S.I.: Concussions

**Piecewise Multivariate Linearity Between Kinematic Features and Cumulative Strain Damage Measure (CSDM) Across Different Types of Head Impacts**

**XIANGHAO ZHAN,**1 **YIHENG LI,**2 **YUZHE LI,**1 **NICHOLAS J. CECCHI,**1 **OLIVIER GEVAERT,**2,3 **MICHAEL M. ZEINEH,**4 **GERALD A. GRANT,**5 and **DAVID B. CAMARILLO**1

1Department of Bioengineering, Stanford University, Stanford, CA 94305, USA; 2Department of Biomedical Data Science, Stanford University, Stanford, CA 94305, USA; 3Stanford Center for Biomedical Informatics Research, Stanford University, Stanford, CA 94305, USA; 4Department of Radiology, Stanford University, Stanford, CA 94305, USA; and 5Department of Neurosurgery, Stanford University, Stanford, CA 94305, USA

(Received 4 February 2022; accepted 12 July 2022; published online 3 August 2022)

Associate Editor Stefan M. Duma oversaw the review of this article.

**Abstract**—In a previous study, we found that the relationship between brain strain and kinematic features cannot be described by a generalized linear model across different types of head impacts. In this study, we investigate if such a linear relationship exists when partitioning head impacts using a data-driven approach. We applied the $K$-means clustering method to partition 3161 impacts from various sources including simulation, college football, mixed martial arts, and car crashes. We found piecewise multivariate linearity between the cumulative strain damage (CSDM; assessed at the threshold of 0.15) and head kinematic features. Compared with the linear regression models without partition and the partition according to the types of head impacts, $K$-means-based data-driven partition showed significantly higher CSDM regression accuracy, which suggested the presence of piecewise multivariate linearity across types of head impacts. Additionally, we compared the piecewise linearity with the partitions based on individual features used in clustering. We found that the partition with maximum angular acceleration magnitude at 4706 rad/s$^2$ led to the highest piecewise linearity. This study may contribute to an improved method for the rapid prediction of CSDM in the future.

**Keywords**—Clustering, $K$-means, Kinematics, Traumatic brain injury, Impact clusters.

**INTRODUCTION**

Traumatic brain injury (TBI) has become a growing public health problem with high mortality and morbidity, as well as a socio-economic problem causing enormous diagnosis and treatment expenses worldwide. In the United States, TBI contributed to a third of all injury-related deaths, affecting 1.7 million people annually. Without directly causing death or disabilities, mild TBI (mTBI), which presents less severe symptoms and is harder to detect and diagnose, is also associated with severe consequences, leading to a form of silent pandemic: evidence has suggested that mTBI can lead to unconsciousness immediately after a head impact and can further result in post-concussive symptoms including cognitive deficits and emotional challenges as well as the risk of long-term neurodegenerative diseases such as Parkinson’s and Alzheimer’s diseases. The causes of TBI/mTBI are not limited to vehicular accidents and military combat, as they can also be sustained in contact sports such as football, mixed martial arts (MMA), ice hockey, water polo, lacrosse, and more. Considering the severity and prevalence of TBI, fast diagnosis and early warning approaches are crucial to preventing repetitive TBI, as the in-time intervention following the early detection can attenuate injury severity to a significant extent.
Because of the thick and hard skull of human beings, the stress wave caused by the direct contacts of head impacts cannot pass the skull and reach the brain. Instead, the mechanical loading resulting from the brain inertia associated with the rapid rotation of skull can trigger the physiopathology of mTBI. Therefore, the brain deformation only depends by the head kinematics. However, due to the complicated structure of head and the viscoelasticity of brain tissue, the relationship between the brain deformation and the head kinematics has not been clearly represented with definite mathematical models. Previous studies simplified the brain dynamics with different assumptions and proposed reduced-order models to estimate the severity of brain deformation, and the machine learning technologies were applied to predict the brain strain based on the head kinematics and the machine learning technologies were applied to predict the brain strain based on the head kinematics. In previous studies, we observed promising linear relationships between some kinematic features and 95th percentile maximal principal strain (MPS95) within a specific type of head impacts, and the linear relationship (slope and interception) varied significantly among different types of head impacts. This result showed that linear relationship existed within the domains defined by the types of head impacts, that is, the linear relationship can vary across different domains. Because of the similar loadings, the kinematic features in the same domain share common characteristics. Therefore, brain strain can be linearly correlated to certain kinematic features. For example, the linearity between MPS95 and angular acceleration peak was found most evident in football, while the linearity between MPS95 and angular velocity peak was found most evident in MMA. This is assumed to be owing that the durations of impact in football were longer than those in MMA, and the different durations led to different correlations.

In head impacts, the head kinematics depend on both impact loadings and head–neck–shoulder system. Across different types of impacts, the impact loadings vary significantly according to considerable factors including the weight, the speed, and the stiffness of impact objects, the helmet types (or bare head), and the frequent impact directions. As results, independent linear relationships were observed with the domains associated with the types of head impacts. Furthermore, the head kinematics are also decided by the properties of the head–neck–shoulder system, like the rotational stiffnesses of the neck and the moving instantaneous rotation of head. Since factors from the head–neck–shoulder system keep the same in different head impacts, kinematic features may share similar characteristics across different types of head impacts. Therefore, it is possible that domains with a linear relationship between brain strain and kinematic features existed across different types of head impacts.

To find these domains, piecewise multivariate linearity in the domains of data-driven partitions was measured. We firstly partitioned our datasets into 80% training data and 20% test data and then on the training data, we applied the $K$-means clustering algorithm with 16 kinematic features extracted from the head impacts in college football, MMA, car crashes, and simulations to re-partition them into different clusters based on the characteristics of kinematic features instead of their source. Then, using the ridge regression models developed for each cluster on the training dataset, we measured the piecewise multivariate linear relationship between kinematic features and brain strain metrics with the data-driven partitions as well as the original partitions according to the types of head impacts on the test impacts. The entire process was done in 20 parallel experiments with random dataset partitions to test statistical significance. Significantly higher piecewise linearity between the cumulative strain damage measure (CSDM) and kinematic features was found in the data-driven partitions instead of the original partitions based on impact sources, which suggested different mechanisms leading to CSDM in data-driven partitions. Furthermore, the crucial kinematic features for clustering and the corresponding critical values were calculated and analyzed.

**METHODS**

**Data Description**

To investigate a variety of head impact types, kinematics from a total of 3161 head impacts from 4 different impact sources were collected: 2130 lab-reconstructed impacts from a validated finite element head model (FEHM) of the Hybrid III anthropomorphic test dummy headform (dataset HM), 15 302 video-confirmed college football impacts recorded by the Stanford instrumented mouthguard (dataset CF), 3,23,24 457 video-confirmed mixed-martial-arts impacts recorded by the Stanford instrumented mouthguard (dataset MMA), 28,38 and 272 reconstructed impacts from National Association for Stock Car Auto Racing (dataset NASCAR). 34

Finite-element (FE) modeling is a state-of-the-art tool for the biomechanical modeling of brain strain during head impacts, and we applied the validated KTH head model to calculate CSDM. Different from MPS and strain rate type metrics that show the most severe deformation of brain tissue, CSDM describes the volume ratio of brain tissue that exerted brain strain.
strain exceeding a certain level and indicates severity of entire brain deformation. In this study, CSDM indicated the volume fraction of the brain with MPS exceeding the threshold of 0.15. Previous work has found CSDM to be an effective predictor of injury, especially for more severe head impacts, and has also been widely used to evaluate risk of head impacts. It should be mentioned that the ground truth CSDM values in this study are calculated by the percentage of brain elements with MPS larger than 0.15 based on the KTH FE modeling. To be specific, if all the brain elements are with MPS larger than 0.15, the CSDM is 1. The distribution and summary statistics of CSDM across four different datasets are shown in Fig. 1. It can be seen that the four datasets show high variance in the CSDM distribution: dataset HM has a higher mean CSDM value and a large portion of HM datasets have a CSDM larger than 0.1/0.2/0.3. Datasets CF and MMA generally have smaller CSDM values but the maximum CSDM values of these two datasets are higher than that in datasets HM and NASCAR.

**Kinematic Feature Extraction**

The head kinematics of impacts are described by groups of features, which are extracted from the curves of translational and rotational kinematics. In this study, two sets of the kinematic features were used: the clustering features set and CSDM regression features set. In clustering features set, 16 kinematic features listed in Table 1 were selected because they are not fully inter-dependent and capable to represent the characteristics of the head impact kinematics. In the CSDM regression features set, more features were adopted including the temporal features and the spectral features.

Previous studies have shown that the temporal features as well as multiple brain injury criteria (BIC) derived from the temporal information, are effective in brain strain estimation. Further, the spectral densities have been found to be effective in classifying the source of head impacts although the predictive power of strain based on these temporal features may not be as high as those temporal features. Therefore, to get an accurate CSDM estimator that can be generalizable across different types of head impacts, in this study, we extracted both temporal and spectral features from the kinematics to leverage the advantages from both types of features and let the regression models leverage these features in a data-driven manner.

The temporal features include the peaks of four types of kinematics: (1) the linear acceleration at the brain center of gravity \(a(t)\), (2) the angular velocity \(\omega(t)\), (3) the angular acceleration \(\alpha(t)\) and (4) the angular jerk \(j(t)\). To calculate the angular jerk, we took a numerical derivative of the angular acceleration with a five-point stencil numerical derivative equation. For each kinematic type, the peaks of four channels were extracted: the components in three axes \((x: \text{anterior-to-posterior}, y: \text{left-to-right}, z: \text{sagittal-to-inferior})\) and the magnitude. To account for non-linearity in the relationship between kinematics and brain strain, we included the square-root and squared features based on the features previously mentioned, because our previous study has shown that the first-power, squared-root, and second-power features are the most predictive of brain strain. The kinematic features selected are based on our previous study on the statistical analysis over the contribution from kinematics factors in prediction of strain. The linear acceleration does not contribute to brain strain, but it includes the information of head impacts. Considering the head impacts are clustered according to their similarity in kinematics instead of contribution to the brain strain and the regression model can decide the contribution of linear acceleration by itself with the current data-feature ratio, we adopted the features based on linear acceleration.

The spectral features were extracted from these four kinematics types in a similar manner as shown previously, but we further optimized this feature extraction approach by adding the number of frequency windows. This allowed more detailed information in the low-frequency range to be extracted: we set 19 frequency windows with a width of 20 Hz from 0 to 300 Hz, and with another width of 50 Hz from 300 to 500 Hz (the Nyquist frequency). In each frequency window, the mean spectral density was extracted.

Furthermore, we extracted 15 BIC which can be regarded as the mathematically transformed temporal features because they were justified to be effective in brain strain estimation, severity index (SI), head injury criterion (HIC), generalized acceleration model for brain injury threshold (GAMBIT), head impact power (HIP), principal component score (PCS), kinematic rotational brain injury criterion (BRIC), power rotation HIC (PRHIC), Kleiven’s linear combination (KLC), rotational injury criterion (RIC), Brain injury criterion (BrIC), the combined probability of concussion (CP), rotational velocity change index (RVCI), the convolution of the impulse response for brain injury criterion (CIBIC), diffuse axonal multi-axis general evaluation (DAMAGE), and brain angle metric (BAM).

Therefore, a total of 367 features were included in the CSDM regression features set (48 temporal features: 4 kinematic types \(\times 4\) channels \(\times 3\) powers; 304 spectral features: 4 kinematic types \(\times 4\) channels \(\times 19\) frequency windows; 15 BIC). Additionally, we tested the clustering the CSDM regression features set, the
resulting partition did not lead to a significant regression accuracy compared with the clustering features set ($p > 0.1$).

**Clustering Model Development**

In this study, we applied the $K$-means clustering algorithm to cluster impacts in a data-driven manner instead of types of head impacts defined by the source of head impacts (e.g., college football, MMAs). $K$-means is an unsupervised clustering algorithm that minimizes the sum of the distance between each sample and its cluster centroid. It is preferred over other clustering algorithms (e.g., Gaussian Mixture Model) because of its simplicity and interpretability as it uses Euclidean distance in the high-dimensional feature space. Given a set of $n$ samples $(x_1, x_2, \ldots, x_n)$, the algorithm aims to partition the samples into $K$ sets $S = \{S_1, S_2, \ldots, S_K\}$, such that the sum of Euclidean distance between a sample and its cluster centroid is minimized:

$$\text{argmin}_S \sum_{i=1}^{K} \sum_{x_j \in S_i} ||x_j - \mu_i||^2.$$

It should be noted that Euclidean distance in high-dimensional feature space is calculated by taking the square root of the sum of squared difference along each feature dimension (each axis in the feature space). The assumption of $K$-means is that the impacts closer in the feature space in the term of Euclidean distance are similar in their kinematics pattern.

| Dataset | Source              | Size | CSDM Mean | CSDM Max | CSDM STD | % of CSDM > 0.1 | % of CSDM > 0.2 | % of CSDM > 0.3 |
|---------|---------------------|------|-----------|----------|----------|-----------------|-----------------|-----------------|
| HM      | ATD simulation      | 2130 | 0.180     | 0.764    | 0.219    | 47.1            | 36.3            | 26.0            |
| CF      | College football    | 302  | 0.046     | 0.894    | 0.154    | 9.3             | 7.0             | 5.6             |
| MMA     | Mixed martial arts  | 457  | 0.029     | 0.942    | 0.117    | 6.8             | 3.3             | 2.6             |
| NASCAR  | Racing car          | 272  | 0.090     | 0.813    | 0.174    | 23.9            | 16.2            | 11.8            |

**FIGURE 1.** The distribution of the CSDM across four different datasets in this study.
CSDM regression is based on two clusters with additional consideration of data partitions instead of features, all kinematic features were adopted in the CSDM regression model. Ridge regression algorithm was used because it is an L2-regularized linear regression model robust to feature collinearity, which balances the model complexity and generalizability, as well as the bias and the variance, to enable a more generalizable CSDM regression model (able to accurately estimate CSDM for different types of head impacts). The implementation of ridge regression was based on the Python package: scikit-learn (version: 1.0.2).

On the training dataset, more flexibility of piecewise linearity led to a better fit and improved goodness of fit ($R^2$), which should not be interpreted as better linearity because of the overfitting: a better fit on the training data is not equivalent to the fact that the models pick up the ground-truth relationship between the predictors and the response (e.g., replacing a linear fit with a polynomial fit can improve the goodness of fit on the training data but may reduce the goodness of fit on the unseen test dataset). To prevent this, we randomly separated impacts in each type into 80% as training sets for model training and 20% as test sets for linearity assessment. Then, all four training sets (from four types of head impacts) were mixed and used to train the clustering model and the regression models in every domain. Then, the models were tested on the test sets (unseen to the model training) for the multivariate piecewise linear model’s accuracy, which was interpreted as linearity.

The piecewise linearity was indicated by the prediction improvement of regression model with data-driven partition upon two reference partitions, which can be referred to as two benchmarks in this study: (1) baseline: all head impacts was used in one single regression model with 80% training data and 20% testing data. The rationale is to make use of the largest quantity of head impacts to develop a model used across head impacts types; (2) classification: independent regression models were built for each type of head impact diagnosed by the classification model with 80% training data and 20% testing data. The rationale is that considering the different characteristics of different types of head impacts, we develop separate models for each type of head impact and categorize new impacts into one of the four types and estimate the CSDM with the associated regression model.

For the model robustness test, the experiments were done with 20 random splits of training set and test set. The Wilcoxon signed-rank test was done on the $R^2$ results to test the statistical significance. The paired $t$-test was not used because the Shapiro–Wilk test rejected the normal distribution assumption of some $R^2$ results. The hyperparameters of the models, such as the L2 penalty strength for each ridge regression model,

### TABLE 1. The 16 temporal features used in the K-means clustering.

| Nos | Feature meaning | Kinematics type |
|-----|-----------------|----------------|
| 1   | $\max(a_x(t))$ | Linear acceleration |
| 2   | $\max(a_y(t))$ | Linear acceleration |
| 3   | $\max(a_z(t))$ | Linear acceleration |
| 4   | $\max(\alpha_x(t))$ | Angular acceleration |
| 5   | $\max(\alpha_y(t))$ | Angular acceleration |
| 6   | $\max(\alpha_z(t))$ | Angular acceleration |
| 7   | $\max(\alpha_{xy}(t))$ | Angular acceleration |
| 8   | $\max(\alpha_{xz}(t))$ | Angular acceleration |
| 9   | $\max(\alpha_{yz}(t))$ | Angular acceleration |
| 10  | $\max(j_x(t))$ | Angular jerk |
| 11  | $\max(j_y(t))$ | Angular jerk |
| 12  | $\max(j_z(t))$ | Angular jerk |
| 13  | $\max(j_{xy}(t))$ | Angular jerk |
| 14  | $\max(j_{xz}(t))$ | Angular jerk |
| 15  | $\max(j_{yz}(t))$ | Angular jerk |
| 16  | $\max(j(t))$ | Angular jerk |

After randomly initializing the $K$ centroids ($\mu_1, \mu_2, \ldots, \mu_K$), the algorithm approaches this problem in an iterative manner until convergence:

Assign each sample to the cluster based on the nearest centroid:

$$S_j^{(t)} = \left\{ x_p : \left\| x_p - \mu_j^{(t)} \right\| \leq \left\| x_p - \mu_j^{(t)} \right\|, \forall j, 1 \leq j \leq K \right\}.$$ 

Update the $K$ centroids by calculating the cluster means:

$$\mu_j^{(t+1)} = \frac{1}{|S_j^{(t)}|} \sum_{x_p \in S_j^{(t)}} x_p.$$ 

Data standardization was performed before clustering to avoid the uneven weights of certain features due to the mismatch of the feature value ranges. The hyperparameter of the K-means clustering algorithm is the number of clusters (K). We set the number of clusters $K$ to be 2. It should be mentioned that the cases when $K$ was more than 2 were also tested but the CSDM regression $R^2$ results generally did not show statistically significant improvement when compared the $K = 2$ case. Therefore, we will report the results based on two clusters with additional consideration of model simplicity and interpretability. The implementation of K-means was based on the Python package: scikit-learn (version: 1.0.2).

### Piecewise Multivariate Linearity Between Kinematic Feature and CSDM in Data-Driven Partitions

Since this study focuses on the influence of impact data partitions instead of features, all kinematic features were adopted in the CSDM regression model. Ridge regression algorithm was used because it is an L2-regularized linear regression model robust to feature collinearity, which balances the model complexity and generalizability, as well as the bias and the variance, to enable a more generalizable CSDM regression model (able to accurately estimate CSDM for different types of head impacts). The implementation of ridge regression was based on the Python package: scikit-learn (version: 1.0.2).

On the training dataset, more flexibility of piecewise linearity led to a better fit and improved goodness of fit ($R^2$), which should not be interpreted as better linearity because of the overfitting: a better fit on the training data is not equivalent to the fact that the models pick up the ground-truth relationship between the predictors and the response (e.g., replacing a linear fit with a polynomial fit can improve the goodness of fit on the training data but may reduce the goodness of fit on the unseen test dataset). To prevent this, we randomly separated impacts in each type into 80% as training sets for model training and 20% as test sets for linearity assessment. Then, all four training sets (from four types of head impacts) were mixed and used to train the clustering model and the regression models in every domain. Then, the models were tested on the test sets (unseen to the model training) for the multivariate piecewise linear model’s accuracy, which was interpreted as linearity.

The piecewise linearity was indicated by the prediction improvement of regression model with data-driven partition upon two reference partitions, which can be referred to as two benchmarks in this study: (1) baseline: all head impacts was used in one single regression model with 80% training data and 20% testing data. The rationale is to make use of the largest quantity of head impacts to develop a model used across head impacts types; (2) classification: independent regression models were built for each type of head impact diagnosed by the classification model with 80% training data and 20% testing data. The rationale is that considering the different characteristics of different types of head impacts, we develop separate models for each type of head impact and categorize new impacts into one of the four types and estimate the CSDM with the associated regression model.

For the model robustness test, the experiments were done with 20 random splits of training set and test set. The Wilcoxon signed-rank test was done on the $R^2$ results to test the statistical significance. The paired $t$-test was not used because the Shapiro–Wilk test rejected the normal distribution assumption of some $R^2$ results. The hyperparameters of the models, such as the L2 penalty strength for each ridge regression model,
were tuned based on five-fold cross-validation on the training data (the training dataset is further partitioned into 80% training data for regression coefficients training and 20% validation data used for hyperparameter tuning. The process is done five times so that every impact in the training set has been in the validation set). The regression root-mean-square error (RMSE) was the optimization goal (the averaged RMSE on the validation data over the fivefold cross-validation).

Effect of Kinematic Features on Clustering

To investigate the contributions of particular kinematic features to the clustering, we further used each individual feature in the 16 temporal features to perform the clustering feature by feature. Each of the 16 features listed in Table 1 was used to cluster the impacts into two domains and this process was done in 20 parallel experiments with randomly partitioned training/test datasets. After clustering the impacts into two domains, the domain-specific ridge regression models for CSDM estimation was developed and the coefficient of determination $R^2$ was computed. Finally, we selected the top three features as critical features based on the mean CSDM regression $R^2$ among 20 experiments. Since the clustering was based on individual feature, a critical point could be found that partition the impacts into two domains. To find the critical point, for each critical feature, we performed $K$-means clustering 100 times and labeled each impact based on the 100 clustering results considering the robustness of labelling. Then, we fitted a logistic regression (LR) model and found the critical point $c$ for a single feature where the probability of the feature value $c$ being in one domain equals 0.5:

$$P(Y = 1|X = c) = P(Y = 2|X = c) = 0.5.$$  

RESULTS

Piecewise Multivariate Linearity with Data-Driven Partitions

As we combined the four different types of head as the training set, we measured the piecewise multivariate linearity with the data-driven partition based on the $K$-means clustering method (labeled as $K$means). $R^2$ of the regression on each of the four types of head impacts is shown in Fig. 2 and the averaged of the regression across four different types of head impacts in Fig. 3. The CSDM regression method with the $K$-means clustering outperformed the baseline method (no partition) and the classification method (partition according the type of head impact), with statistical significance ($p < 0.001$, Wilcoxon signed-rank test) based on the averaged $R^2$ on four types of head impacts (HM/CF/MMA/NASCAR). This suggests significantly higher linearity existed within the domains of data-driven partition than the original partition based on impact sources and no partitions. Furthermore, higher linearity was found within data-driven partitions on all the four impact sources when viewed individually ($p < 0.001$, Wilcoxon signed-rank test). Although kinematics clustering led to significantly better regression of CSDM on all datasets, there is a high variance in the improvement across different types of head impacts in different datasets: the CSDM regression $R^2$ improvement is more evident on the datasets MMA and NASCAR. On dataset HM, the baseline is performing well with high regression $R^2$ and the improvement brought by kinematics clustering is limited. This is the reason why we scaled Fig. 2a differently to clearly show the variation in the boxplots. Additionally, the CSDM regression RMSE results on four datasets are shown in Fig. S1 and the CSDM regression $R^2$ when the clustering was performed on the entire set of features with 2 clusters, 3 clusters and 4 clusters are shown in Fig. S2 (on each of the four datasets) and S3 (mean result over the four datasets).

Impact Partitions Based on Individual Features and the Critical Points

Then, we picked up the top three critical features, based on the results of the clustering on individual features that led to the data-driven partition with the highest mean CSDM regression accuracy in 20 parallel experiments (Fig. 4). The three critical features we found are the maximum resultant angular acceleration ($K$means1), the maximum angular acceleration along the z-axis ($K$means2), and the maximum linear acceleration along the y-axis ($K$means3). With the $K$-means clustering on these three critical features individually, the regression accuracy was improved, although the clustering on the second and third critical features did not show statistically significant improvement over the classification partition ($p > 0.1$, Wilcoxon signed-rank test). According to the results shown in Figs. 2 and 3, clustering on the first critical features ($K$means1) led to significant CSDM regression accuracy improvement when compared with the baseline ($p < 0.001$, Wilcoxon signed-rank test) and the classification partition ($p < 0.05$, Wilcoxon signed-rank test). Furthermore, it should be noted that, clustering on the first critical feature ($K$means1) and clustering on the entirety of 16 features did not show statistically significant difference.
in CSDM regression accuracy ($p > 0.05$, Wilcoxon signed-rank test).

On each of these three critical features, we fitted the LR model for the two clusters and reported the critical point values in Table 1. To better visualize the brain strain profile of all the 4124 brain elements models by the KTH model, we also plotted the heatmaps of all the 4124 impacts with the clusters labeled in Fig. 5. It is shown that the critical points for each critical feature partitioned the impacts into two domains with generally different levels of CSDM, but the impact type partitions based on the clustering with the critical features were not strictly associated with the high/low CSDM values. It is important to note that the clusters separated by the critical points were the same as the robust K-means clustering results because the clustering was performed on one dimension based on Euclidean distance.

**DISCUSSION**

In this study, we observed piecewise multivariate linearity between CSDM and kinematic features presenting across different types of head impacts, and the domains of the piecewise multivariate linearity were according to a data-driven partition based on K-means clustering with 16 standardized temporal features. The linearity with the data-driven partition was evaluated.
as the accuracy of multivariate ridge regression between kinematic features and CSDM, and the CSDM regression accuracy with the data-driven partition was significantly higher than two references: the baseline without any partition and the classification with the partition according to the types of head impacts (i.e., head model simulation, college football, mixed martial arts). Furthermore, among 16 features used in clustering, we found that the clustering just based on angular acceleration magnitude (partitioned at 4706 rad/s²) could provide the partition with piecewise multivariate linearity. The finding of this study suggested that even though the characteristics of head kinematics and the relationships between kinematic features and brain strain varied remarkably among different type of head impacts, a generalizable piecewise multivariate linear relationship existed between kinematics and CSDM regardless of types of head impacts. It should be noted that the piecewise property is reflected by the partitioning of the impact data into two domains in the kinematic features space, while the multivariate linear relationship pertains to the ridge regression with over 300 kinematic features being the predictors and the CSDM being the response variable.

In this study, the piecewise linearity was represented by the accuracy of regression model prediction, and it should be mentioned that the improvement of accuracy was not contributed by more degrees of freedom in regression. Usually, replacing a linear model with a piecewise linear model improves the fit on the training set, but does not necessarily improve the regression accuracy on unseen test set. In this study, what is remarkable is that after performing clustering and modeling the relationship in a piecewise multivariate linear model, the CSDM regression accuracy tested on the unseen test set was significantly improved, which is owing to the physics of how head kinematics result in CSDM in head impacts. Furthermore, the clustering model was based on the head kinematics without any information about the CSDM, so the data-driven partition was different from the partitions obtained by optimizing the fitting of $x$–$y$ relationships in every domain.

In previous studies, better correlation between the kinematic features and 95th percentile maximum principal strain (MPS95) was also found with the partition based on the impact duration. For impacts with short impulse duration, MPS95 was found to be correlated with angular velocity. For impacts with long impulse duration, MPS95 was found to be correlated with angular acceleration. The similar finding about CSDM was not reported as far as we know. Both as indicators to represent the mechanical loading on brains, MPS95 represents the highest strain across the entire brain and CSDM represents the overall per-

![Figure 3](image3.png)

**FIGURE 3.** The averaged CSDM regression $R^2$ with ridge regression and different methods across four different types of head impacts. Kmeans-1/2/3: the $K$-means clustering method with the first/second/third critical feature: the maximum resultant angular acceleration, the maximum angular acceleration along the $z$-axis, the maximum linear acceleration along the $y$-axis.

![Figure 4](image4.png)

**FIGURE 4.** The distribution of the two clusters partitioned by the critical points for the critical features. The critical points $c$ for the critical features: the maximum resultant angular acceleration (a); the maximum angular acceleration along the $z$-axis (b); and the maximum linear acceleration along the $y$-axis (c).
The relationship between kinematics and MPS95/CSDM could be different. In this study, we have also tested the effect of kinematics clustering on the regression of the MPS95 by performing clustering on the kinematic features, partitioning the impacts into domains and developing domain-specific ridge regression models for MPS95 within each domain. However, the similar statistically significant improvement in CSDM regression was not found in MPS95 regression with the clustered partitions. This indicates that the piecewise multivariate linearity may not exist between the kinematic features and MPS95. It should be mentioned that the clustering was based on the kinematic features. In this study, we adopted the peaks of linear and angular acceleration in each direction and magnitude. Then, considering that previous studies suggest that angular velocity and angular jerk will influence the brain strain, we also include the peaks of angular velocity and angular jerk. We also tested the clustering with 367 features and did not found significant difference comparing $R^2$ of the prediction. In the regression model, we included the translational feature although previous studies showed that brain strain was only decided by head rotation. This is because in the regression, the effectiveness of the linear acceleration features and the weights to be put onto the linear acceleration features are determined by the models and data themselves in a completely data-driven manner. We aim to provide the model with as many predictive kinematics predictors as possible for better CSDM regression accuracy as the ability of the union of the predictors to explain variance gets higher, and let the regression model leverage the predictors according to the data. In this study, we reported the clustering that partitions the impacts into two domains. We have also tested clustering with three domains in our preliminary experiments with all the temporal and spectral features, which turned out to show similar significant accuracy improvement over the baseline method and the classification method but slightly inferior CSDM estimation accuracy when compared to the two domains case. Therefore, we focused on the binary divisions of impacts with $K$-means clustering. It should be noticed that some information is missing when the kinematics profiles are transformed into kinematic features for regression. As a result, we include more kinematic features in the CSDM regression features set. To avoid missing the information, some other approaches took the kinematic profile as input instead, such as DAMAGE and BAM that were based on a physical model and the CNN layers in machine-learning model.

This study is limited in the following aspects: although we have verified that the clusters found by $K$-means clustering contribute to better CSDM estimation, how exactly the different clusters differ in injury mechanism is still not fully understood. Imaging results can be incorporated to further investigate the clusters partitioned by the kinematics critical features and critical points. Additionally, in this study, we included the translational kinematic features in the regression model, which have been shown not predictive of strain. The effect of translational kinematic features will be investigated in the future. Another limitation of this study is that we only used CSDM with the threshold of 15%. Higher thresholds like 20% and 25% were used in other studies as well, but we did not use them in this study because of the limitation of the datasets: a great portion of impacts in our on-field datasets were mild impacts, and their CSDM with higher thresholds of 20% and 25% were close to zero. With the larger datasets in the future with more medium and severe impacts as we can expect, the piecewise linearity can be tested with higher CSDM thresholds. Furthermore, we used the KTH model to calculate brain strain. This model is limited when compared to recently developed state-of-the-art FEHMs. For example, the KTH model does not take the gyri or sulci into modeling, which have been shown to have significant influences on FEHM behavior. In the future, more recently developed FEHMs can be applied to validate the results on brain strain. Furthermore, in this study, we only investigated the relationship between the kinematics and the whole-brain strain pattern reflected by CSDM. There has been research showing that there are different spatial covariation patterns in the strain and strain rate in the brain and on the same impact datasets different brain regions can have different variance in strain and strain rate. In the future, the relationship between the kinematics and the strain patterns across different brain regions can be investigated.

SUPPLEMENTARY INFORMATION

The online version contains supplementary material available at https://doi.org/10.1007/s10439-022-03020-0.
ACKNOWLEDGMENTS
This research was supported by the Pac-12 Conference’s Student-Athlete Health and Well-Being Initiative, the National Institutes of Health (R24NS098518), Taube Stanford Children’s Concussion Initiative and Stanford Department of Bioengineering.

AUTHOR CONTRIBUTIONS
XZ, YL and YuL conceived this study, XZ and YL did the experiment and analyzed the data, YL, DC supervised this study, XZ, YL and YL wrote the manuscript, OG, MZ and GG revised the manuscript.

CONFLICT OF INTEREST
The authors declare no competing interests.

REFERENCES
1Beckwith, J. G., R. M. Greenwald, J. J. Chu, J. J. Crisco, S. Rowson, S. M. Duma, S. P. Broglio, T. W. McAllister, K. M. Guskiewicz, and J. P. Mihalik. Timing of concussion diagnosis is related to head impact exposure prior to injury. Med. Sci. Sports Exerc. 45:747, 2013.
2Bourdet, N., C. Deck, A. Trog, F. Meyer, V. Noblet, and R. Willinger. Deep learning methods applied to the assessment of brain injury risk. In: Proceedings of International Research Conference on the Biomechanics of Impacts, 2021.
3Camarillo, D. B., P. B. Shull, J. Mattson, R. Shultz, and D. Garza. An instrumented mouthguard for measuring linear and angular head impact kinematics in American football. Ann. Biomed. Eng. 41:1939–1949, 2013.
4Carlsen, R. W., A. L. Fawzi, Y. Wan, H. Kesari, and C. Franck. A quantitative relationship between rotational head kinematics and brain tissue strain from a 2-D parametric finite element analysis. Brain Multiphys.2:100024, 2021.
5Casswell, S. V., A. E. Lincoln, H. Stone, P. Kelshaw, M. Putukian, L. Hepburn, M. Higgins, and N. Cortes. Characterizing verified head impacts in high school girls’ lacrosse. Am. J. Sports Med. 45:3374–3381, 2017.
6Cecchi, N. J., A. G. Domel, Y. Liu, E. Rice, R. Lu, X. Zhan, Z. Zhou, S. J. Raymond, S. Sami, and H. Singh. Identifying factors associated with head impact kinematics and brain strain in high school American football via instrumented mouthguards. Ann. Biomed. Eng. 49:2814–2826, 2021.
7Cecchi, N. J., D. C. Monroe, G. M. Fote, S. L. Small, and J. W. Hicks. Head impacts sustained by male collegiate water polo athletes. PLoS ONE.14:e2016369, 2019.
8Doherty, C. P., E. O’Keeffe, E. Wallace, T. Loftus, J. Keany, J. Kealy, M. M. Humphries, M. G. Molloy, J. F. Meaney, and M. Farrell. Blood–brain barrier dysfunction as a hallmark pathology in chronic traumatic encephalopathy. J. Neuropathol. Exp. Neurol. 75:656–662, 2016.
9Fahlstedt, M., F. Abayazid, M. B. Panzer, A. Trotta, W. Zhao, M. Ghajari, M. D. Gilchrist, S. Ji, S. Kleiven, and X. Li. Ranking and rating bicycle helmet safety performance in oblique impacts using eight different brain injury models. Ann. Biomed. Eng. 49:1097–1109, 2021.
10Fanton, M., C. Kuo, J. Sganga, F. Hernandez, and D. B. Camarillo. Dependency of head impact rotation on head–neck positioning and soft tissue forces. IEEE Trans. Biomed. Eng. 66:988–999, 2018.
11Fanton, M., J. Sganga, and D. B. Camarillo. Vulnerable locations on the head to brain injury and implications for helmet design. J. Biomech. Eng. 2019. https://doi.org/10.1115/1.4043837.
12Friedman, J., T. Hastie, and R. Tibshirani. The Elements of Statistical Learning. Springer Series in Statistics. New York: Springer, 2001.
13Gabler, L. F., H. Joodaki, J. R. Crandall, and M. B. Panzer. Development of a single-degree-of-freedom mechanical model for predicting strain-based brain injury responses. J. Biomech. Eng. 2018. https://doi.org/10.1115/1.4038357.
14Ghazi, K., S. Wu, W. Zhao, and S. Ji. Instantaneous whole-brain strain estimation in dynamic head impact. J. Neurotrauma. 38(8):1023–1035, 2020.
15Giudice, J. S., G. Park, K. Kong, A. Bailey, R. Kent, and M. B. Panzer. Development of open-source dummy and impactor models for the assessment of American football helmet finite element models. Ann. Biomed. Eng. 47:464–474, 2019.
16Hernandez, F., L. C. Wu, M. C. Yip, K. Laksari, A. R. Hoffman, J. R. Lopez, G. A. Grant, S. Kleiven, and D. B. Camarillo. Six degree-of-freedom measurements of human mild traumatic brain injury. Ann. Biomed. Eng. 43:1918–1934, 2015.
17Hoerl, A. E., and R. W. Kennard. Ridge regression: biased estimation for nonorthogonal problems. Technometrics. 12:55–67, 1970.
18James, S. L., A. Theadom, R. G. Ellenbogen, M. S. Banick, W. Montjoy-Venning, L. R. Lucchesi, N. Abbasi, R. Abdulkader, H. N. Abraha, and J. C. Adsuar. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 18:56–87, 2019.
19Kleiven, S. Predictors for Traumatic Brain Injuries Evaluated Through Accident Reconstructions. SAE Technical Paper, 2007.
20Kuo, C., M. Fanton, L. Wu, and D. Camarillo. Spinal constraint modulates head instantaneous center of rotation and dictates head angular motion. J. Biomech. 76:220–228, 2018.
21Laksari, K., M. Fanton, L. C. Wu, T. H. Nguyen, M. Kurt, C. Giordano, E. Kelly, E. O’Keeffe, E. Wallace, and C. Doherty. Multi-directional dynamic model for traumatic brain injury detection. J. Neurotrauma. 37:982–993, 2020.
22Li, X., Z. Zhou, and S. Kleiven. An anatomically detailed and personalizable head injury model: significance of brain and white matter tract morphological variability on strain and white matter strain rate in American football. Ann. Biomed. Eng. 49:2791–2804, 2021.
Liu, Y., A. G. Domel, S. A. Yousefsani, J. Kondic, G. Grant, M. Zeineh, and D. B. Camarillo. Validation and comparison of instrumented mouthguards for measuring previous studies simplified head kinematics and assessing brain deformation in football impacts. *Ann. Biomed. Eng.* 48:2580–2598, 2020.

Liu, Y., X. Zhan, A. G. Domel, M. Funtowicz, Z. Zhou, S. J. Raymond, H. V. Alizadeh, N. J. Cecchi, M. Zeineh, and G. Grant. Theoretical and numerical analysis for angular acceleration being determinant of brain strain in mTBI. arXiv preprint (2020). arXiv:2012.13507.

MacQueen, J. Some methods for classification and analysis of multivariate observations. In: *Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability*, Oakland, CA, USA, 1967, pp. 281–297.

Montenigrò, P. H., M. L. Alosco, B. M. Martin, D. H. Daneshvar, J. Mez, C. E. Chaisson, C. J. Nowinski, R. Au, A. C. McKee, and R. C. Cantu. Cumulative head impact exposure predicts later-life depression, apathy, executive dysfunction, and cognitive impairment in former high school and college football players. *J. Neurotrauma* 34:328–340, 2017.

O’Keeffe, E., E. Kelly, Y. Liu, C. Giordano, E. Wallace, M. Hynes, S. Tiernan, A. Meagher, C. Greene, and S. Hughes. Dynamic blood–brain barrier regulation in mild traumatic brain injury. *J. Neurotrauma* 37:347–356, 2020.

Ponsford, J., C. Willmott, A. Rothwell, P. Cameron, G. Ayton, R. Nelms, C. Curran, and K. Ng. Impact of early intervention on outcome after mild traumatic brain injury in children. *Pediatrics*. 108:1297–1303, 2001.

Prins, M., and C. C. Giza. Repeat traumatic brain injury in the developing brain. *Int. J. Dev. Neurosci.* 30:185–190, 2012.

Sanchez, E. J., L. F. Gabler, A. B. Good, J. R. Funk, J. R. Crandall, and M. B. Panzer. A reanalysis of football impact reconstructions for head kinematics and finite element modeling. *Clin. Biomech.* 64:82–89, 2019.

Shi, L., Y. Han, H. Huang, J. Davidsson, and R. Thomson. Evaluation of injury thresholds for predicting severe head injuries in vulnerable road users resulting from ground impact via detailed accident reconstructions. *Biomech. Model. Mechanobiol.* 19:1845–1863, 2020.

Somers, J. T., B. Granderson, J. W. Melvin, A. Tabiei, C. Lawrence, A. Feiveson, M. Gernhardt, R. Ploutz-Snyder, and J. Patalak. Development of head injury assessment reference values based on NASA injury modeling. *Stapp Car Crash J.* 55:49, 2011.

Takahashi, Y., and T. Yanoaka. A study of injury criteria for brain injuries in traffic accidents. In: 25th *International Technical Conference on the Enhanced Safety of Vehicles (ESV)*. National Highway Traffic Safety Administration, 2017.

Takhounts, E. G., S. A. Ridella, V. Hasija, R. E. Tannous, J. Q. Campbell, D. Malone, K. Danielson, J. Stutzel, S. Rowson, and S. Duma. *Investigation of Traumatic Brain Injuries Using the Next Generation of Simulated Injury Monitor (SIMon) Finite Element Head Model*. SAE Technical Paper, 2008.

Taylor, C. A., J. M. Bell, M. J. Breiding, and L. Xu. Traumatic brain injury-related emergency department visits, hospitalizations, and deaths—United States, 2007 and 2013. *MMWR Surveill. Summ.* 66:1, 2017.

Tiernan, S., A. Meagher, D. O’Sullivan, E. O’Keeffe, E. Kelly, E. Wallace, C. P. Doherty, M. Campbell, Y. Liu, and A. G. Domel. Concussion and the severity of head impacts in mixed martial arts. *Proc. Inst. Mech. Eng. H.* 2020. https://doi.org/10.1177/0954411920947850.

Versace, J. A Review of the Severity Index. SAE Technical Paper, 1971.

Wallace, T., and J. Morris. Development and testing of a technology enhanced intervention to support emotion regulation in military mTBI with PTSD. *Arch. Phys. Med. Rehabil.* 100:e5, 2019.

Wilcoxon, B. J., J. T. Machan, J. G. Beckwith, R. M. Greenwald, E. Burmeister, and J. J. Crisco. Head-impact mechanisms in men’s and women’s collegiate ice hockey. *J. Athl. Train.* 49:514–520, 2014.

Wu, S., W. Zhao, K. Ghazi, and S. Ji. Convolutional neural network for efficient estimation of regional brain strains. *Sci. Rep.* 9:1, 2019.

Wu, S., W. Zhao, and S. Ji. Real-time dynamic simulation for highly accurate spatiotemporal brain deformation from impact. *Comput. Methods Appl. Mech. Eng.* 394:114913, 2022.

Zhan, X., Y. Li, Y. Liu, N. J. Cecchi, S. J. Raymond, Z. Zhou, H. V. Alizadeh, J. Ruan, S. Barbat, and S. Tiernan. Classification of head impacts based on the spectral density of measurable kinematics. arXiv preprint (2021). arXiv:2104.09082.

Zhan, X., Y. Li, Y. Liu, A. G. Domel, H. V. Alizadeh, S. J. Raymond, J. Ruan, S. Barbat, S. Tiernan, and O. Gevaert. The relationship between brain injury criteria and brain strain across different types of head impacts can be different. *J. R. Soc. Interface*. 18:20210260, 2021.

Zhan, X., Y. Li, Y. Liu, A. G. Domel, H. V. Alizadeh, Z. Zhou, N. J. Cecchi, S. J. Raymond, S. Tiernan, J. Ruan, S. Barbat, O. Gevaert, M. M. Zeineh, G. A. Grant, and D. B. Camarillo. Predictive factors of kinematics in traumatic brain injury from head impact based on statistical interpretation. *Ann. Biomed. Eng.* 49:2901–2913, 2021.

Zhan, X., Y. Liu, N. J. Cecchi, O. Gevaert, M. Zeineh, G. Grant, and D. B. Camarillo. Find the spatial co-variation of brain deformation with principal component analysis. *IEEE Trans. Biomed. Eng.* 2022. https://doi.org/10.1109/tbme.2022.3163230.

Zhao, W., and S. Ji. Brain strain uncertainty due to shape variation in and simplification of head angular velocity profiles. *Biomech. Model. Mechanobiol.* 16:449–461, 2017.

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.