Comparison of Flexion–Extension Responses between Male and Female sub-Axial Cervical Spine Segments

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Comparison of Flexion–Extension Responses between Male and Female sub-Axial Cervical Spine Segments

Pranav Duraisamy, Davidson J. Jebaseelan, Jobin D. John

Abstract While finite element human body models enable virtual representation of diverse populations, validation of female models remains a challenge due to limited sex-differentiated experimental data. We modelled the segmental rotation of C3-C7 cervical spine segments at a flexion and extension load of 3 Nm using Bayesian linear regression. Results showed sex-dependent asymmetry in flexion and extension. In male segments, the differences between flexion and extension were minimal, while female segments exhibited greater flexibility in flexion (approximately 4° difference). When comparing flexion and extension separately, the rotation of male and female segments in extension tends to be similar. However, for flexion, the female rotation was 4.5° more than male in average. These findings suggest that female cervical spines may not be a volumetrically scaled version of male spines. The observed sexual dimorphism likely results from the asymmetry in load-bearing structures of the cervical vertebrae, where the articular processes limit the rotation in extension while there is no similar skeletal obstruction in flexion. The findings provide information for development and validation of HBM lineups that represent both sexes. This may be particularly relevant to investigating neck injuries in low-speed crashes where the kinematics tend to be close to physiological ranges. Despite limitations in sample size and unavailability of spinal measurements, through the use of a Bayesian approach that considers uncertainties in the analysis, this study provides insights to inform the development of more accurate sex-differentiated physical and virtual models.

Keywords Bayesian regression, Cervical spine, Segmental rotations, Sex-differences, Sexual dimorphism.

I. INTRODUCTION

Finite element (FE) human body models (HBMs) open new possibilities for representing wider sections of the human population through virtual testing. For instance, though the development of a physical crash test dummy representing an average female anthropometry was considered not feasible previously [1] there have been multiple virtual counterparts (both dummies and HBMs) representing the average female developed in recent years [2–5]. Many of the FE HBMs representing females are obtained through mesh morphing methods that transform the geometric coordinates of the nodes of an existing FE model to represent a new anthropometry [6–7]. This approach has also been used to obtain average female HBM from male or vice versa [3–4]. The validation of female models, however, remains a challenge because of the lack of female-specific experimental data – either because of the lack of experiments or because the biomechanical responses were analysed without differentiating for sex [8–9] Hence, sex-specific calibration and validation of the current female HBMs are either limited or non-existent.

This study addresses this lack of knowledge, with a focus on neck biomechanics. Neck injuries have been seen to have a gender-dependent pattern in traffic injuries with female tending to be at a higher risk of injury [10]. The flexion–extension rotation of cervical spine segments was the focus of this study. There are only few previous studies that have reported responses of female cervical spine segments. When this is available, it is common to consider the male and female segments together for reporting [11] or the responses are reported separately with no or limited comparison between the male and female segments [12–13].

The objective of this study was to quantify the differences between the male and female cervical spine

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segments in flexion and extension, with the goal to inform the ongoing developments of both physical and virtual models of the average female.

II. METHODS

Flexion–extension responses of lower cervical spine segments (C3-C7) from previously published experiments were analysed [12–13]. In these experiments, osteoligamentous spine segments (consisting of two vertebrae and the soft tissues in between them) from unembalmed post-mortem human subjects (PMHS) were loaded in pure moment loads after preconditioning. The raw data from these experiments was accessed from the United States National Highway Traffic Safety Administration (NHTSA) Biomechanics database (Table AI). This series consisted of spine segments from 16 female and 16 male post-mortem human subjects (PMHS). The female segments mostly consisted of C3-C4 and C5-C6 levels, while the male segments consisted mostly of C4-C5 and C6-C7 levels. (Table AII). The segments were tested repeatedly in flexion and extension; however, this is not expected to influence the results as the moment loading was limited to low moments of 3 Nm.

Bayesian Model and Analysis

Bayesian linear regression was used to model the rotation of cervical spine segments at a moment of 3 Nm. An exploratory visualisation of the data showed that the distributions of the female and male segmental rotations were different (Fig. A1). Hence, sex and loading mode (flexion/extension) were considered for the regression model. In addition, a multi-level (hierarchical) modeling approach was used to capture the effect of sex on flexion and extension.

$$R \sim L_i + l_{ij} + E \tag{1}$$

where *i* and *j* stands for loading mode (extension/flexion) and sex (female/male) respectively.

$$R = \text{segmental rotation angle at 3 Nm}$$

$$L_i = \text{coefficient for loading mode}$$

$$l_{ij} = \text{coefficient for loading mode specific to the sex}$$

$$E = \text{residual random error}$$

The common effect, the loading term L_i is defined as

$$L_i \sim \text{Normal}(\mu_i,\ \sigma_i) \tag{2}$$

$$\mu_i = \begin{cases} 5.3 & \text{for Extension} \\ 5.8 & \text{for Flexion} \end{cases}$$

$$\sigma_i = \begin{cases} 2.3 & \text{for Extension} \\ 2.9 & \text{for Flexion} \end{cases}$$

The loading mode effects are specific to the sex. In other words, the effect of the predictor loading mode varies for each sex (group effect).

$$l_{ij} \sim \text{Normal}\big(0,\ \sigma_{l_i}\big) \tag{3}$$

The hyperprior is given by

$$\sigma_{l_i} \sim \text{HalfNormal}(\tau_i)$$

$$\tau_i = \begin{cases} 2.3 & \text{for Extension} \\ 2.9 & \text{for Flexion} \end{cases}$$

The residual error is given by, $E \sim \text{Normal}(0,\ \sigma)$, $\sigma \sim \text{HalfStudentT}(\nu,\ \sigma)$ with ν = 4, σ = 3.4, computed as weakly informative.

Information on cervical spine segmental stiffness from other studies was used to define the priors. The priors were centered on the means for flexion and extension reported in [14]. This study, however, consisted of only Male PMHS data and hence the standard deviations of the priors were defined to be 1.5 times of that reported in [14] . This served as weakly informative priors. Distributions of the priors are shown in Figure A2. MCMC NUTS Sampler was used for model fitting, sampling the joint posterior distribution of the parameters. Tuning draws were done for step size adaptation initially, which was discarded later and not included in inference data. The Bayesian model was fit using 4 MCMC chains, each with 1500 draws. Python package Bambi (v0.14.0) was used for building the Bayesian models [15].

The female and male posterior predictive distributions in flexion and extension were used to evaluate the differences in responses.

III. RESULTS

The posterior distribution was verified using various checks as follows. The posterior predictive distributions after the model was fit compares well with the distribution of observed data from experiments (Fig. A4). R_hat and Effective Sample Size (ESS) were used to evaluate the chains [16]. The summary of the inference data, with description of R_hat and ESS values are given in Table AIII. The marginal posterior distributions for predictors/regression coefficients and the path traced by the sampler are shown as trace plot (Fig. A5).

The posterior distributions for 94% High Density Interval (HDI) are shown in Fig. 1. For the common-level effects, the mean rotation in flexion is similar to extension, with the HDI overlapping. For the group-level effects, the distributions of the coefficients for females were seen to be different than males, with flexion showing lesser overlap than extension.

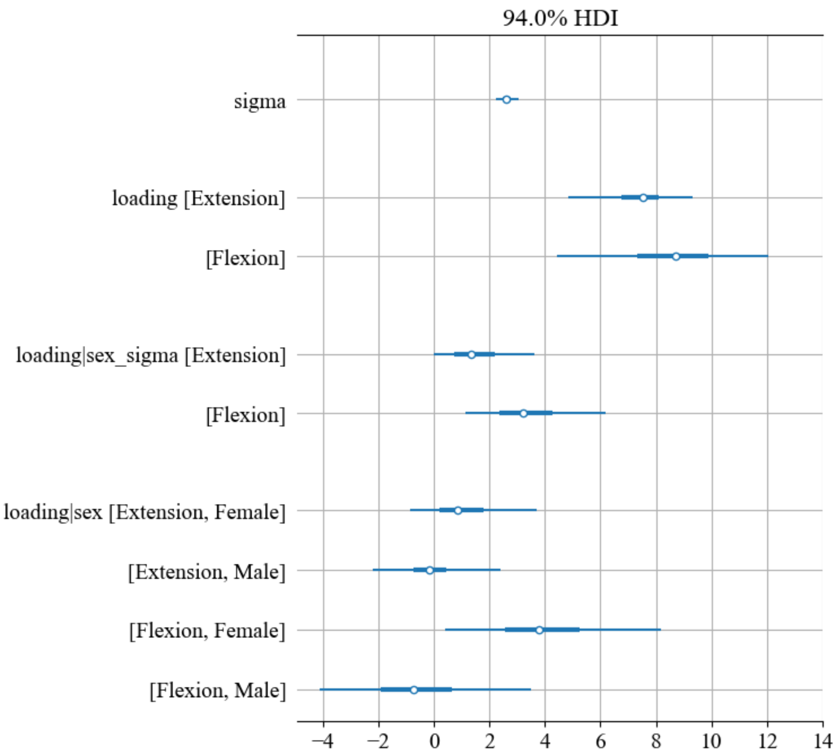

Fig. 1. Posterior distributions of the model parameters, shown with the mean and 94% High Density Internal (HDI)

The posterior predictive distributions are shown for loading mode (flexion/extension) and sex in Fig. 2 and 3, respectively. Contrast distribution is the difference between the two posterior predictive distributions being compared. First, the difference between flexion and extension for each sex was compared (Fig. 2). With a difference of less than 1° between them, flexion and extension were not dissimilar for male. However, the female cervical segments showed a distinction in responses, with the segmental rotations in flexion being more flexible by an average of 4° approximately. Second, the difference between female and male was made for each of the loading scenarios (flexion and extension). In extension, the male and female were different only by 1.2° with part of the contrast distributed across zero. On the other hand, for flexion, the female segments were about 4.5° more flexible.

IV. DISCUSSION

Bayesian approaches to modeling data give the opportunity to include domain knowledge in the modeling workflow. Previous scientific knowledge can be used in modeling through the use of informed priors. With the traditional focus on the average male anthropometry, most of the experimental corridors are typically scaled to an average male even when female samples are part of the study. Given the lack of female-specific biomechanical corridors for many body regions and load cases, Bayesian approaches can serve as an approach to estimate sex-differences with limited data or biomechanical principles.

Mean and standard deviation used to define priors in this study were taken from another study that had segments tested in the range of 3 Nm [14]. Even though the priors were centered around the flexion and extension-specific means, they were defined with wider standard deviations to serve not as strong priors. This was done to account for the lack of female PMHS and also to consider the larger uncertainties when female PMHS were included in previous studies [11]. Study [11] was not considered for priors as the experiments were performed only till a maximum of 2 Nm.

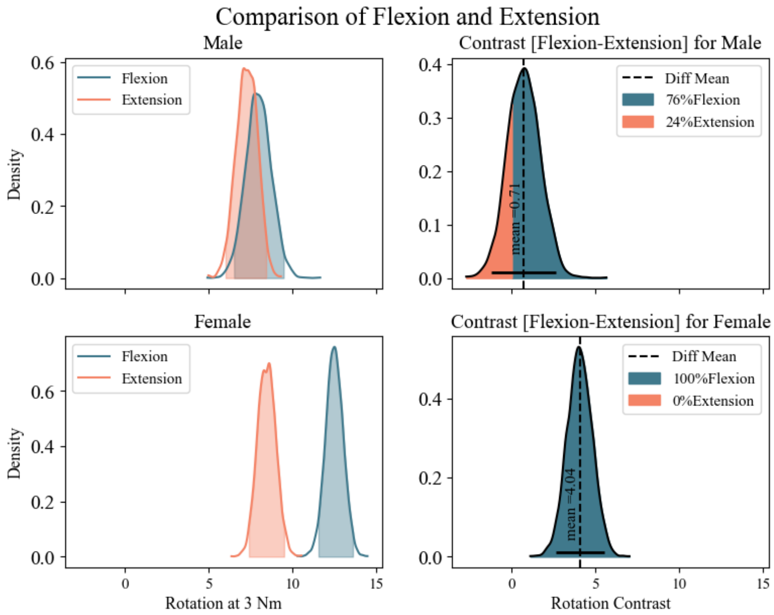

Fig. 2. Posterior predictive distributions of flexion and extension cervical spine segmental rotations (in degrees) at 3 Nm and their contrasts, corresponding to (top) Male and (bottom) Female.

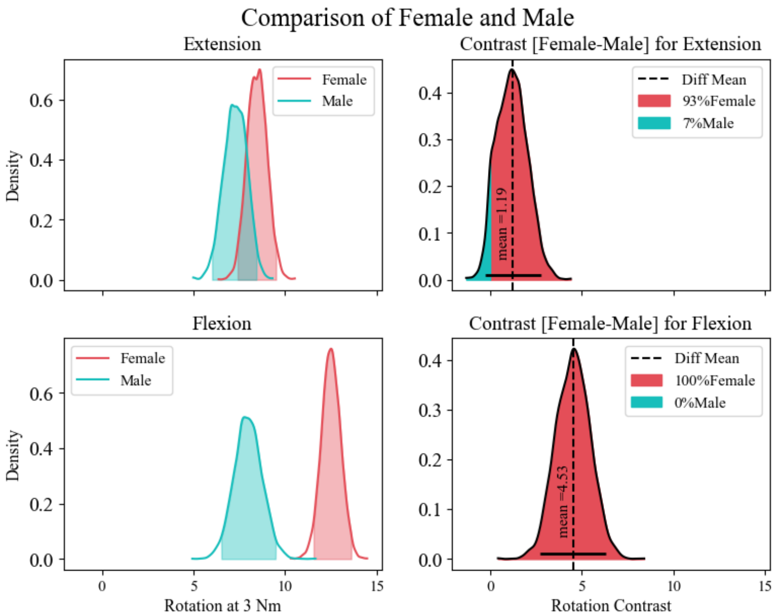

Fig. 3. Posterior predictive distributions of female and male cervical spine segmental rotations (in degrees) at 3 Nm and their contrasts, corresponding to (top) Extension and (bottom) Flexion.

Sex-dependent Cervical Spine Biomechanics

The posterior predictive distributions show that sub-axial cervical spine segments exhibit sex-dependent asymmetry in their flexion–extension response. While the male flexion and extension has overlapping distributions, the female responses did not show similar overlap indicating potential differences in the load-bearing patterns between male and female segments (Fig. 2). This is evident in the contrast plot while comparing the differences between male and female distributions in extension (Fig. 3). When compared to flexion, it has an overlap and the difference between male and female extension is negligible (partly distributed across zero). This indicates that the female and male cervical spine segments are more similar when loaded in extension, than in flexion.

This difference could perhaps be attributed to the asymmetry in the spinal structure. In extension, the articular processes in the posterior part of the vertebra provide interfaces for intervertebral interaction and load bearing through the articular processes. In flexion, however, there are no similar load bearing skeletal structures and the resistance to deformation is provided by soft tissues. For a moment of 3Nm applied on a cervical spine segment, the rotation in a smaller-sized female can be restricted by the articular processes, while there will be no similar restriction in flexion. In addition, he vertebral structures in the anteroposterior direction are shown to have sex-dependent variations, with males exhibiting longer dimensions [17–19]. Hence, the soft tissues (intervertebral disc and ligaments) resisting load in flexion may exhibit sex-dependent variations, such as longer moment arm for ligaments in a male spine segment resulting in lower rotation.

Considerations for Human Body Models

The findings in this study provide the basis for validation of the recent female models, which so far lack sex-dependent validation of the cervical spine [4,20]. Given the asymmetry in flexion-extension between male and female cervical spine segments, morphed HBMs may need to verify that derivative models capture this asymmetry in cervical spine rotations, especially where cervical spine injuries are investigated. This may be important to consider in low-speed crashes, where whiplash-associated disorders are commonly reported to have sex-based differences, and where the cervical spine kinematics tend to remain closer to the physiological ranges of motion similar to this study.

Limitations

Although the study made an attempt to quantify sex-differences in cervical spine flexion–extension kinematics, the analysis is based on the limited number of PMHS that lack other anatomical information such as spinal dimensions that could influence the spinal rotations. It should also be noted that in the experimental data, the male segments consisted more of the lower cervical spine levels. Whether the level of cervical spine segment acts as a confounding factor needs to be further evaluated. An initial evaluation with the data used as priors did not show any relationship (Fig A10). Also, female PMHS can be expected to have smaller vertebral and intervertebral dimensions that can influence the segmental rotations. It could as well be the case that a proportion of the differences shown in Fig. 2 and 3 could arise from variations in morphological measurements such as vertebral depth and disc height. However, as these measurements are not available from the experiments currently reported in literature, the estimates in this study quantify the overall difference in sub-axial cervical spine rotations between men and women.

V. CONCLUSION

This study used a Bayesian model to analyse cervical spine segmental rotations and identified sex-dependent asymmetry in flexion–extension response. The sexual dimorphism in spinal rotations show that the female cervical spine segmental kinematics cannot be considered as size-scaled versions of male.

VI. SUPPELMENTARY MATERIAL

Code and data used for the analysis is available at https://github.com/pranavduraisamy/cervical-segmental-stiffness-ircobi

VII. ACKNOWLEDGEMENTS

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IX. APPENDIX

Data and Exploratory Analysis

A brief overview of the experiments performed in [12,13] is given here. The cervical spine segments were sectioned from unembalmed human cadaveric cervical spines. Before the experiments, surrounding musculatures were cleaned and cast into aluminium cups with fiber reinforced polyester resin. A testing apparatus with a couple of free-floating pneumatic pistons, were used to apply pure bending moments to the superior cast. The inferior cast was rigidly attached to the base of the test frame by threaded fasteners. A counterweight balances the mass of the assembly and applies 0.5N of tension to the upper cast after mounting. Same apparatus is used for all the studies. The specimens were preconditioned and tested for quasistatic load of different magnitudes. Angular displacement data was acquired using digital camera. The specimens were preconditioned with 30 cycles of +/-1.5 Nm of moment. Then each specimen was loaded with pure flexion and extension moments in approximately 0.5 Nm increments. A creep of 30 s was allowed prior to data acquisition, and the load was released between load steps. The peak applied moment was approximately 3.5 Nm.

The data was accessed from the NHTSA Biomechanics database through API (Table AI). It is found that for each test the data was recorded at random intervals, so linear interpolation was done to find the rotation angle at 3 Nm. Female segments were tested for both flexion and extension in a single test, whereas male FSUs were evaluated separately for flexion and extension in distinct tests. To generalise the data, Female segmental responses were split into two separate rows/records with 'f' denoting flexion and 'e' denoting extension, appended to the test ID. To maintain relative scale, All the responses were taken as absolute values.

After filtering and processing, there were 48 female and 29 male FSUs (Table AII) from 16 female and 16 male PMHS. Out of which 36 are tested for flexion while 41 are tested for extension.

TABLE AI
NHTSA BIOMECHANICS DATABASE TEST IDS

Sex	Loading Mode	Test ID
Female	*Extension & Flexion* *	4394, 4396, 4429, 4431, 4911, 4913, 6349, 6350, 6366, 6368, 6374, 6376, 6380, 6382, 6452, 6454, 6460, 6462, 6466, 6468, 6474, 6476, 6482, 6484
Male	*Extension*	6356, 6358, 7398, 7404, 7407, 7413, 7422, 7431, 7452, 7461, 7465, 7474, 7477, 7483, 7486, 7492, 7495
Male	*Flexion*	6356, 6358, 7400, 7406, 7409, 7415, 7424, 7436, 7445, 7476, 7497, 7506

** Both responses were recorded on the same test ID for females*

TABLE AII
COUNT DATA

Cervical Level	Male		Female	
	Flexion	Extension	Flexion	Extension
C3C4	1	1	11	11
C4C5	6	11	1	1
C5C6	1	1	11	11
C6C7	4	4	1	1

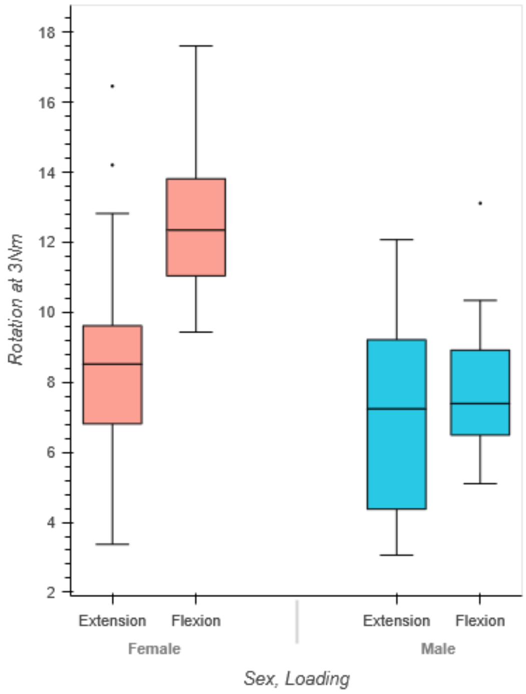

Fig. A1. Box Plot representation of segmental rotation (in degrees) at 3 Nm

Bayesian Analysis – without Age

TABLE AIII
INFERENCE DATA SUMMARY

Variables	Mean	S.D.	HDI_3%	HDI_97%	ESS_bulk	ESS_tail	R_hat
sigma	2.64	0.23	2.23	3.06	4645	3705	1
loading [Extension]	7.35	1.19	4.83	9.31	2151	1817	1
loading [Flexion]	8.52	2	4.43	12.03	2381	2917	1
loading|sex_sigma [Extension]	1.59	1.12	0	3.63	1925	1958	1
loading|sex_sigma [Flexion]	3.45	1.45	1.13	6.19	2694	3061	1
loading|sex [Extension, Female]	1.12	1.26	-0.84	3.72	1994	2205	1
loading|sex [Extension, Male]	-0.07	1.16	-2.2	2.42	2423	2270	1
loading|sex [Flexion, Female]	4	2.06	0.43	8.18	2377	2975	1
loading|sex [Flexion, Male]	-0.53	2.01	-4.1	3.52	2551	2991	1

R-hat diagnostic for all the predictors were found to be 1, which indicates the model has converged and all chains have mixed effectively in MCMC sampling process. Effective sample size in the bulk and tail regions were greater than 200 (4 chains x 50), which ensures that the sampled data and inference of the model are sufficiently reliable.

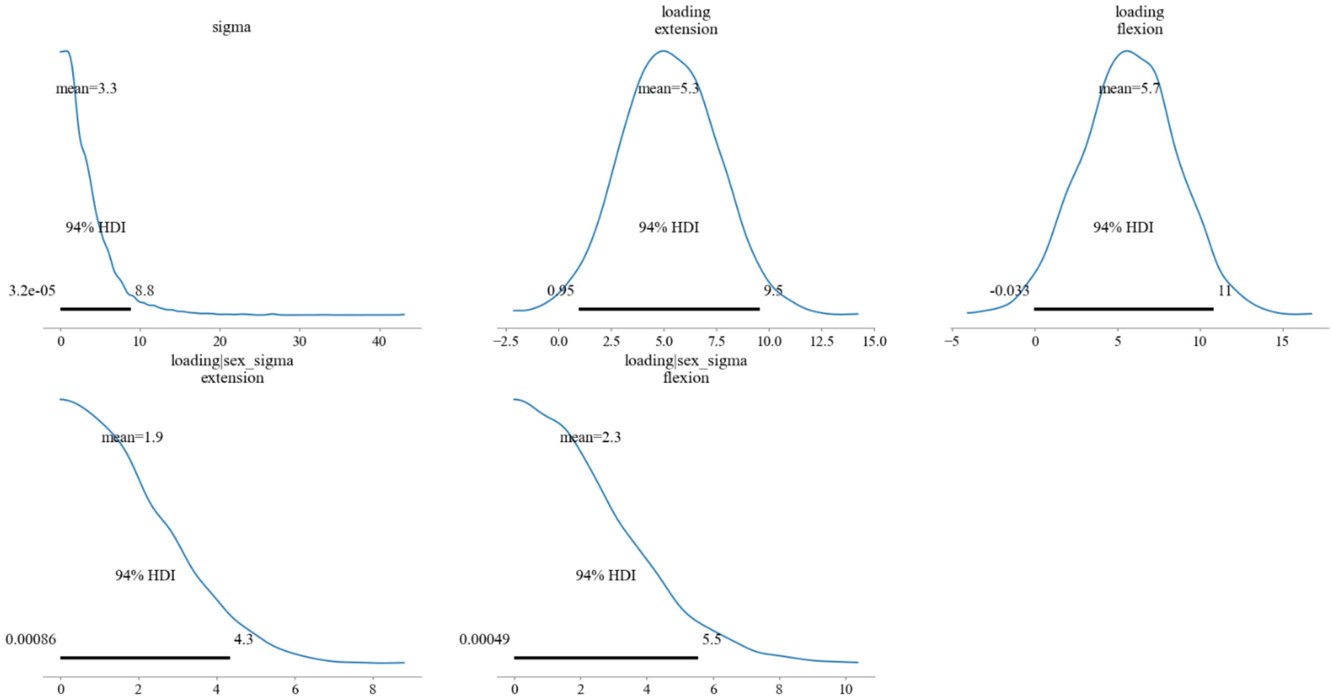

Fig. A2. Prior Distribution for regression coefficients

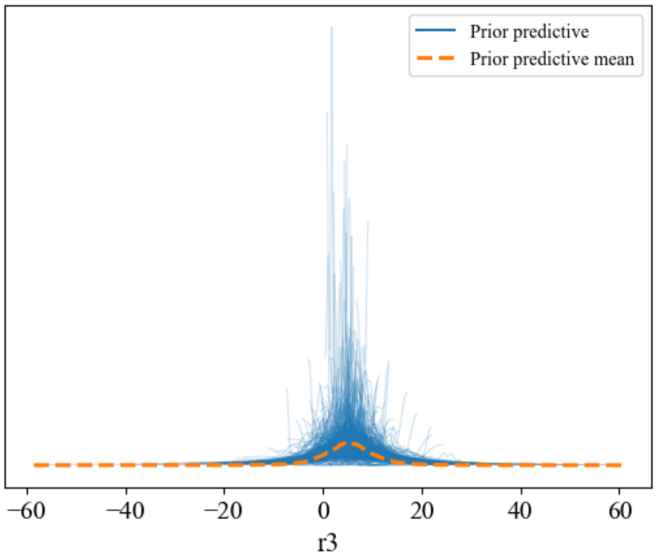

Fig. A3. Weakly informative Prior Predictive distribution, showing the distribution of rotation at 3 Nm, before fitting the model.

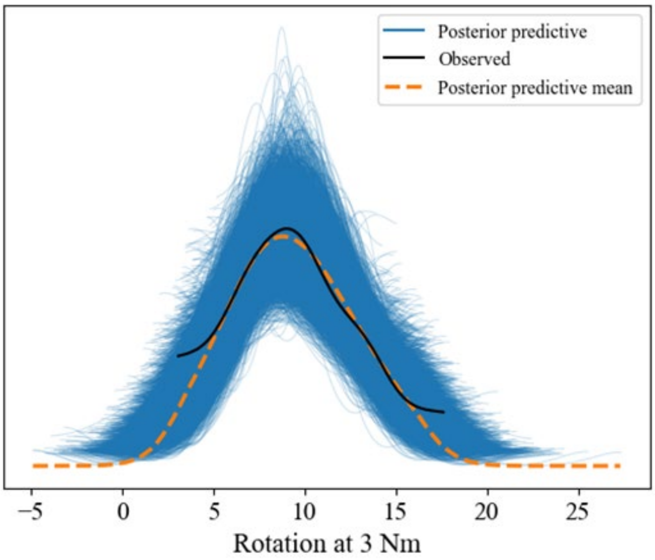

Fig. A4. Posterior Predictive Curves, showing the distribution of rotations at 3 Nm after the model is fitted

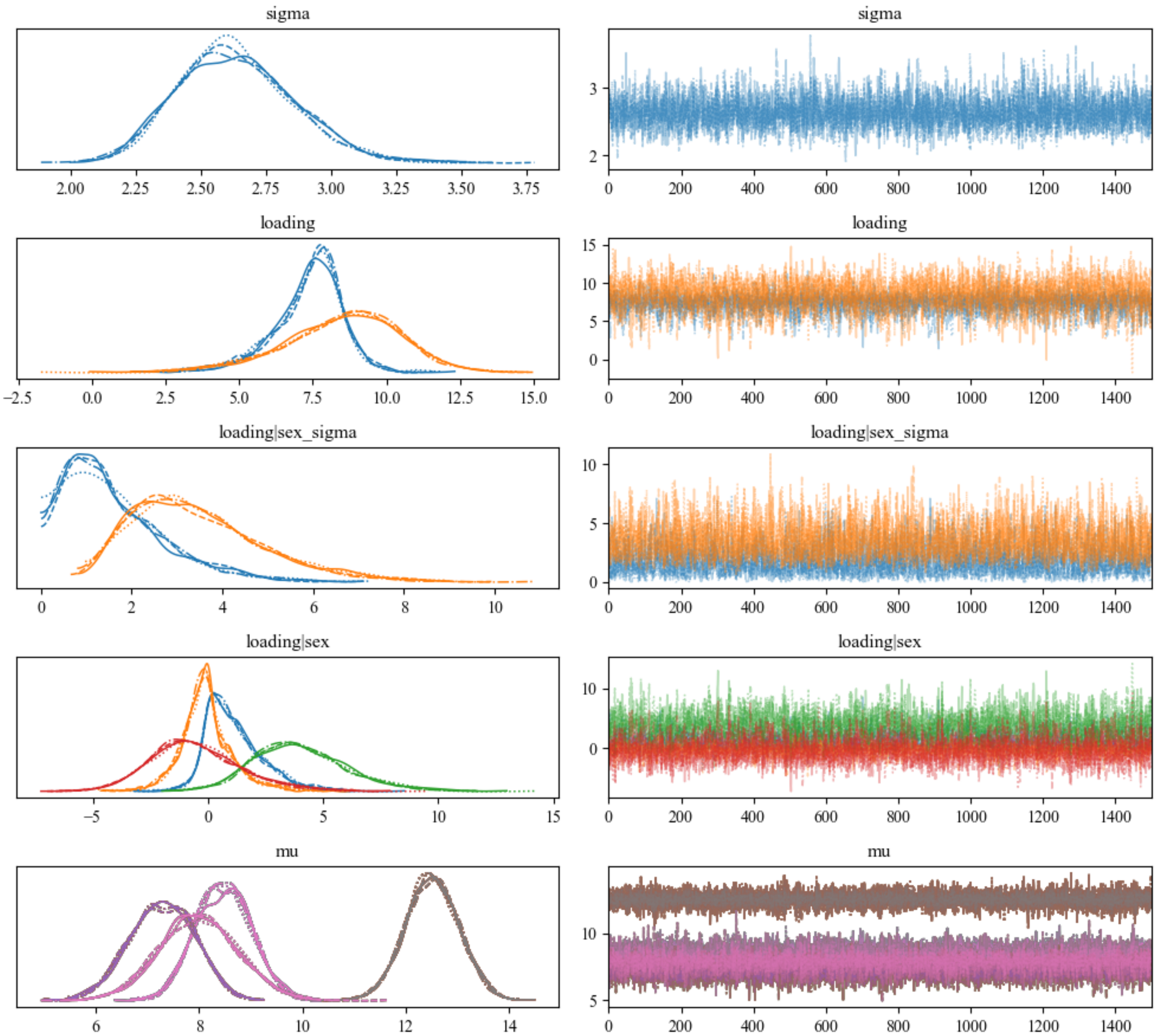

Fig. A5. (a) Left: Marginal posterior distribution for all parameters in the model. (b) Right: Sampling paths

Bayesian Analysis – with Age

TABLE AIV

INFERENCE DATA SUMMARY

Variables	Mean	S.D.	HDI_3%	HDI_97%	ESS_bulk	ESS_tail	R_hat
sigma	2.66	0.23	2.24	3.08	4719	4047	1
age	0.01	0.03	-0.05	0.06	3477	3442	1
loading [Extension]	7.08	1.71	3.80	10.23	3428	3443	1
loading [Flexion]	8.36	2.16	4.40	12.51	3745	3642	1
loading|sex_sigma [Extension]	1.59	1.10	0.00	3.60	2511	2138	1
loading|sex_sigma [Flexion]	3.36	1.40	1.01	5.88	3425	3532	1
loading|sex [Extension, Female]	1.03	1.24	-0.95	3.66	3574	3876	1
loading|sex [Extension, Male]	-0.24	1.22	-2.68	2.18	4173	4122	1
loading|sex [Flexion, Female]	3.80	2.10	0.18	8.08	3807	3642	1
loading|sex [Flexion, Male]	-0.81	2.15	-4.92	3.30	3902	3983	1

The model's performance remains identical despite the inclusion of age as a predictor. The model's outputs are hardly affected by age, as the coefficient/slope is negligible. All other coefficient's values were not influenced by the inclusion of age as a predictor in the model. The prior predictive distribution became much wider when age is included (Fig A7).

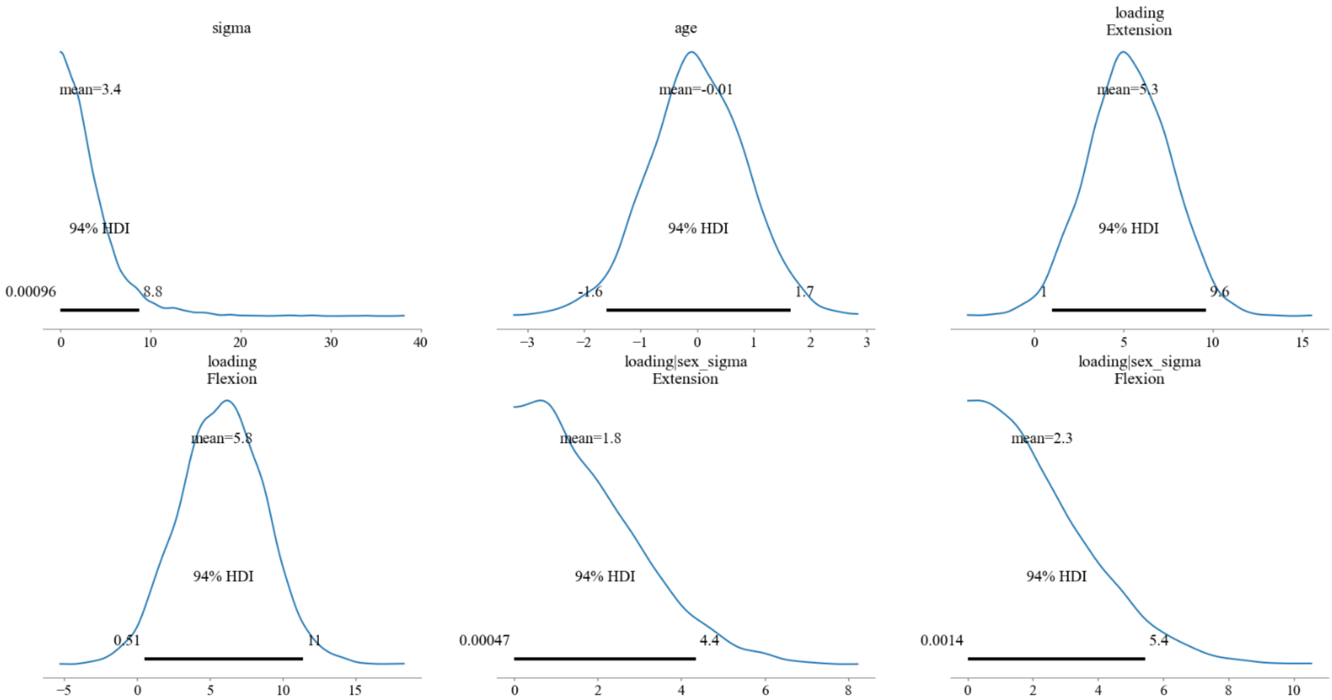

Fig. A6. Prior Distribution for regression coefficients

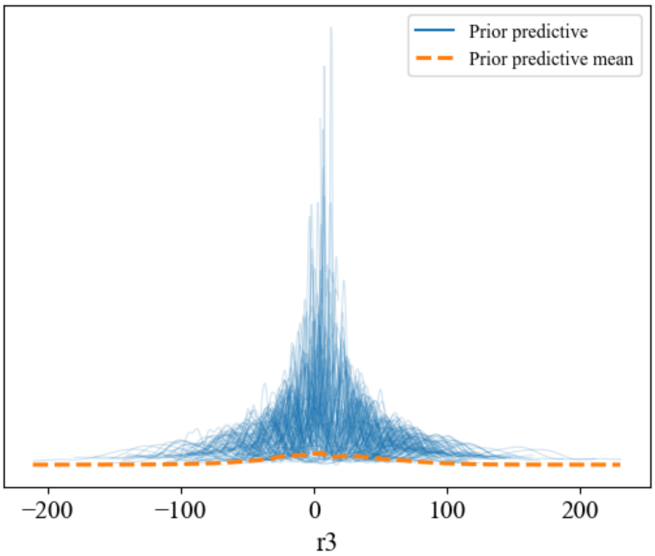

Fig. A7. Prior Predictive Curves for fitted model

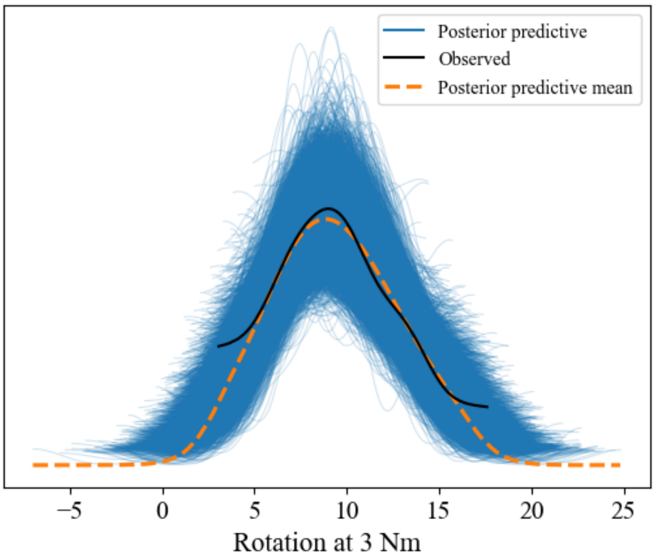

Fig. A8. Posterior Predictive Curves for fitted model

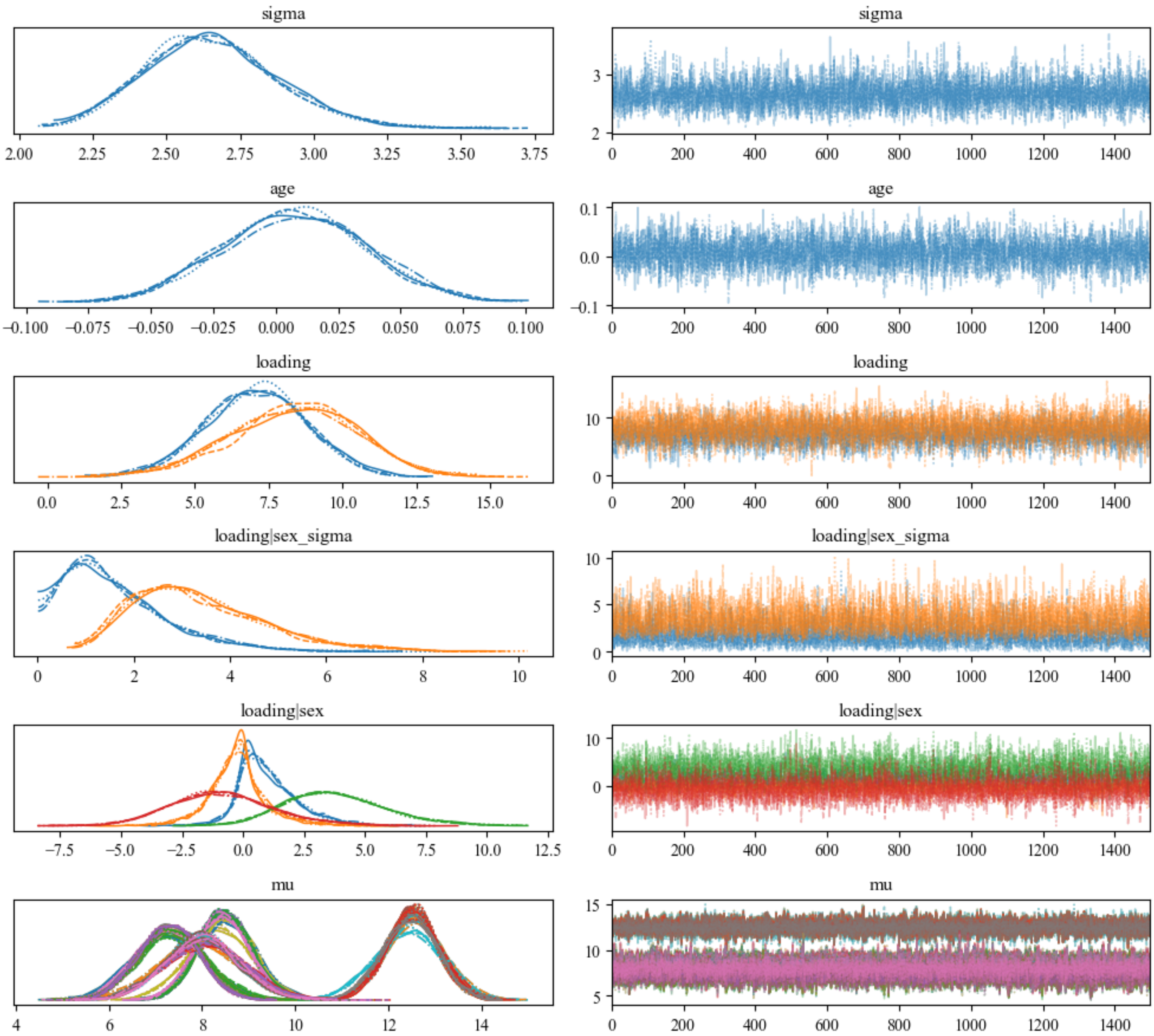

Fig. A9. (a) Left: Marginal posterior distribution for all parameters in the model. (b) Right: Sampling paths

Effect of Height and Weight on Rotation

To understand the influence of anthropometry on the cervical spine segmental rotation, the rotation at 3 Nm from [14] is shown in Fig A10. This information is not reported in other studies unfortunately and limits our ability to study the size and gender effects. Future studies will also need to consider local morphological dimensions of spine segments for analysis.

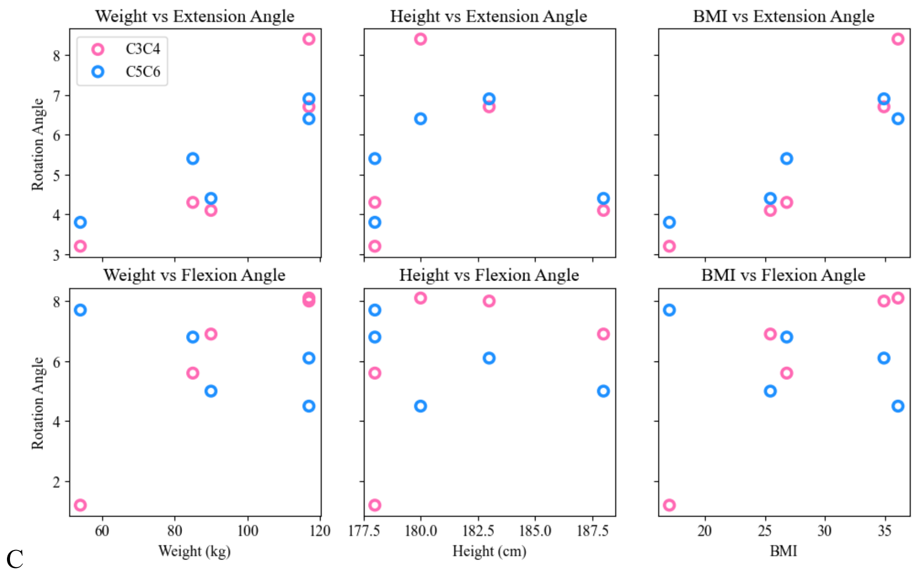

Fig. A10. Segmental rotation at 3 Nm from [14], with respect to weight, height, and BMI (top) Extension (bottom) Flexion