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Sharing Data to Understand Spatial Variation in the Musculoskeletal System: Can the Uptake being seen in Open-access Online Journals Extend to Data Repositories?

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The use of finite element (FE) analysis has increased substantially with the development of computational and imaging technology, helping extend our understanding of the relationship between form and function in the orthopaedic and muscular system. In some biological systems detail in these models can become extremely fine, with micro-structural data being combined with data on the macro scale to better understand the functional link across multiple scales [1]. Increasingly model development is being driven by data, leading to approaches that combine highly specialised experimental and computational techniques. The difficulty and expense involved in obtaining the data and developing these models means that sample sizes are often modest, limiting researchers' ability to investigate the (spatial) variation in the imaged data (namely, differences in the shape and arrangement of structural components). As more data is collected by research groups, an important question related to this drive to understand the link between form and function is whether investigation of the spatial variation within the micro-scale can yield methods for early detection of disease or degradation in function. What is most needed to answer this question is more data.

Modelling of shape has been significantly advanced by research in the area of computer vision. The use of spatial and mathematical landmarks has allowed considerable progress to be made in modelling a particular object's shape [2,3], as well as in comparing shapes of a given type and quantifying the shape variation through Principal Component Analysis [4] or Independent Component Analysis [5]. However, identifying the appropriate number and location of landmarks to accurately model variation in shape across a collection of objects is a difficult problem in itself, especially in the medical setting where the object of interest is 3-dimensional and may consist of highly deformable biological tissue. Some progress has been made, with varying degrees of automation, in using splines to identify landmarks (b-splines for fitting to curves [6] and radial basis splines for higher dimensions [7]). Such an approach not only positions the landmarks for each object, but also determines the correspondence required for the subsequent shape analysis (in fact the coefficients in the fitted model associated with each knot can also be included in the subsequent PCA if they are of interest). Where radial basis splines are fit to the object data from multiple 2-dimensional slices, this approach has the advantage of producing a 3-dimensional realisation of the object of interest. PCA identifies the modes of variation in the shape of the object across the sample collected, and can be used to simulate candidate objects from the population of interest, not seen in the sample collected. Given an "average" FE model with corresponding landmarks, PCA can also be used to expedite the FE modelling process, as information contained in the principal modes can be used to deform the "average" model to best fit a particular object. The effectiveness of this approach improves as the size of the training set increases. With all aspects of shape analysis, sharing data across research groups improves model precision.

Approaches for modelling variation in structure (or spatial arrangement) are not as advanced as those for capturing variation in shape. In other biological systems some progress has been made in capturing the arrangement of organelles in 2-dimensional slices by using object centroids to identify their position, and then modelling their arrangement in space as a point process [8]. Such a model enables the investigation of point intensity, inter point dependence (attraction or repulsion), and even the inclusion of covariates to explain position. Furthermore, it is possible to simulate point patterns from a model for the point process, which is particularly valuable at the micro-scale (for example enabling both immunofluorescence data and 3-dimensional electron tomography data to drive the same model). This approach can be extended to 3-dimensions where appropriate [9], but many features in a biological system cannot have their location modelled this way (for example fibre strands or neural pathways). Other approaches are required to consider the complex arrangement of 3-dimensional structure, but where the theory of spatial point processes is fairly limited (being a reasonably recent discipline [10]), approaches to modelling components best represented by lines or networks are virtually non-existent. There is certainly potential to apply the theory of spatial point processes at the micro-scale of the muscular-skeletal system, but with the growing sophistication and power of the various imaging modalities it is necessary for the development of statistical techniques to keep pace. As with existing methods; future theoretical developments will be data driven.

Our understanding of the relationship between the properties of the objects that constitute a biological system and how that system functions can be increased, verified, and put to use by developing more comprehensive models that include features at multiple scales. The clinical benefits from these models can be profound, but this model development is dependent on the use of data that is extremely expensive and time-consuming to collect. To expedite the modelling process it is important that research groups share their data. I urge those who collect this data to consider making it available to other researchers, via open-source software and data repositories, such as the Musculoskeletal Atlas Project [11].

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