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Simultaneously assessing amplitude and temporal effects in biomechanical trajectories using nonlinear registration and statistical nonparametric mapping

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Abstract

Biomechanical trajectories generally embody amplitude and temporal effects, but these effects are generally analyzed separately. Here we demonstrate how amplitude-phase separation techniques from the statistics literature can be used to simultaneously analyze both. The approach hinges on nonlinear registration, which temporally warps trajectories to minimize timing effects, and the resulting optimal time warps can be combined with the resulting amplitudes in a simultaneous test. We first analyzed two simulated datasets with controlled amplitude and temporal effects to demonstrate how amplitude-timing separation can avoid incorrect conclusions from common amplitude-only hypothesis testing. We then analyzed two experimental datasets, demonstrating how amplitude-phase separation can yield unique perspectives on the relative contributions of amplitude and timing effects embodied in biomechanical trajectories. Last, we show that the proposed approach can be sensitive to procedural and parameter specifics, so we recommend that these sensitivities should be explored and reported.

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1. Introduction

Biomechanical trajectory analysis often involves temporal registration, whereby trajectories with variable temporal lengths (Fig.1A) are interpolated over a homologous time domain like percent stance, stride or movement time (Fig.1B). This process is often referred to as temporal 'normalization' in the biomechanics literature (e.g. Weiske et al., 2021), but this paper uses 'registration' (Sadeghi et al., 2000) to follow the broader literature (Ramsay and Li, 1998; Srivastava et al., 2011; Tucker et al., 2013; Marron et al., 2015; Wrobel et al., 2019).

Temporal registration can be either linear (Fig.1B) or nonlinear (Fig.1C). Linear registration interpolates each trajectory at n equally spaced time points between movement start and end, where n is often 101. Nonlinear registration contrastingly interpolates at non-constant intervals (Fig.2A), resulting in temporal displacement fields (Fig.1D,Fig.2B) which nonlinearly map a trajectory (Fig.2C) to the common, target time domain (Fig.2D).

Many nonlinear registration approaches exist for trajectory data including: event landmarking (Crane et al., 2010; Moudy et al., 2018) and manual warping (Pataky et al., 2019) along with many automated, algorithmic techniques (Ramsay and Li, 1998; Sadeghi et al., 2000; Marron et al., 2015). Nonlinear registration has been employed in the biomechanics literature to demonstrate both reduced variance (Sadeghi et al., 2000; Weiske et al., 2021) and improved correlation with performance measures (Moudy et al., 2018). Nonlinear registration algorithms remain in active development in the statistics literature (e.g. Cheng et al., 2016; Luca and Alessio, 2019; Wrobel et al., 2019).

There has been extensive recent work on amplitude-phase separation and analysis (Tucker et al., 2013; Marron et al., 2015; Lee and Jung, 2017; Tucker et al., 2019) including hypothesis testing (Henning and Srivastava, 2016). These approaches consider both amplitude, in the form of registered trajectories (Fig.1C) and phase (or 'timing'), as manifested in optimal warping functions (Fig.2A). As far as we are aware, these techniques have not yet been introduced to the biomechanics literature.

The purpose of this study was to demonstrate how amplitude-phase separation techniques can be applied to biomechanical data. We use statistical nonparametric mapping (SPM) (Nichols and

Holmes, 2002; Pataky et al., 2015) to conduct simultaneous inference on nonlinearly registered data and their optimal temporal warp functions. We first use two simulated datasets to demonstrate the proposed approach. We then analyze two experimental datasets to demonstrate potential practical benefits.

2. Methods

All analyses were conducted in Python 3.8.11, (van Rossum, 2021) using Anaconda 4.10.3 (Anaconda, 2021) along with the packages `fdasrsf` (Tucker, 2021) and `spm1d` (Pataky, 2012). All data and code associated with this paper are available on GitHub: `https://github.com/0todd0000/nlreg1d`.

2.1. Simulated Datasets

Two simulated datasets were constructed and analyzed. As these datasets were designed to illustrate specific cases of amplitude vs. timing effects, their relevance to experimental data analysis is left to the reader to interpret.

Dataset A (Fig.3-A.1) consisted of six trajectories for each of two groups. Each trajectory had a Gaussian pulse centered at different temporal locations. The true population mean pulse amplitudes for the two groups were 20 and 25, respectively. Temporally smooth Gaussian noise (amplitude=1) was added to each trajectory to ensure nonzero variance.

Dataset B (Fig.4-A.1) consisted of ten trajectories for each of two groups. Like Dataset A, each trajectory had a Gaussian pulse, and temporally smooth Gaussian noise (amplitude=1). Unlike Dataset A, the true population pulse amplitude mean for both groups was 20, and the temporal centers for the two groups' pulses were approximately 55 and 50, respectively.

2.2. Experimental Datasets

Two previously published datasets were reanalyzed in the main text:

Dataset C (Fig.5-A.1) (Besier et al., 2009) consisted of estimated vastus lateralis forces during the stance phase of walking for 15 Controls and 27 Patellofemoral (PFP) patients. This muscle was selected from a set of ten estimated muscle forces. Like the simulated datasets this muscle was selected for illustrative purposes. Analyses of the remaining nine muscles did not yield any results contrary to this paper's conclusions, so are excluded in the interest of brevity.

Dataset D (Fig.6-A.1) (Pataky et al., 2014) consisted of mediolateral center of pressure (COP) trajectories during the stance phase of walking in 10 healthy individuals (28.8 $\pm$ 8.3 years) for both Normal and Fast walking, where walking speeds were subjectively determined. Similar to above, analysis of the anteriorposterior COP component is excluded for brevity.

2.3. Nonlinear registration

All trajectories were first linearly registered by linearly interpolating between time=0% and time=100%. Next, the square-root slope framework (Srivastava et al., 2011; Tucker et al., 2013) as implemented in the `fdasrsf` package (method name: `srsf_align`) (Tucker, 2021) was used to nonlinearly register all datasets. This process is depicted in Fig.1; while the original, linearly registered data (Fig.1B) embody both amplitude and temporal variation, the nonlinearly registered data (Fig.1C) embody predominantly amplitude information, and the optimal deformation fields (Fig.1D) embody predominantly timing information.

2.4. Statistical analysis

We first used statistical non-parametric mapping (SnPM) (Nichols and Holmes, 2002) to conduct trajectory-level hypothesis testing (simulataneous inference) on linearly registered data, using either a two-sample test (Datasets A–C) or a paired test (Datasets D); SnPM is equivalent to the so-called 'F-max' procedure (Ramsay and Silverman, 2005; Pataky et al., 2021). Nonparametric inference was used because warp functions are geometrically constrained to monotonically increase, which can generally lead to non-normal distributions at arbitrary domain points.

We next analyzed the data using our proposed multivariate test which simultaneously considers both amplitude and timing effects. Noting that 't' is used later to represent the t-statistic, let q represent temporal location and let $a_i(q)$ represent the ith linearly registered trajectory (Fig.1B). For each $a_i(q)$ we assembled a multivariate trajectory $\boldsymbol{y}_i(q)$ as follows:

$$\boldsymbol{y}_i(q) = \begin{Bmatrix} a_i(q) \\ w_i(q) \end{Bmatrix} \tag{1}$$

where $a_i(t)$ is the ith nonlinearly registered trajectory (Fig.1C) and $w_i(q)$ is its corresponding displacement field (Fig.1D).

These multivariate trajectories were analyzed using two-sample (Datasets A–C) or paired (Dataset D), nonparametric Hotelling's T^2 tests, for which parametric versions are described elsewhere (Worsley et al., 2004; Pataky et al., 2013; Pataky, 2016); see also the 'Assumptions' notebook in this repository: `https://github.com/0todd0000/nlreg1d/tree/main/Notebooks`. *Post hoc* univariate tests were then conducted separately on the $a_i(q)$ and $w_i(q)$ components to augment interpretations of the main multivariate tests. This *post hoc* analysis of $w_i(q)$ follows Taylor and Worsley (2008).

The key distinctions between the common and proposed approaches are: (i) linear vs. nonlinear registration, and (ii) univariate analysis of amplitude effects vs. multivariate analysis of both amplitude and timing effects. While linear vs. nonlinear registration differences have been extensively considered elsewhere (e.g. Sadeghi et al., 2000; Srivastava et al., 2011; Tucker et al., 2013), to our knowledge, the proposed simultaneous inference, multivariate approach has been previously reported in neither the biomechanics nor statistics literatures.

3. Results

3.1. Simulated Datasets

Univariate analysis of Dataset A failed to yield significance (Fig.3-A.2), but the proposed multivariate approach yielded a large and significant effect (Fig.3-B.3). *Post hoc* analyses revealed that this effect was due mainly to amplitude effects (Fig.3-B.4) as opposed to timing effects (Fig.3-B.5). These results show that temporal variability can hide true amplitude effects (Fig.3-A.1), and that — in the face of temporal variability — nonlinear registration is generally required to elucidate true amplitude effects.

Univariate analysis of Dataset B yielded significance (Fig.4-A.2), with a suprathreshold cluster spanning approximately time = 30-50%. The proposed multivariate analysis similarly yielded significance (Fig.4-B.3). *Post hoc* analyses suggested that this effect was due mainly to timing differences (Fig.4-B.5). These results show that: (i) typical SPM results can be ambiguous in terms of amplitude vs. timing effects, and (ii) the proposed multivariate approach can detect even small (but systematic) timing differences.

3.2. Experimental Datasets

Univariate analysis of Dataset C failed to yield significance (Fig.5-A.2), in disagreement with multivariate results (Fig.5-B.3). *Post hoc* analyses suggested a significant timing difference between Controls and PFP patients (Fig.5-B.5) but not a significant amplitude difference (Fig.5-B.4). While the original article reported a significant maximum force (amplitude) effect for these data (Besier et al., 2009), the present results refute that interpretation, and suggest that only temporal effects are significant.

Univariate analysis of Dataset D yielded significance (Fig.6-A.2), largely in agreement with multivariate results (Fig.6-B.3). *Post hoc* analyses suggested that these effects were predominantly temporal (Fig.6-B.5). These results emphasize that common univariate analyses do not distinguish between amplitude and temporal effects in experimental datasets.

4. Discussion

This study has demonstrated how amplitude-phase separation (Tucker et al., 2013; Lee and Jung, 2017; Tucker et al., 2019) can be used, along with a single hypothesis test, to simultaneously analyze amplitude and timing effects in biomechanical trajectories. This approach requires that (i) amplitude effects are suitably isolated in nonlinearly registered trajectories (Fig.3B.1), and that (ii) the resulting temporal warps suitably embody timing information (Fig.3B.2). The importance of nonlinear registration for reducing variance improving homology has been extensively demonstrated in previous research (Ramsay and Li, 1998; Sadeghi et al., 2000; Weiske et al., 2021; Moudy et al., 2018), but its relevance to amplitude-phase separation has not, to our knowledge, been previously reported in the biomechanics literature.

The proposed technique is especially applicable to biomechanics studies for which amplitude and timing effects are of empirical interest, and where null hypotheses encompass both amplitude and timing effects. Null hypotheses are often of the form: 'no kinematic effects' or 'no changes in joint moments', a form which does not identify specific dependent variables, implying that amplitude or timing effects, or both, can be used to reject, or fail to reject, such hypotheses. The proposed approach tightly matches this type of hypothesis. Distinguishing between amplitude and timing effects may be biomechanically important because amplitude and timing are generally associated with fundamentally different biomechanical constructs: amplitude is generally associated with mechanical capacity (strength, loading magnitude, etc.) and timing is generally associated with coordination and control (neural activation patterns, kinematic style, etc.). This distinction is of course imperfect: strength and force transmissibility are directly related by kinematics through the Jacobian of the kinematic chain. Regardless of their specific interpretations, a method that can distinguish between amplitude and timing effects may provide a novel paradigm for empirically probing a potentially wide set of biomechanical problems.

In this study we considered only two-sample and paired comparisons, but through SPM our proposed method extends to the full family of experimental designs (Friston et al., 1995; Pataky, 2016) including regression, ANOVA, ANCOVA and ultimately MANCOVA (Worsley et al., 2004). We do not expect that the proposed approach would exhibit experimental design dependencies because nonlinear registration can be conducted at the trajectory set level (Tucker et al., 2013; Marron et al., 2015) in a manner that excludes experimental design information.

Like any analysis tool, the proposed approach has the potential to be abused. Different nonlinear registration algorithms generally yield different displacement fields (Fig.7), and algorithm parameters can generally be tweaked to produce (Fig.7g) or eradicate (Fig.7f) significance in datasets with relatively large effects. This is generally true for all data processing steps including common steps like smoothing. It is the responsibility of the investigator to ensure that their conclusions are robust to the particulars of these processing parameters, and sensitivities to procedural tweaks should be reported.

A final important limitation is that the proposed *post hoc* analyses of amplitude vs. timing effects may be inconsistent with the main multivariate test (e.g. Fig.5B3,B5). This is nevertheless a standard limitation of multivariate analyses: dependent variables are generally non-independent, exhibiting some correlation, which implies that multivariate results cannot always be interpreted when independently analyzing individual variables.

In summary, we have demonstrated how existing nonlinear registration frameworks can be used to simultaneously test for amplitude and timing effects in biomechanical trajectories. In the absence of a specific null hypothesis to the contrary, default null hypotheses (of 'no effect') pertain to both amplitude and timing effects. Since both amplitude and timing effects are generally of empirical interest, we submit that amplitude-phase separation is necessary to robustly test the default null hypotheses of many biomechanics studies.

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Conflict of Interest Statement

The authors report no conflict of interest, financial or otherwise.

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275 # Figures

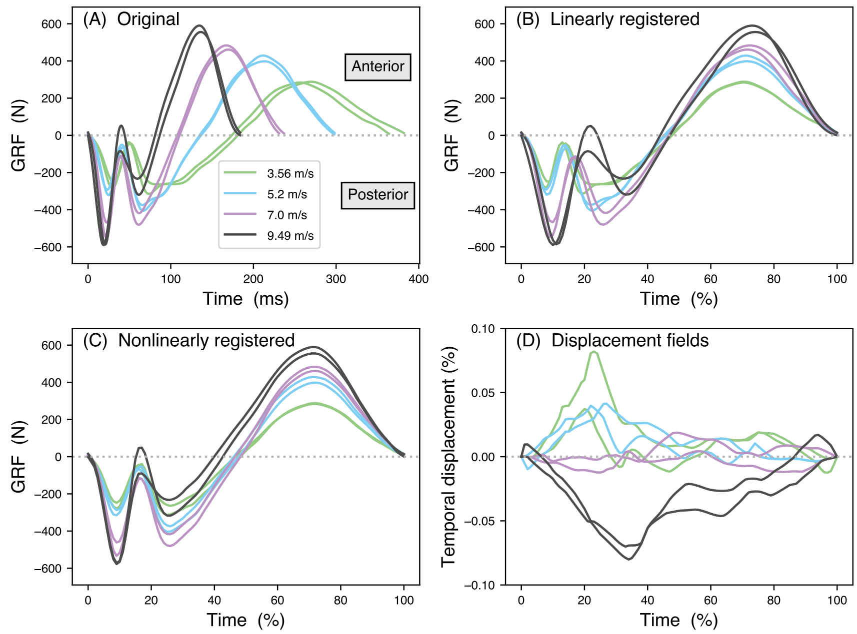

Figure 1: Example nonlinear registration. (A) Original anterioposterior ground reaction force (GRF) data from Dorn et al. (2012) containing two observations for each of four running / sprinting speeds. (B) Linearly registered data, wherein each trajectory has been interpolated at 101 equally spaced time points from the start to the end of the trajectory. (C) Nonlinearly registered data using the method of Tucker et al. (2013). (D) Temporal displacement fields associated with the optimum nonlinear time warps; positive/negative values indicate that the specified time location has been moved forward/backward in time by the specified amount, relative to the full temporal domain. For example, at approximately time=35% the fastest speeds have displacement values of approximately -0.08, implying that points in this vicinity from panel B have been moved backward in time by about 8% to achieve the nonlinear registration in panel C.

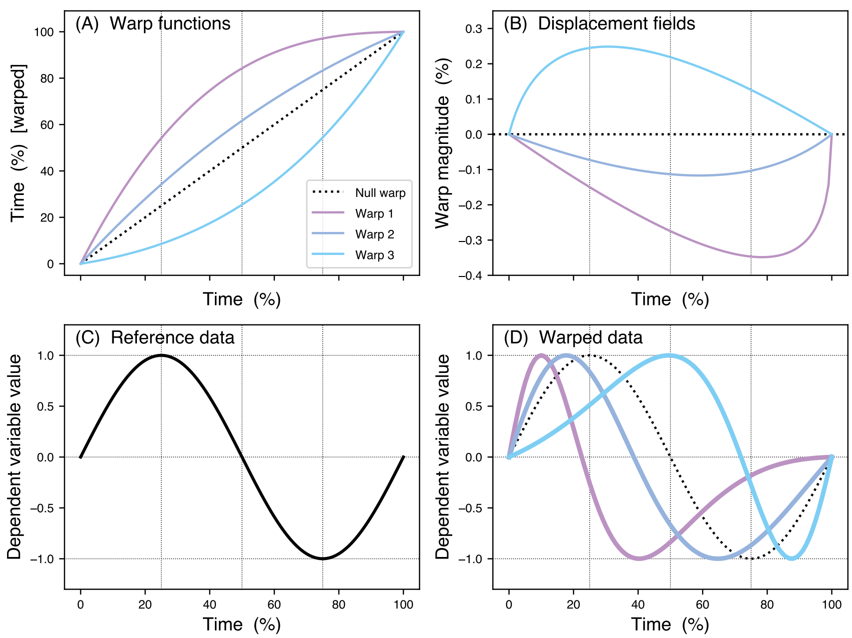

Figure 2: Depiction of temporal warping. (A) Three example warp functions along with the null warp. (B) Displacement fields corresponding to the warps from panel A. (C) A simple sine wave reference datum. (D) The reference datum from C after warping.

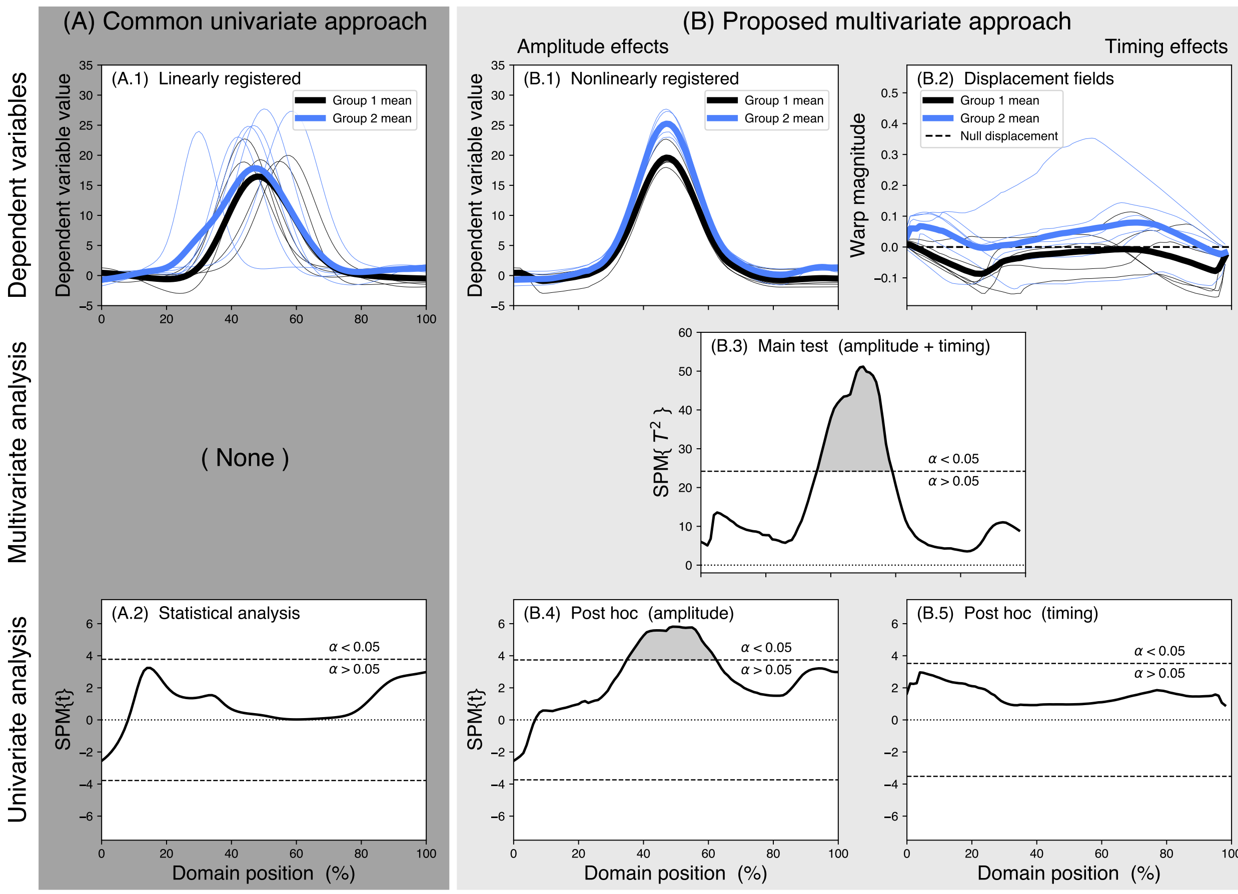

Figure 3: Dataset A (simulated), embodying a true amplitude effect, with temporal variability. (A) Depiction of the common SnPM approach where (A.1) linearly registered data are analyzed, for which in this case (A.2) no significance is found. (B) Depiction of the proposed method, which starts with (B.1) nonlinear registration, which yields (B.2) displacement fields, one per observation, where each displacement field represents the magnitude of temporal displacement required to register the data, and where the total warp energy — across all observations — is minimized. (B.3) The two-sample Hotelling's T2 test simultaneously considers the nonlinearly registered data and the displacement fields, and in this case yields significance. *Post hoc* analysis clarifies that group differences are predominantly due to (B.4) amplitude effects as opposed to (B.5) temporal effects. Key result: the proposed approach correctly identifies the true amplitude effects in this synthetic dataset, but the common approach does not.

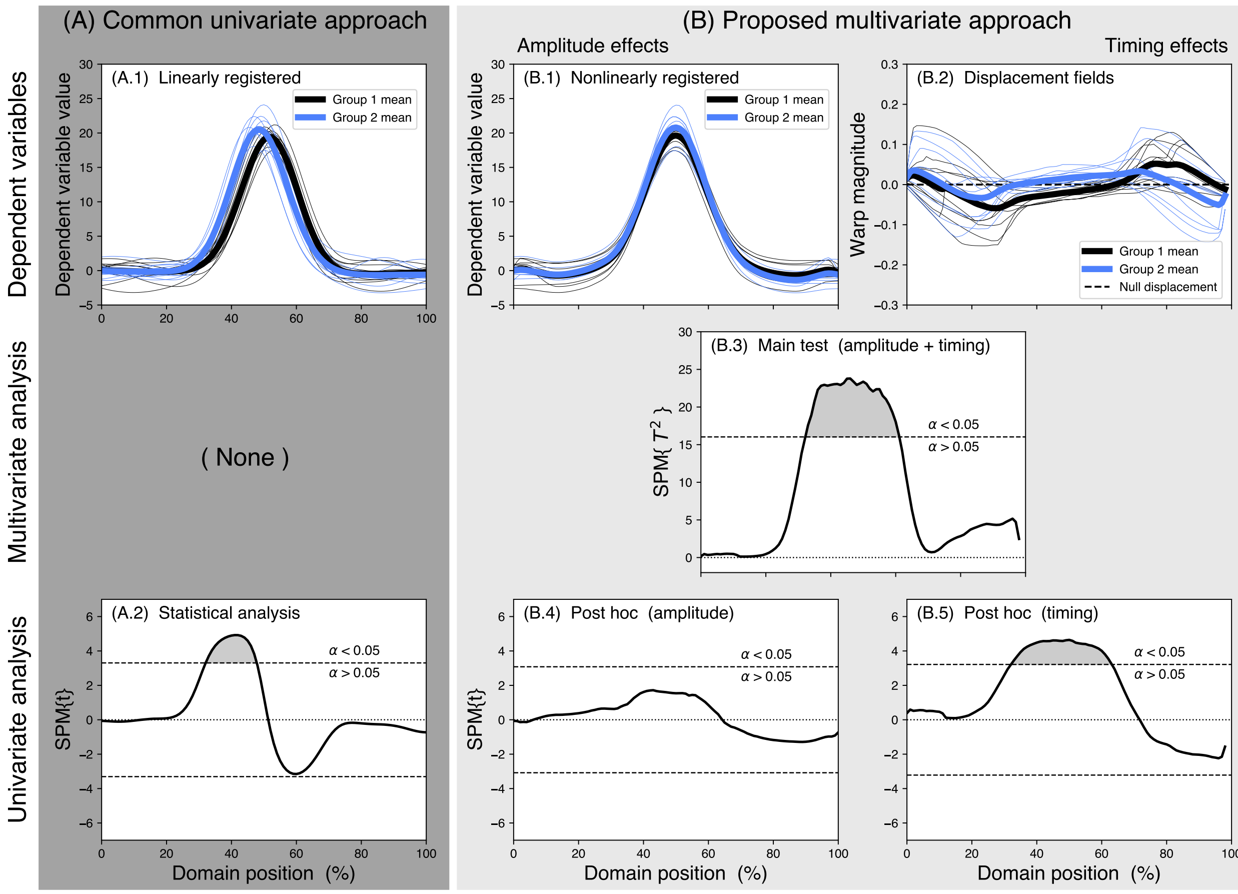

Figure 4: Dataset B (simulated), embodying a true temporal effect, but no true amplitude effect. Data presented as in Fig.3. Key result: the proposed approach correctly isolates the true temporal effect (B.3-5). Although the common approach also reaches significance (A.2), based on only that result it is unclear whether this is due to an amplitude or a timing effect.

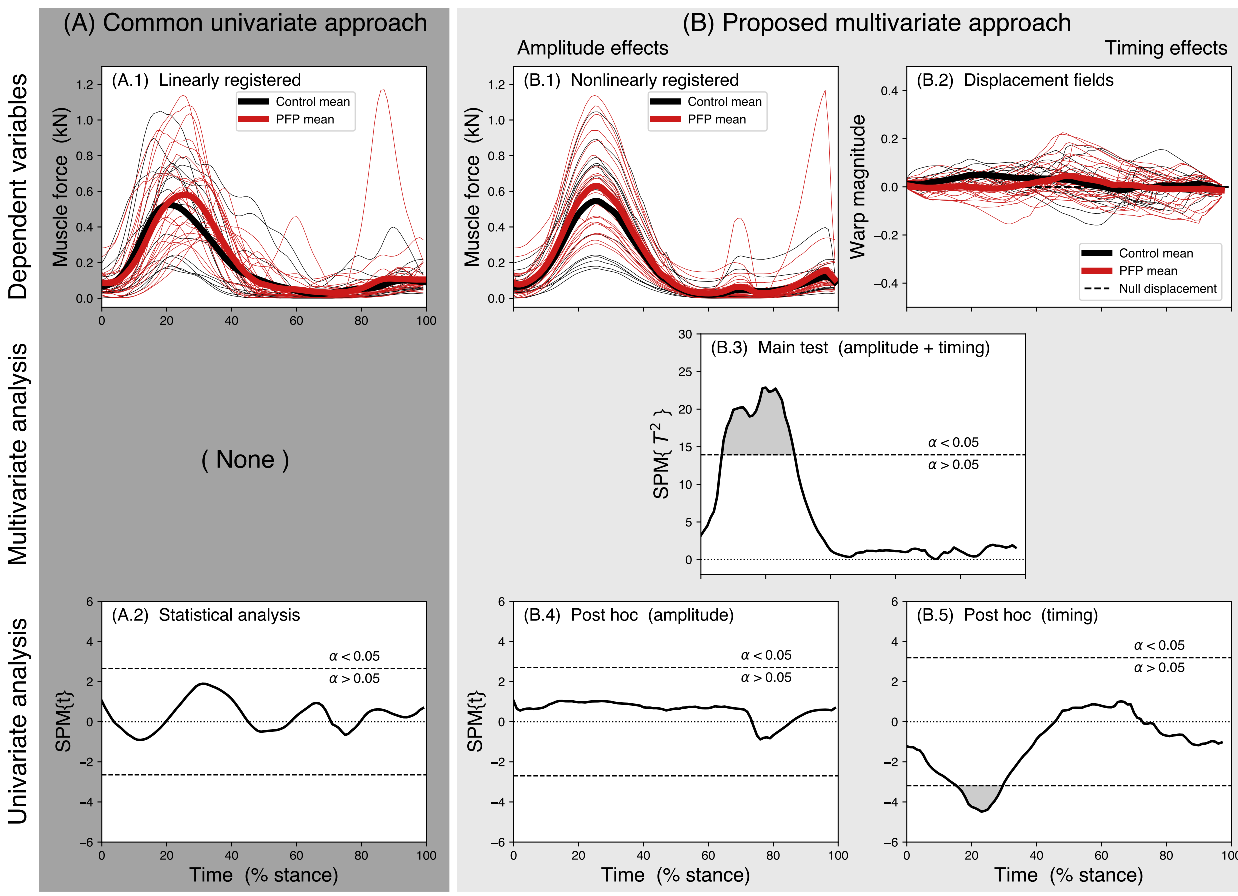

Figure 5: Dataset C (experimental) (Besier et al., 2009): vastus lateralis forces in patellofemoral pain (PFP) patients and Controls during walking. (A) The common approach fails to yield significance. (B) The proposed approach suggests that there is a significant temporal delay in the PFP in early-stance vastus lateralis forces.

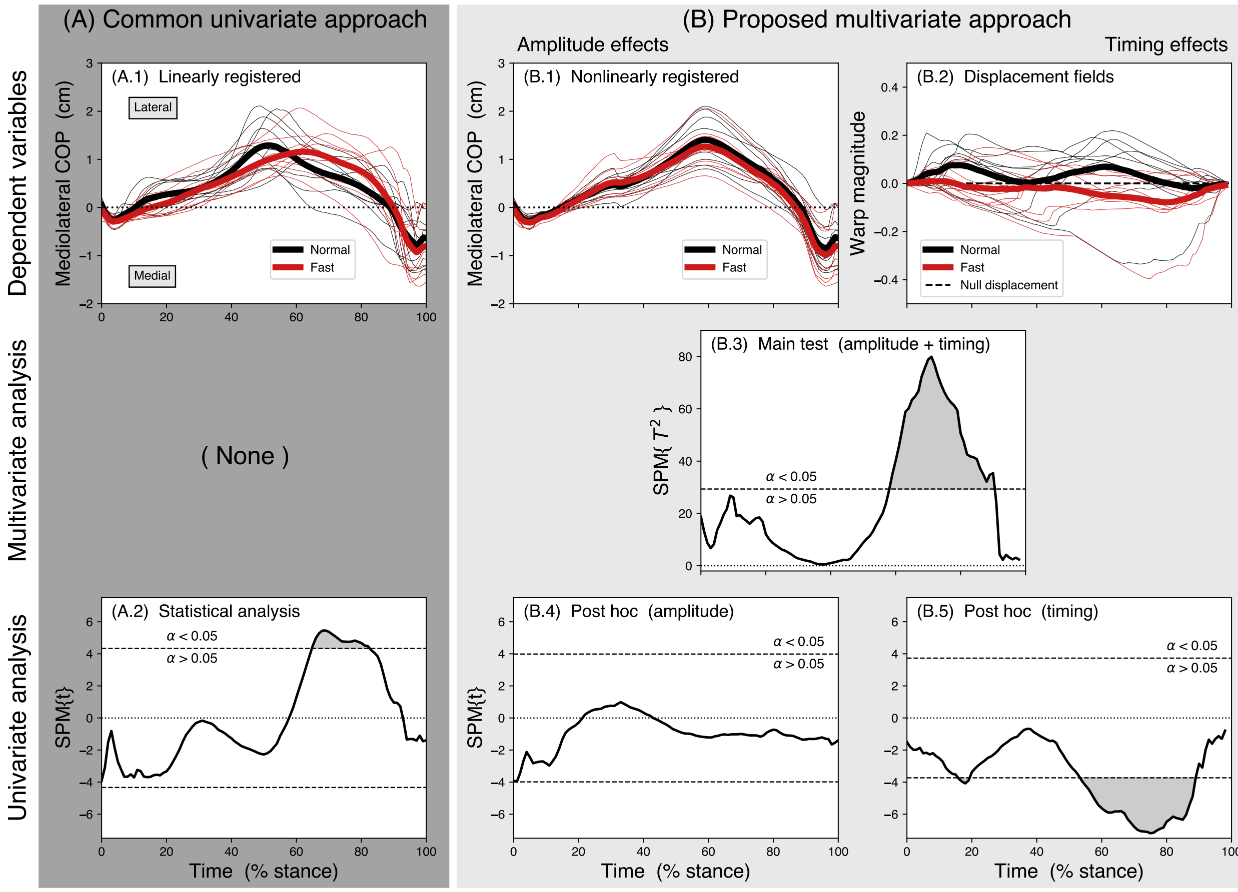

Figure 6: Dataset D (experimental) (Pataky et al., 2014): mediolateral center-of-pressure (COP) excursions during Normal and Fast walking. Both approaches yield significance, but the proposed approach suggests that the effect is primarily temporal (B.5), suggesting that the common approach's result (A.2) could be misinterpreted as an amplitude effect.

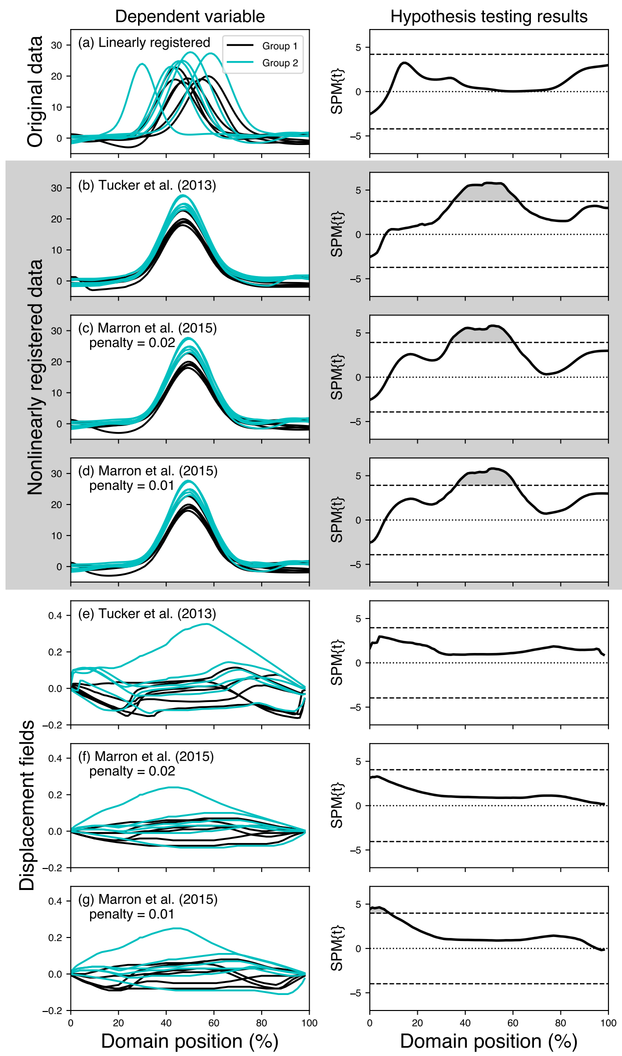

Figure 7: Example sensitivity to nonlinear registration algorithms / parameters. (a) Original data and SnPM results; same as Fig.3A . (b) Nonlinearly registered data using the approach from Tucker et al. (2013), along with SnPM results; same as Fig.3B1,B4. (c-d) Nonlinearly registered data using the approach in Marron et al. (2015) with penalty parameters of 0.02 and 0.01, respectively. (e-g) Displacement fields and SmPM analysis for the registration results from panels b-d. Changing the penalty parameter from 0.02 (f) to 0.01 (g) causes a change in the null hypothesis rejection decision.