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1 **Title Page**

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3 **Title:** Passive Intervertebral Motion Characteristics in Chronic Mid to Low Back  
4 Pain: a Multivariate Analysis.

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19 Passive Intervertebral Motion Characteristics in Chronic Mid to Low Back Pain: a  
20 Multivariate Analysis.

21 **Key words**

22 Multivariate analysis, low back pain, kinematics, motion analysis.  
23

24 **Introduction**

25 Low back pain is now the leading cause of disability globally [1] . Despite this, approximately  
26 90% of cases are of unknown origin (hence nonspecific low back pain - NSLBP) [2] . However,  
27 certain features of the spine are associated with an increased probability of back pain, such as  
28 Modic type 1 changes, disc extrusion, and spondylolysis [3] . These findings, and the typical  
29 mechanical symptoms of NSBLP, indicates that mechanical characteristics may play a part in back  
30 pain.

31 The spine, typical of the musculoskeletal system, operates with redundant degrees of freedom.  
32 Adequate motor control is therefore important in preventing buckling and stress concentrations  
33 [4] . Reeves et al. pointed to the importance of passive, as well as muscular restraints, in  
34 maintaining spinal performance and structural integrity [5] . Where the passive restraints are a  
35 function of the material properties of the discs, vertebral bodies and ligaments etc, which, while not  
36 actively used to control spine motion, can be seen as a slowly-changing control system that provides  
37 restraint in rate and range of movement.

38 Passive motion quantitative fluoroscopy (QF) is a method of measuring intervertebral (IV) motion  
39 in recumbent subjects, where trunk motion is induced by a motorised table [6–8]. Using QF, joint  
40 kinematics of a spinal region can be assessed throughout a motion cycle, providing information on  
41 its passive mechanical properties. This ability is important, given the putative role of the neutral  
42 zone in spinal stability, a region of IV motion around the neutral position, where little resistance to  
43 force is offered by the passive tissues [9] . QF has been found to have 'good' to 'excellent'  
44 reliability (ICC > 0.737) for range of motion (ROM) [10] , with errors of <0.7 degrees in an in-  
45 vitro study [7] .

46 Studies that have compared back pain populations to controls using QF support the hypothesis that  
47 characteristics of passive IV motion can discriminate back pain. Mellor et al, in a study of 40  
48 chronic back pain sufferers and matched controls, found that groups differed on 'combined  
49 proportional range variances' (CPRV)[10] . This measure is based on the fact that individual IV  
50 joint's contribution to overall spinal bending varies over the course of the motion. CPRV is a  
51 measure of this variation, combined across all bending directions, and this study showed it was  
52 higher in patients. Breen and Breen found that chronic low back pain (LBP) patients had greater  
53 motion sharing inequality (MSI) between IV joints in a study comparing 20 patients with 20  
54 matched controls [11] .

55 The high dimensionality of QF data (801 per motion in Mellor et al's study [10] ) requires the  
56 selection of scalar variables of interest to make analysis tractable [12] . Hitherto, this selection has  
57 been based on *a priori* theoretical assumptions about which features are important. An alternative is  
58 to adopt a multivariate approach, in which the choice of features to analyse is based on objective  
59 criteria, and where between-groups differences can be made on the basis of the simultaneous

60 consideration of all chosen features, rather than a one-variable-at-a-time approach with its inherent  
61 weaknesses [13] . In this study, well-established linear multivariate methods were chosen for their  
62 relative simplicity and invertibility, which facilitates plotting and examining features in the original  
63 data space.

64 Previous studies, being based on the proportional contribution to total spinal angle, suffer from  
65 problems related to division by small numbers when the total spinal angle is small. Hence,  
66 approximately 20% of the data needs to be discarded near the neutral position. The present study  
67 avoids this problem by using IV angles directly [14,15] .

68 This study aims to obtain and describe the main dimensions of passive IV motion variations from  
69 passive QF data using principal components analysis (PCA). Using this lower dimensional  
70 description of the motion, assess if and how passive motion differs between back pain sufferers and  
71 controls.

## 72 **Methods**

### 73 *Recruitment and Data Acquisition*

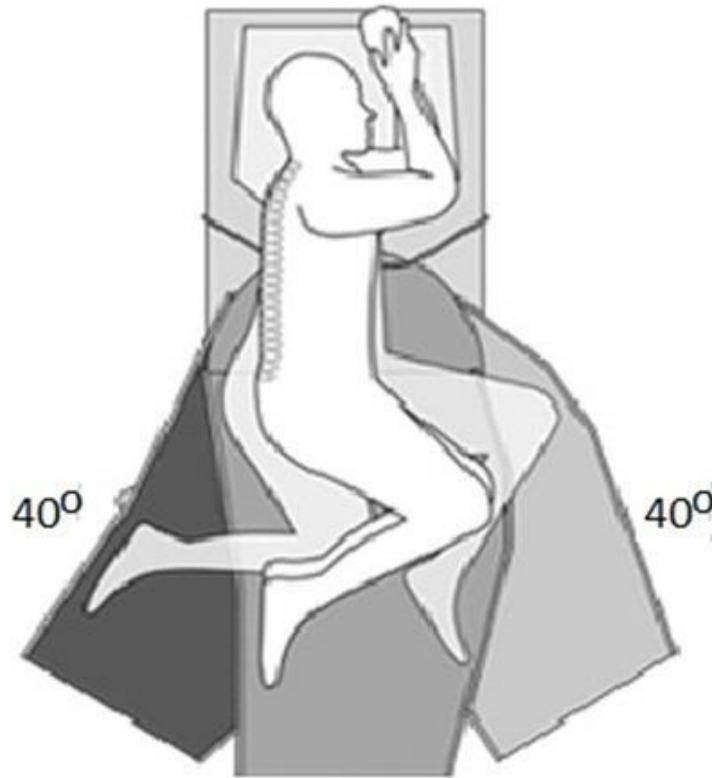
74 This study is a re-analysis of data obtained from F Mellor's PhD study [16] . Recruitment, imaging  
75 protocol and initial processing of the images have been described in detail elsewhere [10,16] . In  
76 summary, 40 patients and 40 controls, matched for gender, age group (mean patients: 35.9, controls:  
77 35.7), and BMI (mean patients: 24.5, controls: 24.5) were recruited and underwent passive motion  
78 QF.

79 Patients were otherwise healthy, aged 21-50, with low back pain lasting greater than three months.  
80 Their back pain was required to have mechanical aggravating and relieving factors, a Von Korff  
81 chronic pain grade II or higher [17] , a score of four or greater on the Roland Morris Disability  
82 questionnaire [18] , and positive prone instability tests [19] between L2 and L5.

83 Controls were those without back pain in the previous year, which had prevented normal activity for  
84 one day or more, and negative prone instability tests between L2–L5. Imaging protocol and  
85 preprocessing is listed below:

- 86 • Participants were asked to lie on a custom moveable table that rotated the lower half of the  
87 body with the axis of rotation placed at the L3/4 joint (see figure 1, used with permission  
88 [20] ).
- 89 • For 'right' and 'left' motions, subjects were placed supine in the neutral position and rotated  
90 40° to the right and left, each time returning to the neutral position.
- 91 • For 'flexion' and 'extension' motions, subjects were placed in a lateral recumbent position  
92 and the table was rotated 40° to flex and extend the spine, each time returning to the neutral  
93 position.
- 94 • Each motion (bending and return) took 12 seconds, and vertebrae L2 to L5 were imaged and  
95 analysed.
- 96 • Images were obtained at 15Hz using videofluoroscopy (Siemens Arcadis Avantic VC10A).

97 • Tracking templates were constructed manually to encompass each vertebral body in one  
98 frame. The templates were then registered to vertebral positions in other frames using a  
99 cross-correlation similarity measure to obtain relative vertebral body orientations [21] . IV  
100 angles for each IV joint were obtained from differences between adjacent vertebral body



101 *Figure 1: Diagram of passive motion table for sagittal plane motion.*  
orientations.

102

103 For each motion direction ('left', 'right', 'flexion', 'extension'), 801 IV angles were obtained. In  
104 some cases there were missing data at the extremity of each motion. To address these gaps, to  
105 smooth the data, and to reduce the number of data points, this study divided the data into two  
106 halves: from neutral to end of range, and end of range to neutral. Each half was separately fitted to a  
107 smoothing spline, whose smoothing parameters were chosen using generalised cross-validation  
108 (GCV)[22] . GCV is based on a random, zero mean, serially uncorrelated model for the noise, and  
109 seeks to estimate a smoothing parameter just sufficient to eliminate this noise, but preserving as  
110 much of the signal as possible. Using the fitted spline, data were resampled to 40 points per half and  
111 the two halves were rejoined. 40 points were chosen as this far exceeds the expected number of PC  
112 dimensions of interest. Numbers of points in excess of the numbers of participants results in PC  
113 dimensions with zero eigenvalues, which would not be retained in further analyses.

114 *Data Analysis*

115 The resulting sequences of angles, one for each direction, were analysed using PCA. The aim of  
116 PCA is to describe the data more efficiently by using a new (often much smaller) set of variables  
117 called principal components (PCs). The underlying assumption behind PCA, and other dimension  
118 reduction methods, is that the data resides in a lower dimensional space than the space of the  
119 observed variables. For example, imagine points within a three dimensional space, where the points  
120 all lie in a plane. Each are represented by three coordinates, but one of these coordinates is, in a  
121 sense redundant, given that all points lie in a plane. This redundancy is reflected in correlations  
122 between the coordinates. PCA exploits correlations in the data in order to estimate the  
123 dimensionality of the underlying space in which the data resides (see figure 2). Observations,  
124 however, are often contaminated with noise, which are usually uncorrelated. PCs are ordered  
125 according to how much variance in the data they explain (indicated by their eigenvalues), which can  
126 be plotted on a ‘scree plot’ (see figure 3). The choice of how many PCs to retain was aided by  
127 observing inflection points in the scree plots [23] , and by using the broken stick method [13] .  
128 Both of these methods estimate the underlying dimensionality of the data by identifying PCs whose  
129 eigenvalues are greater than what would be expected from observing pure uncorrelated noise. Each  
130 PC represents different features of motion, which require interpretation, with each subject having  
131 different weightings on these (PC scores), depending on how these features are represented in  
132 subject’s motions. These PCs were plotted in the original data space of IV angles to aid  
133 interpretation, i.e. PC scores were converted back into angles and plotted (see figure 4, for an  
134 example).

135 Using the retained PCs, differences between back pain and control groups were tested for each  
136 motion using the Hotelling T2 test, a multivariate equivalent of the Student’s t-test [24] . This test  
137 relies on the assumption of multivariate normality, so a distribution-free permutation test was used  
138 in addition[25] to guard against violations of this assumption.

139 To determine how groups differed, linear discriminant analysis (LDA) was carried out. LDA  
140 calculates a linear combination of input variables which best discriminates two groups, based on  
141 maximising the ratio of between and within group sum of squares, termed the linear discriminant  
142 (LD), with each subject having a score placing them on this scale (the LD score) [26] . LD scores  
143 were visualised by plotting them in the original space of IV angles to aid interpretation of group  
144 differences (see figure 2).

145 LD scores were used to predict which group each subject belonged to. The quality of this prediction  
146 was assessed with leave-one-out cross-validation. In this, an LDA model is calculated on the  
147 remaining data after one subject’s data is removed. This model is used to calculate an LD score for  
148 the left out subject, from which a prediction of class membership is made. The proportion of  
149 correctly classified subjects was used as a measure of quality of the LDA classifier. To see how  
150 sensitive the results were to the choice of number of retained PCs, a variable number of PCs (1-10)  
151 were used in the cross-validations.

152 LDA is somewhat restrictive in specifying that scores are a linear function of the input variables.  
153 Quadratic discriminant analysis (QDA) is more flexible in allowing quadratic terms in this function.  
154 QDA was used to assess whether more complex non-linear dimension reduction methods are  
155 needed, which would be indicated by a significantly better classification performance in QDA over  
156 LDA.

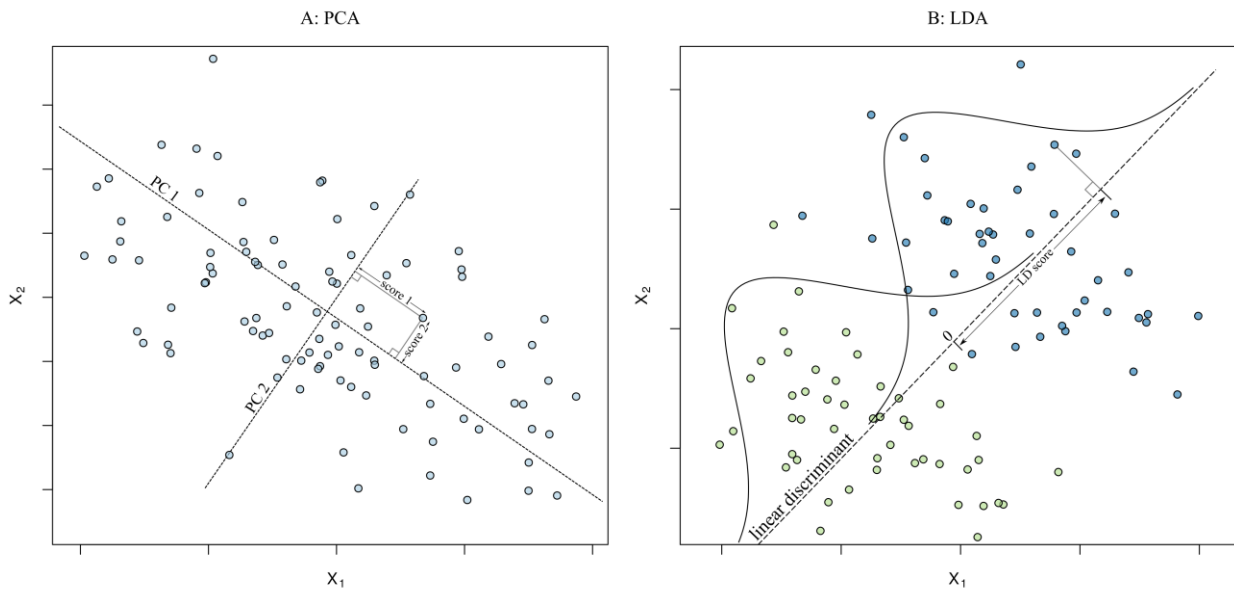


Figure 2: Geometrical interpretation of PCA and LDA, showing how input variables ( $X_1$  &  $X_2$ ) become PC and LD 'scores'. **Graph A** - PCA. PC 1 is a straight line whose direction is chosen to maximise the variance of orthogonal projections of data on to it. The point at which a data point projects onto the PC gives its score for that PC. PC 2 is similarly defined, subject to it being orthogonal to PC 1. In high dimensional cases, less important PCs (i.e. those explaining less variance) are dropped to provide a more succinct representation of the data. **Graph B** - LDA. Here there are group labels (green and blue data). A straight line (the 'linear discriminant') is obtained whose direction maximises the group difference of the orthogonal projections of data onto it. The position of the projection of a data point on to the line is called its LD score.

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## 160 Results

### 161 PCA Results

162 Estimation of the number of PCs to retain gave similar results for the broken stick method and scree  
 163 plot examination, both indicating that three PCs should be retained for all motion directions (see  
 164 figure 3 for flexion, see link to data repository for others). For all motions, ~95% of the variance is  
 165 explained by 5-6 PCs.

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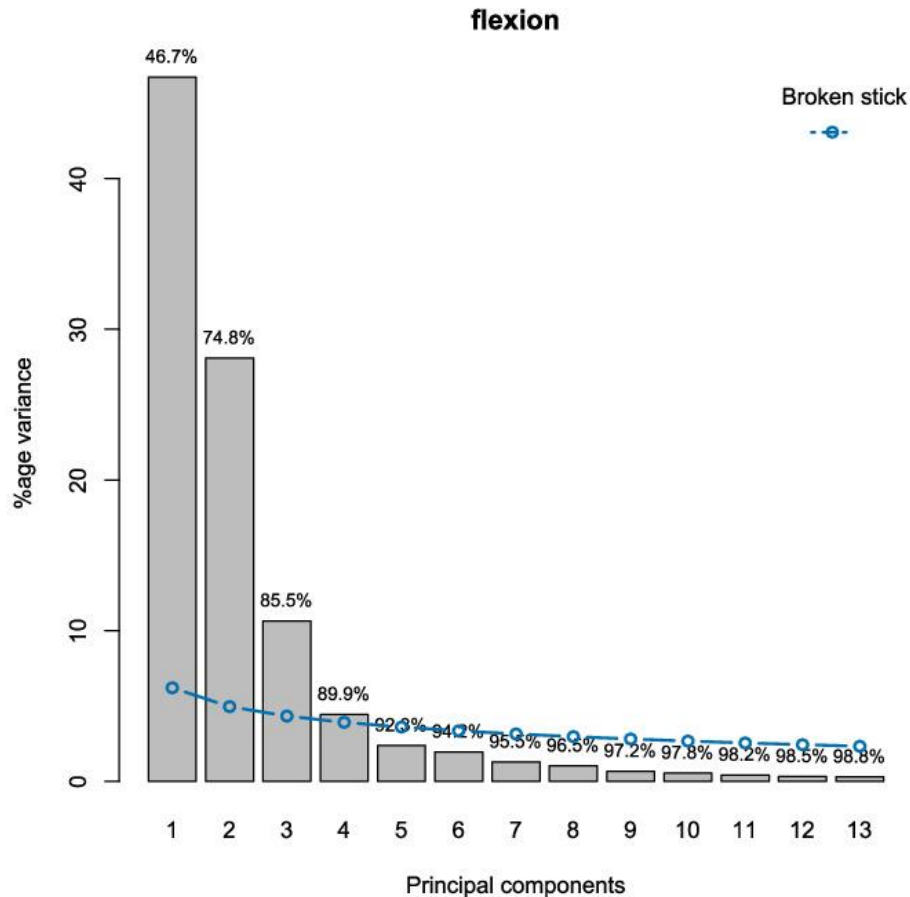


Figure 3: Screeplot for flexion motion. Broken stick model and 'knee' of plot indicate three PCs should be retained, by distinguishing PCs whose eigenvalues are greater than what would be expected from observing uncorrelated noise.

167

168 Plotting and interpreting each PC pointed to similar patterns across all four motions. The first PC  
 169 represented mainly a variation in ROM across all joints, in which motion is distributed evenly  
 170 between joints (see figure 4 for flexion, see link to data repository for others). Positive PC scores  
 171 represent above-average ROM, negative scores represent below-average ROM. The second (figure  
 172 5) and third (not shown) PCs represented mainly variation in the distribution of motion between  
 173 joints. In PC 2, positive scores correspond to above average ROM at L4/5 but less than average  
 174 ROM at the other joints. For PCs greater than 3, the variations captured represent mainly different  
 175 'shapes' in the motion curve. That is, PCs 1-3 represent variation in joint ROM, but with similar  
 176 patterns of acceleration/deceleration, whereas PCs > 3 represent variations in  
 177 acceleration/deceleration beyond that due to a variation in ROM. (see figure 6 for example). The  
 178 one exception to this pattern was extension, where ROM variation was correlated with some degree  
 179 of variation in shape of the motion curve (see figure 7).



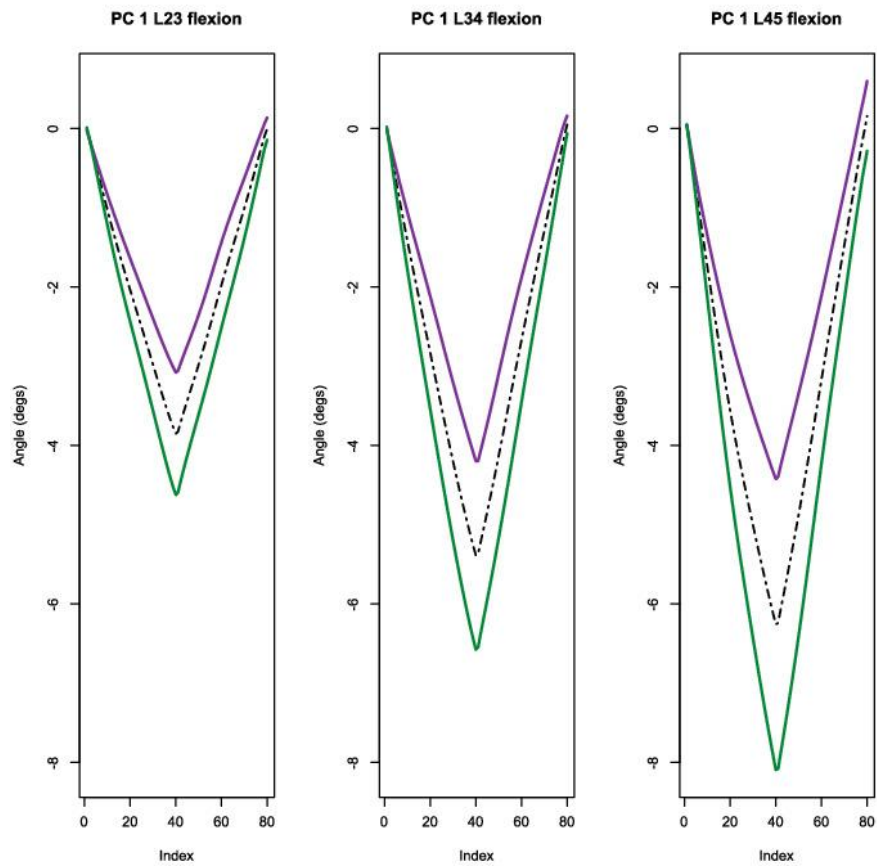


Figure 4: PC 1 flexion. This shows the main way IV motion varies across the sample. This mode of variation can be interpreted as variation in uniform ROM across all joints. Mean motion: black dotted line, +1 s.d.: green solid line, -1 s.d.: purple solid line. The data index is used as a surrogate for table motion on the horizontal axis.

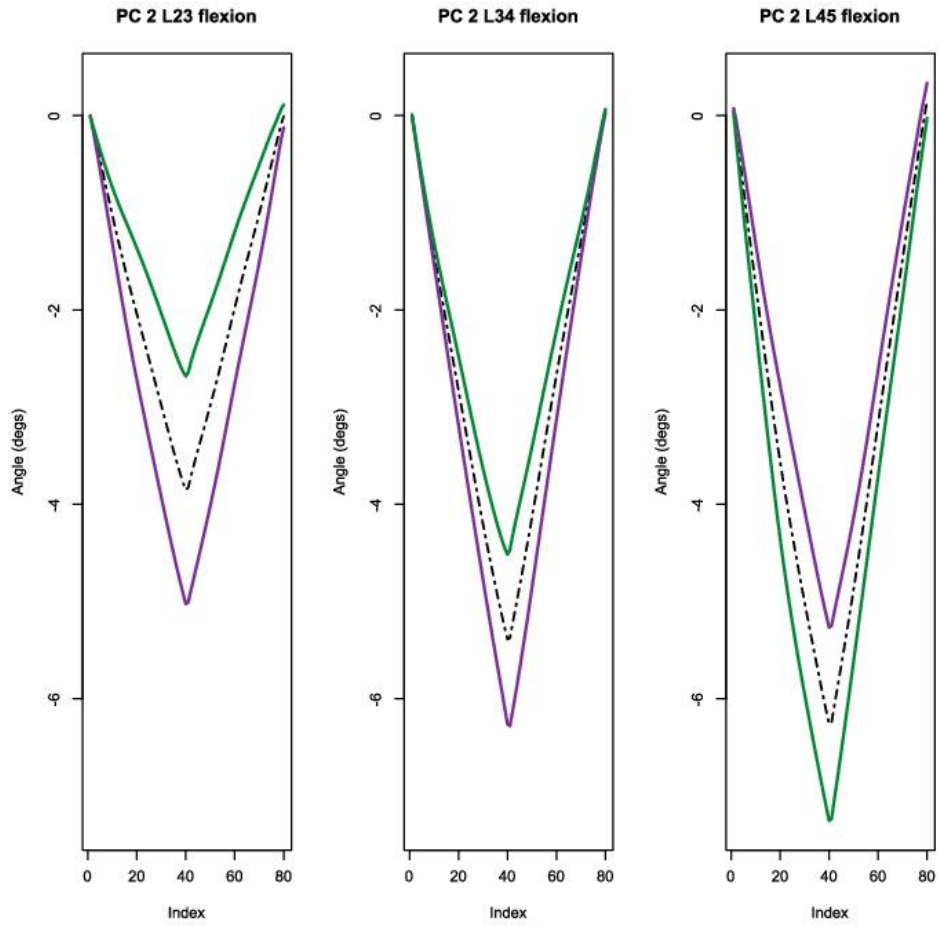


Figure 5: PC 2 for flexion motion, showing remaining main mode of variation, after having accounted for PC 1 variation. For positive scores (green), ROM is greater than average at L4/5, whilst it is less than average at other joints. Mean: black dotted line, green solid line: +1 s.d., purple solid line: -1 s.d. The data index is used as a surrogate for table motion on the horizontal axis.

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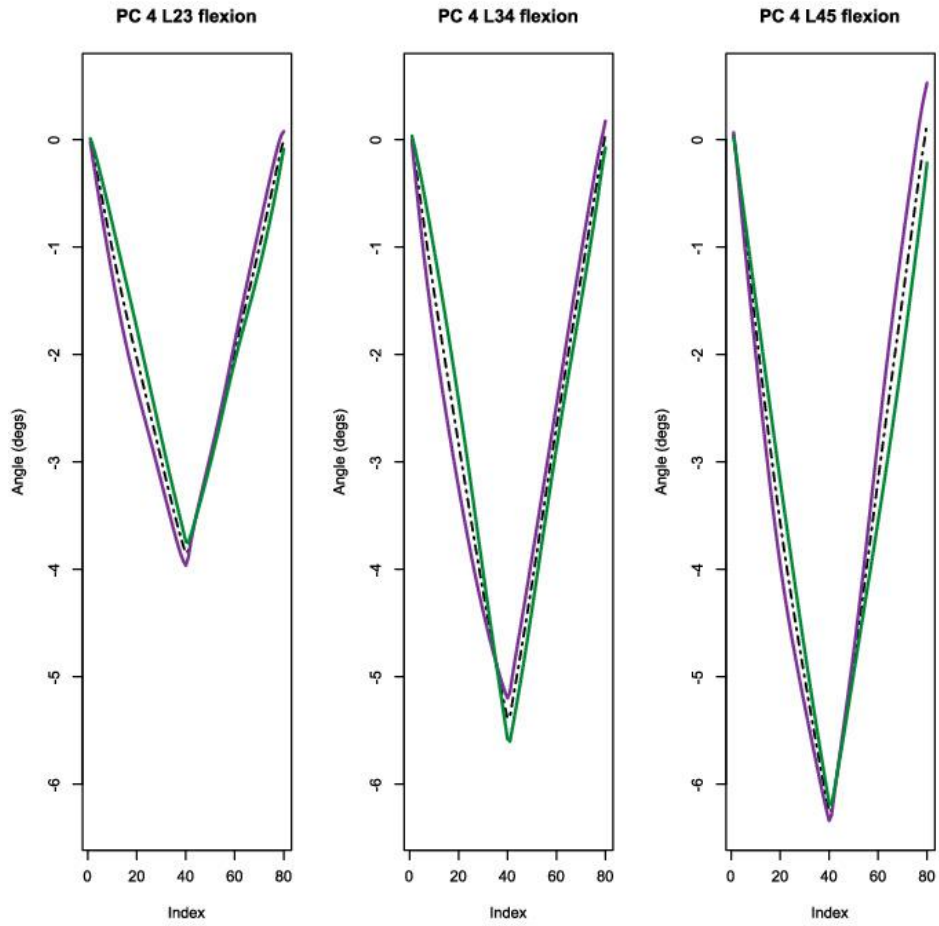


Figure 6: PC 4 for flexion motion. Main feature is variation in the shape of the motion curve, e.g. increased angular velocity (greater negative gradient) of the purple curve during the first part of the motion. Mean: black, green: +1.5 s.d., purple: -1.5 s.d.. The data index is used as a surrogate for table motion on the horizontal axis.

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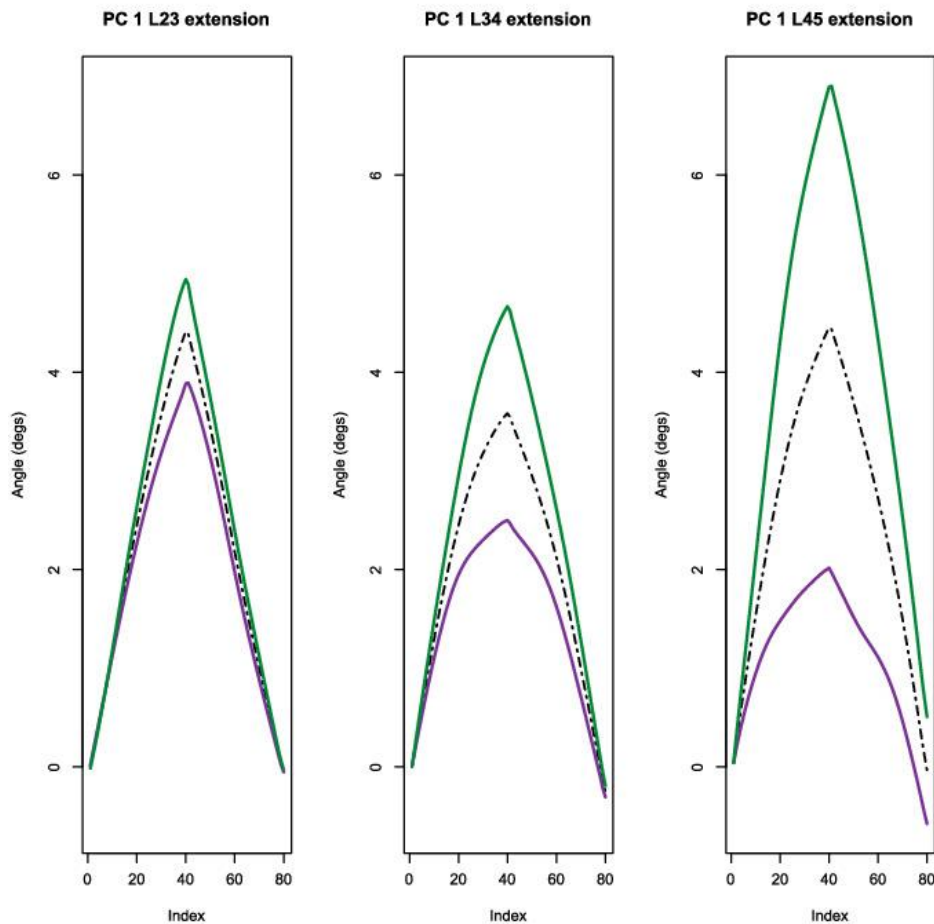


Figure 7: PC 1 extension. Variation in ROM is correlated with some variation in the shape of the motion curve, seen mainly at L4/5, where negative scores are associated with a flattening of the peak & asymmetry. Mean: black, green: +1 s.d., purple: -1 s.d. The data index is used as a surrogate for table motion on the horizontal axis.

185

186

187 Representing motion using the first three PC scores, a Hotelling T-squared and a permutation test  
 188 were used to compare groups. This showed a significant difference between groups for coronal  
 189 plane motions only ('right':  $T_2 = 10.62$ ,  $p = 0.02$  and 'left':  $T_2 = 9.67$ ,  $p = 0.03$ ). The permutation test  
 190 gave the same p-values as the Hotelling T-squared test.

#### 191 *LDA and QDA Results*

192 The performance of LDA and QDA as predictors of back pain status for the coronal motion  
 193 directions are shown in figure 8, relative to the number of PCs used to represent motions. For  
 194 sagittal plane motions (extension and flexion), neither LDA nor QDA achieved statistically  
 195 significant classification accuracy (not shown – see supplementary material). For coronal plane  
 196 motions ('right' & 'left') groups were variably distinguishable, depending on the number of PCs  
 197 used to represent motion. There was no clear advantage of using QDA over LDA, although there is  
 198 a marginal improvement when using QDA for the 'right' motion. Separability does not appear to  
 199 increase with the number of PCs used, with no more than 4 PCs sufficing (first two for 'left', first  
 200 four for 'right').

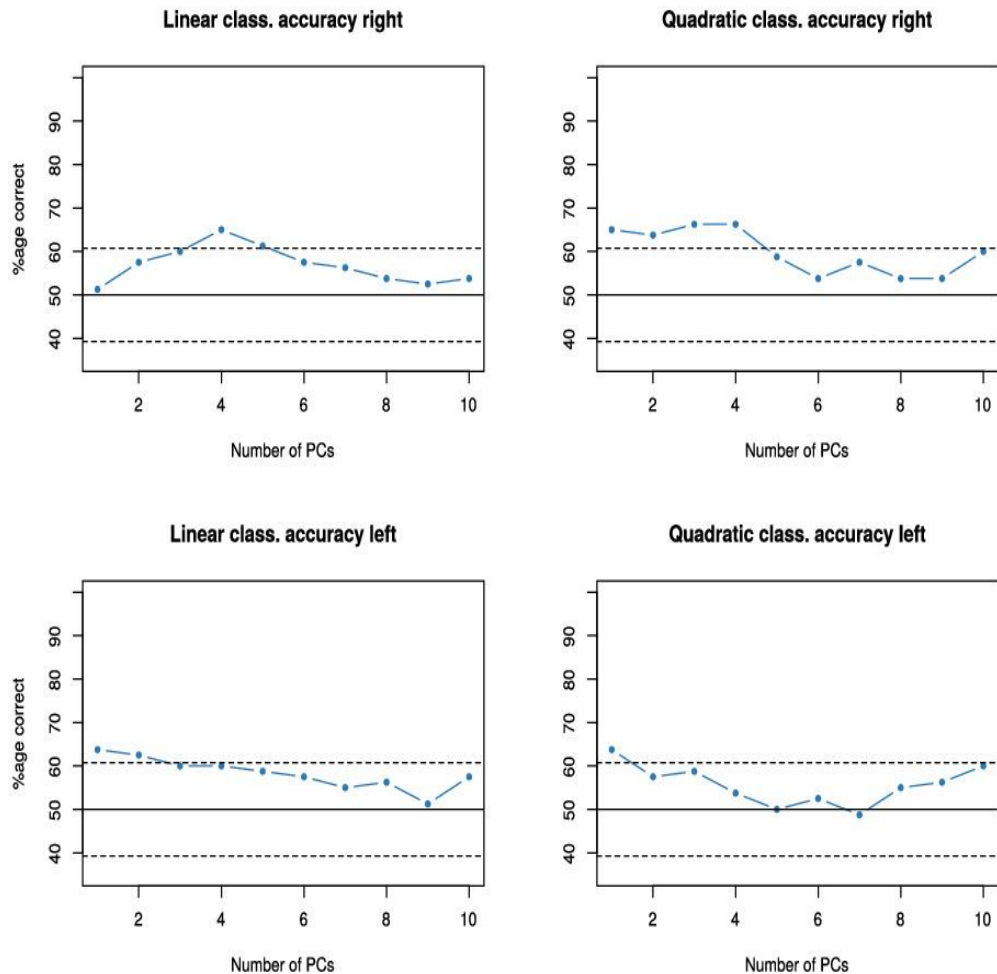


Figure 8: Prediction accuracy (percentage correctly classified) for coronal plane motions using leave-one-out cross-validation versus number of input PCs. Linear (left) and quadratic (right) discriminant analysis. Dotted horizontal lines show the  $H_0$  rejection region; points outside these dotted lines achieve statistical significance at the 0.05 level.

201

202 LD scores were plotted and interpreted for coronal plane motions only, as sagittal plane motions  
 203 showed no significant differences (see, instead, see link to data repository). The ‘left’ motion  
 204 showed that the control group had a greater ROM at L4/5, but smaller ROM at L2/3 and L3/4  
 205 (figure 9). For the ‘right’ motion, there is greater ROM at L4/5 for the controls, but a lower ROM at  
 206 L3/4. There is also a difference in shape of the motion curve for this motion, although this might be  
 207 due to the presence of an outlier (figure 10),

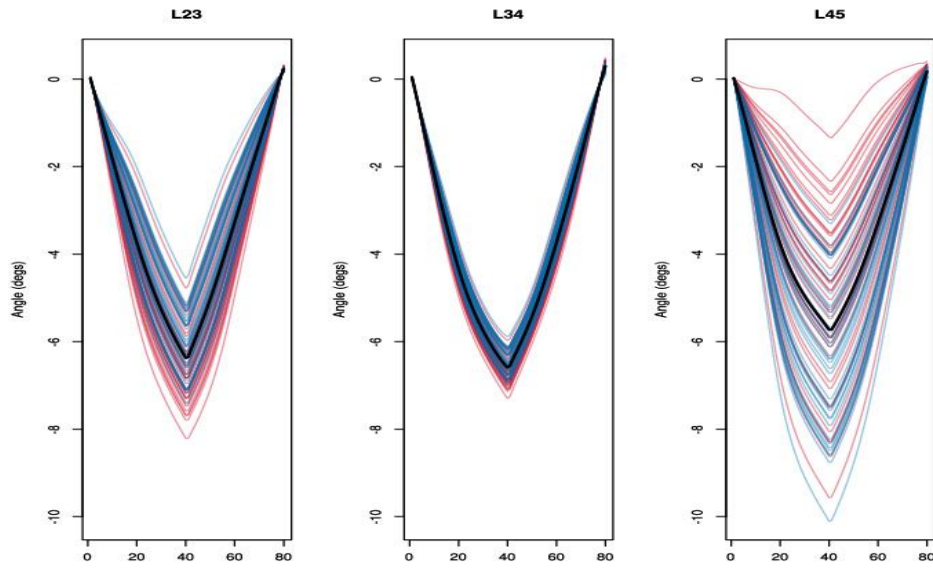


Figure 9: Projection of data onto linear discriminant of the LDA model using the first 2 PCs, 'left' motion. This shows the features by which the two groups differ maximally. The control group (blue) has a smaller ROM at L2/3 and L4/5, but greater ROM at L4/5 than the back pain group (red). The data index is used as a surrogate for table motion on the horizontal axis.

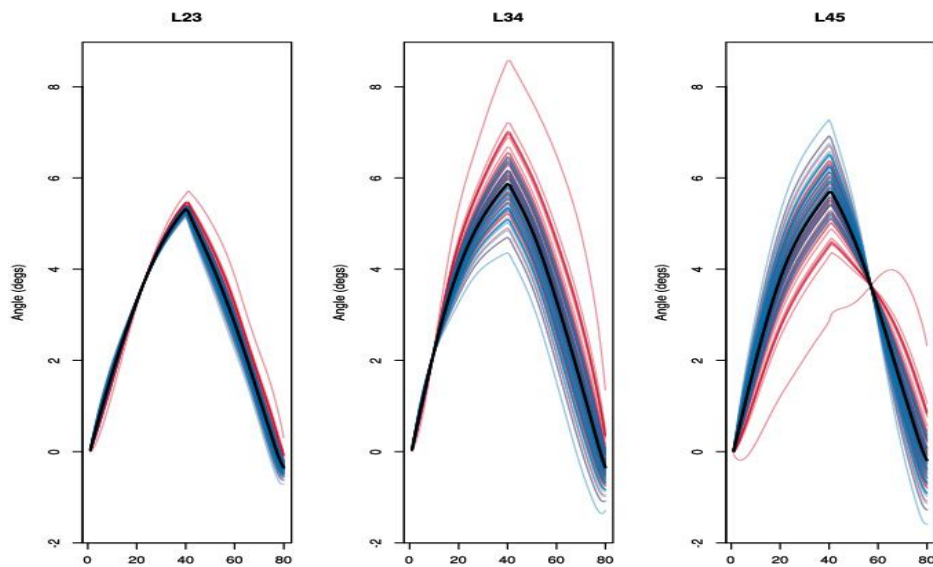


Figure 10: Projection of data onto linear discriminant of LDA model using the first 4 PCs as input, 'right' motion. This shows the features by which the two groups differ maximally. The control group (blue) has a smaller ROM at L3/4, but greater ROM at L4/5. There also appears to be differences in shape of the motion curve, due to differences in angular velocity (gradients) at different points in the motion. There is an extreme value visible in the L4/5 motion curves which may be skewing the results. The data index is used as a surrogate for table motion on the horizontal axis.

## 210 Discussion

211 PCA identified three main modes of variation for passive IV motion. PC 1 was associated with  
212 uniform variation in ROM across the whole of this spinal region. PCs 2 & 3 were associated with  
213 variations in how ROM was shared within the spinal region. In these first three modes, there was  
214 little shape variation, with curves resembling that of the mean, which had a simple, smooth and  
215 symmetrical shape. The one exception was extension, where reduced ROM correlated with peak  
216 flattening and asymmetry. The nature of this association of shape change with ROM is unclear, but  
217 may indicate that relatively stiff spines exhibit hysteresis in lower lumbar joints, leading to  
218 asymmetry between outward and return movements.

219 Statistically significant differences in passive IV motion between NSLBP subjects and matched  
220 controls were found for coronal plane motions only, using low dimensional PC representations.  
221 LDA indicated there was reduced motion ROM at the most caudal joint in NSLBP participants,  
222 compensated for by higher ROM in the more cranial joints. In both cases, differences related largely  
223 to ROM and its distribution between joints, and little to the shape of the motion curve. Studies of  
224 distribution of motion between IV joints for flexion of the lumbar spine in healthy people indicate a  
225 gradual decrease of ROM from caudal to cranial, which they term the 'spine rhythm' [27] . If this  
226 finding can be translated to coronal plane motion, it would support the idea that increased motion in  
227 the cranial joints is deviation from normal.

228 The relative lack of motion curve shape variation appearing in the first few PCs may be because  
229 shape varies on an individual basis, and not in a consistent pattern across the sample. Examining the  
230 individual motion curves demonstrates wide variation in shape (see link to data repository), which  
231 shows that this mode of variation cannot be reduced to a few dimensions, at least not with PCA.  
232 Theoretically, an expanded neutral zone might cause a difference in shape of motion curve between  
233 groups [28] . However, this effect maybe obscured by the mechanical properties of adjacent joints.  
234 For example, an increased neutral zone would alter the leverage exerted on neighbouring joints.  
235 This altered stress applied to adjacent joints would be expected to confound the observation of their  
236 stress-strain curves, and may explain why the neutral zone is more important in in-vitro studies of  
237 intervertebral mechanics [10] .

238 These results are similar to studies that have shown that motion sharing inequality can distinguish  
239 back pain subjects from controls, in so far as both point to alteration in how motion is distributed  
240 between IV joints [11,29] . An inequality or alteration in restraint may predispose to mechanical  
241 back pain through a greater tendency to buckle. The spine, without active muscular control, has  
242 been shown to buckle with axial loads far less than typical in-vivo axial loads [30] . It could be  
243 speculated that alterations in motion sharing in the spine over the lifetime of an individual, due to  
244 degenerative changes or alterations in soft-tissue mechanical properties, may undermine the  
245 dynamic stability of its coordination patterns, an important consideration in the motor control of  
246 redundant systems, such as the spine [31,32] . It has been shown that motion sharing inequality  
247 correlates with age and degenerative changes [11] .

248 The reason why only coronal plane motions distinguished groups may be due to lower mean lumbar  
249 ROM for coronal plane active motions [33] . Presumably, the greater force required to obtain the  
250 same ROM during imposed passive motions may highlight the effect of differences in passive  
251 restraints. In addition, greater accuracy for tracking vertebral bodies in coronal plane motions may

252 mean these measurements are less contaminated with noise. Breen et al found that RMS error in IV  
253 angles obtained by vertebral tracking from videofluoroscopy images was 0.32 degrees for coronal  
254 plane and 0.52 degrees for sagittal plane motions [7] . The smoothing of the motion data due to  
255 spline interpolation should reduce the noise, but may not have been entirely successful, especially if  
256 the noise was not random and serially uncorrelated.

257 A limitation of the method used in this study is that it was limited to consideration in only two  
258 planes. Assessing dynamic motion in the transverse plane would require dynamic 3D imaging,  
259 which is not possible with 2D videofluoroscopy. There is some evidence of altered distribution of  
260 ROM in axial rotation between spinal segments being associated with back pain [34] .

261 This study undertook the first multivariate analysis of continuous passive IV motion data in a  
262 matched sample of back pain sufferers and controls, confirming the importance of altered passive  
263 restraints between vertebrae. Back pain is an enduring mystery, but in recent decades expanding the  
264 scope from just considering tissue pathology to incorporating psychosocial mechanisms, has led to  
265 deeper insights into this condition. Between these two lies the study of low-level control of  
266 intersegmental coordination, which may offer a better understanding of symptom variation over  
267 shorter time scales, which often are associate with variation in motion and posture. It may also help  
268 explain why NSLBP often remits and relapses without apparent reason [35] . Future longitudinal  
269 studies should focus on the time course of alterations in intersegmental coordination, to understand  
270 how they relate to the time course of NSLBP.

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