterative registration method, followed by a thin-plate spline method with a radial basis function to interpolate the 3D points. The method was recently introduced to generate subject-specific FE brain models of the subjects in this dataset [4]. The registration process was applied to the initial position and displacement time-histories (after the scaling process in Step 1).

Step 3: To account for the variation in sensor initial positions (even after registration), a common, average cluster initial position for each of the 24 sensors was computed. The displacement time-history at this common

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cluster point was calculated using inverse distance weighting (IDW) by using the 3D Euclidean distance (d_i) of the cluster point to each of the six subject sensor positions. A weighting factor was applied to the distances $w_i = \frac{1}{[d_i]^u}$, where the exponent was chosen to be $u = 3$ based on a calibration with synthetic data generated using simulated GHBMC model brain displacements under three loading conditions in the dataset (40 rad/s – 60 ms in the sagittal, coronal, and axial directions). The average and standard deviation displacement of the cluster points were calculated using IDW with the weighting factors using the following equations.

$$X_{avg} = \frac{\sum_{i=1}^{n} X_i * w_i}{\sum_{i=1}^{n} w_i}, X_{std} = \sqrt{\frac{\sum_{i=1}^{n} (X_i - X_{avg})^2 * w_i}{(n-1) * \sum_{i=1}^{n} w_i}} \quad (1)$$

III. INITIAL FINDINGS

The numerical transfer functions had an average CORA score of 0.88-0.92, indicating an excellent prediction to the original data. Once the transfer functions were created and validated, they were used to generate scaled responses for each crystal for each test for every subject for a common set of 12 head kinematics curves. The registration and morphing used to account for geometric differences among subjects did not significantly alter the initial position of the sensors, with a shift of less than 10 mm for all sensors. The final cluster point average responses were calculated after scaling the data using the kinematic transfer function, then normalising to a common anthropometric space, and lastly using the IDW method to average the displacement of all subjects with nearby data points. The displacement corridors for two cluster points for the 40 rad/s – 60 ms case under sagittal and axial loading are depicted in Fig. 1.

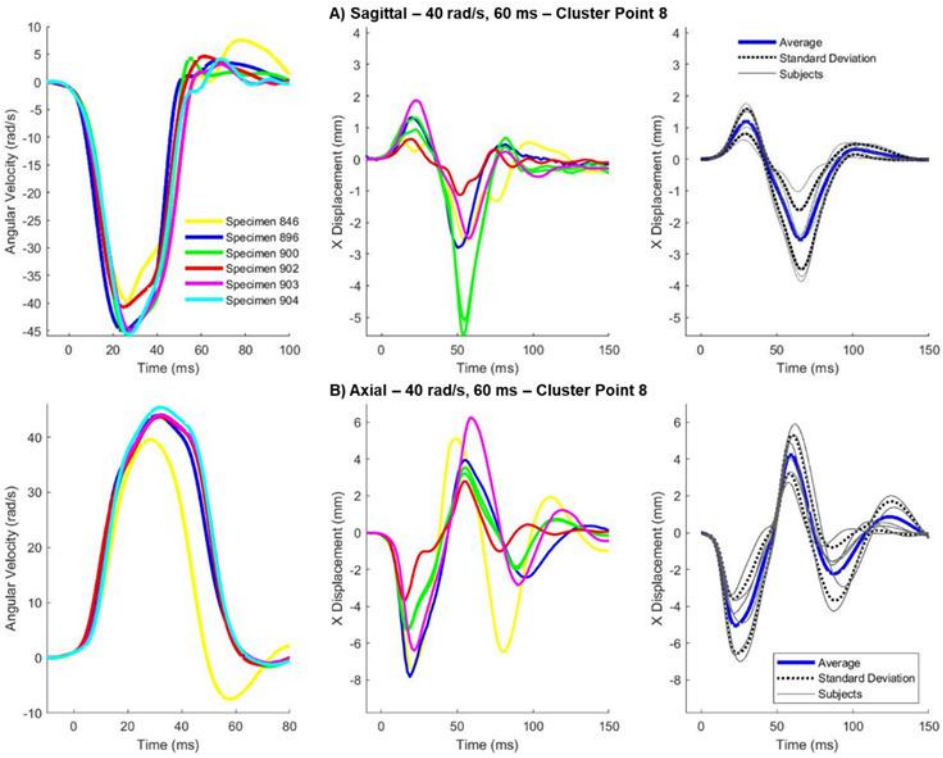

Fig. 1. The averaged 3D dynamic displacements for a cluster point for the 40 rad/s – 60 ms case for sagittal (A) and axial (B) rotations. The head kinematics (left) and associated subject-specific brain displacements (middle) are harmonised and used to compute the resulting average and standard deviation of the cluster point (right).

IV. DISCUSSION

Calculation of average time-history responses of PMHS biomechanics data to study population-variance are often confounded by unavoidable differences in test conditions and specimen geometry. While methods have been utilised in the biomechanics field to normalise this variation and apply results to a standardised anthropometric space, methods for soft tissue response at the organ level are not well established. This study investigates some methods to create average responses in a reliable set of dynamic brain displacement responses to represent the variability in the underlying dataset. This is a first step in understanding how population-average FE brain models can be evaluated against sample-average biomechanical data.

V. References

[1] Alshareef et al., J Neurotrauma,2020.
[2] Gehre et al., ESV Conference, 2009.
[3] Mao et al., J Biomechanical Engineering, 2013.
[4] Alshareef et al., Biomech & Modeling in Mechanobiology, 2021.