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DEEP 3D CONVOLUTION NEURAL NETWORK METHODS FOR BRAIN WHITE MATTER HYBRID COMPUTATIONAL SIMULATIONS

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ABSTRACT

Material properties of brain white matter (BWM) show high anisotropy due to the complicated internal three-dimensional microstructure and variant interaction between heterogeneous brain-tissue (axon, myelin, and glia). From our previous study, finite element methods were used to merge micro-scale Representative Volume Elements (RVE) with orthotropic frequency domain viscoelasticity to an integral macro-scale BWM. Quantification of the micro-scale RVE with anisotropic frequency domain viscoelasticity is the core challenge in this study.

The RVE behavior is expressed by a viscoelastic constitutive material model, in which the frequency-related viscoelastic properties are imparted as storage modulus and loss modulus for the composite comprised of axonal fibers and extracellular glia. Using finite elements to build RVEs with anisotropic frequency domain viscoelastic material properties is computationally very consuming and resource-draining. Additionally, it is very challenging to build every single RVE using finite elements since the architecture of each RVE is arbitrary in an infinite data set. The architecture information encoded in the voxelized location is employed as input data and is consequently incorporated into a deep 3D convolution neural network (CNN) model that cross-references the RVEs' material properties (output data). The output data (RVEs' material properties) is calculated in parallel using an in-house developed finite element method, which models RVE samples of axon-myelin-glia composites. This novel combination of the CNN-RVE method achieved a dramatic reduction in the computation time compared with directly using finite element methods currently present in the literature.

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1. INTRODUCTION

The brain white matter (BWM) is comprised of networks of nerve fibers called axons, which are covered by myelin, a lipid-rich substance, and are embedded in glia, the extracellular matrix. Due to the heterogeneity of the BMW tissue, its mechanical properties vary considerably with the local microstructural architecture, i.e., geometry, location, and orientation of BWM, and need to be analyzed at the micro-scale level [1-4]. According to those considerations, this paper focuses on the quantification of the mechanical properties of micro-scale Representative Volume Elements (RVE) of the BWM with anisotropic frequency domain viscoelasticity [5, 6]. The primary purpose of these RVEs is to produce the numerical linkages between the heterogeneity of the microstructure of BWM and the anisotropic mechanical material properties [7-11].

Finite elements (FE) offer great freedom in discretizing a composite structure at the microstructural scale and analyze its stress-strain response [8-12]. However, the computational resources required for the FE discretization and analysis are usually very demanding. Especially for BWM microstructural composites, the complex geometric architecture necessitates mesh refinement increasing the computational cost. Additionally, considering that the complex interactions of the composite tissues will also call for further mesh refinement of the FE model to increase the accuracy of the results, the increase of the computational cost can be dramatic [1-5].

Apart from the high computational requirements of the FE method, a more significant disadvantage is the mesh complexities that arise for the intricate geometric 3D model. Mesh intricacies are owed to the arbitrary and random nature of axons groupings in the BWM, which create the 3D geometric models of the RVEs. It's noteworthy that different regions of the BMW offer different microstructural architectures ranging from uniform isotropic parallel configurations of axons to completely random ones. *These axons will unavoidably include some irregular extremely sharp angles, which will cause mesh failure or even simulation failure.*

The Convolution Neural Network (CNN) has been proved as a high-performance, practical approach for computer vision and image analysis applications [13-15]. Here, the CNN is employed as a deep learning method, which is ideally suited to resolve the computational cost and mesh failure issues. In essence, the FE method is used to create the RVEs and collect training data from the stress-strain analysis, while the CNN is utilized to establish structure-property linkages for RVEs. It is expected that the CNN model will provide a much faster answer compared to the FE model with only a modest loss accuracy.

2. MATERIALS AND METHODS

2.1. Representative volume element model

In our study, the RVE scale has to be large enough to capture the microstructural tissue interactions within the BWM, but also small enough to account for the detailed geometric information within a reasonable-sized model at an affordable computational cost [13-15].

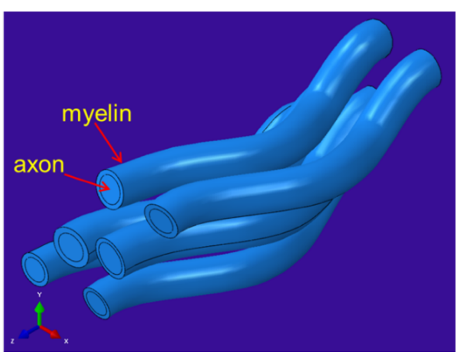


Figure 1. Six (6) axons covered by myelin bionic with random walk direction and location. The radii of axon and myelin are randomly changed based on a certain value range (15 ~ 20 μm). The ratio of the internal/external radius is 0.7 ~ 0.8.

Since the BWM is a complex anisotropic structure, the location and direction of axons can be randomly assigned in space. The RVEs used in this study were generated by starting with a 3D axon bionic random walk algorithm in python (**Figure 1**). Based on this algorithm, the model randomly generates geometric structures mimicking 3D axons. The axons and myelin are assigned random radii congruent to the geometric constraints asserted by real BWM microtome data [1-2]. This algorithm automatically avoids intersecting axons while it maintains a minimum interaxonal distance to maximize the axonal volume fraction.

After the geometric reconstruction of the axon, myelin, and glia composite by the aforementioned reconstruction model, a 3D RVE cutting algorithm based on Abaqus Python API was built (**Figure 2**). Based on this algorithm, the RVEs are created for building the FE model (**Figure 3**).

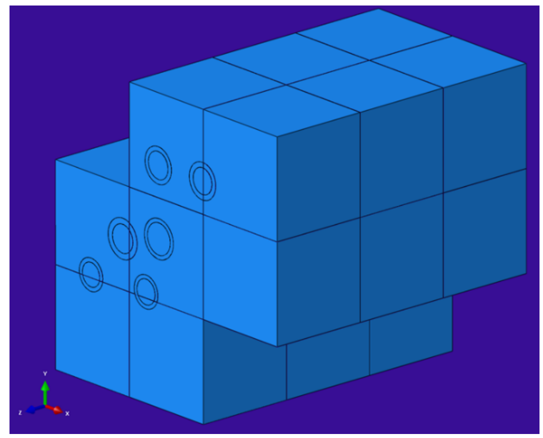


Figure 2. Anisotropic RVEs cutting algorithm. The length of the RVEs' edge is 25 μm. Twenty-two (22) RVEs containing six (6) axons are depicted. The axons were generated using a bionic random walk algorithm.

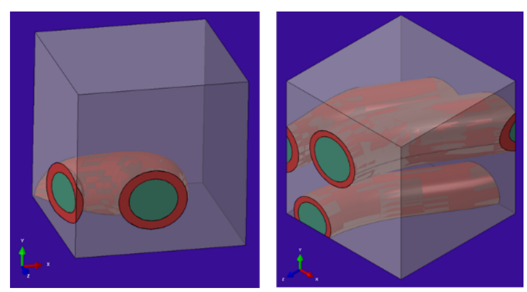


Figure 3. Anisotropic RVEs created from the cutting method. The green, red, and grey parts are the axons, myelin, and glia, respectively.

2.2. Finite element analysis

In order to represent the accurate constitutive relation of the RVEs, the full anisotropic stress-strain relation is considered in the FE analysis. Six directional harmonic excitation loads at 50Hz frequency of 0.1 kPa are independently applied to the RVEs (**Figure 4**).

Since the full anisotropic material properties have 32 independent constants, the total number of independent constants of the RVEs' material properties should be 72 in the viscoelastic frequency domain. That data will be used in the training of the CNN as the output section.

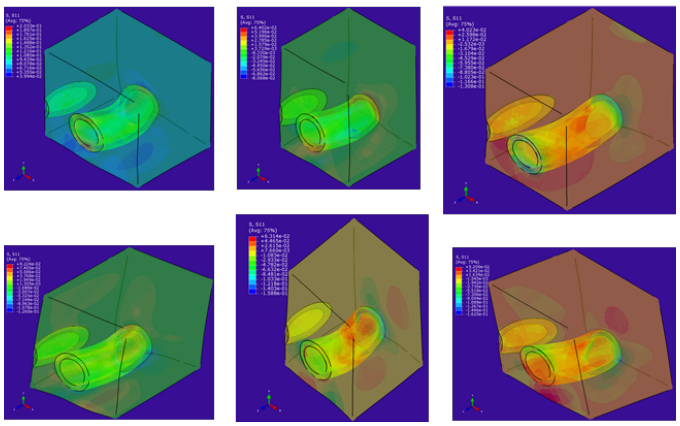


Figure 4. The six (6) loading directions for anisotropic RVEs. From the upper left to lower right corners, the six directions are three tensile in x-axis, y-axis, z-axis, and three shear directions in the x-y, y-z, and x-z planes. (The deformation is scaled to illustrate the loading directions).

2.3. 3-D CNN for homogenization of RVE

The purpose of CNN is to utilize finite samples of RVEs to reach an answer quickly to offset the high computational cost and possible mesh failure (**Figure 5**). The final trained CNN can generate anisotropic material properties based on the input of geometric information of RVEs.

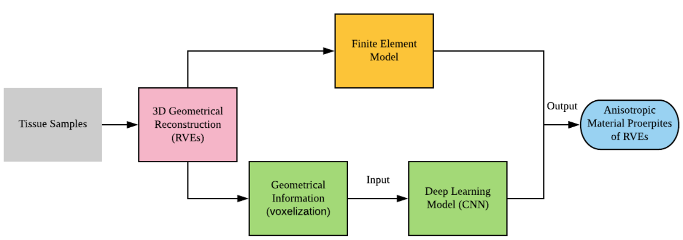


Figure 5. Methodology combining FEs and deep learning. The tissue samples provide information for the reconstruction of RVEs. The RVEs would be used for building the FE model and extracting geometric information. The FE model outputs the anisotropic RVE material properties, which is the stiffness tensor of RVEs (output part of the training set for CNN). The voxelization process generates the voxelized 3D NumPy array to represent the geometric information (input part of the training set for CNN).

The geometric information and input data of each anisotropic RVE includes volume fraction (VF), axonal orientation, and the three distinct material properties (axon, myelin, and glia) with their location information in the RVE cube. It is noteworthy that, using the VF, axon/myelin ratio, axonal orientation, and material properties is not enough to represent the uniqueness of each RVE. Therefore, a more accurate and distinctive method should be employed to implement the geometric information as training inputs. Based on these considerations, the voxelization method is selected to extract the geometric information and the 3D location of the RVEs in space (**Figure 6**).

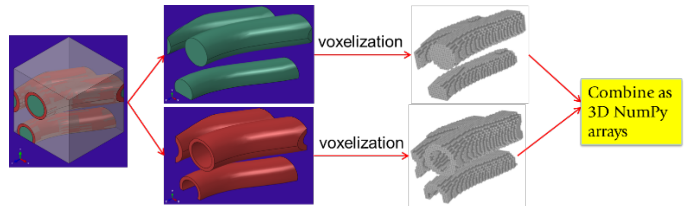
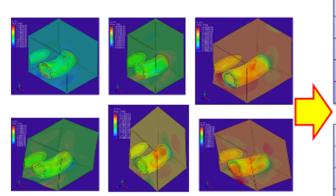


Figure 6. The voxelization method for RVE. The green and red parts are the axons and myelin geometric constructs. The voxelization method creates the 3D NumPy arrays based on the occupation of axons and myelin in 3D space.

The voxelization method scans the full 3D cubic space of the RVEs to get the occupation (points of material occupied by) of axons and myelin. 3D NumPy arrays (n×n×n dimension, where n is the number representing the “occupation” value in each edge of the RVE cubes) are generated based on the spatial locale information. If the point of the current scan in 3D space is an axon, the occupation value on this point is set to 1. If the point of the current scan in 3D space is myelin, the occupation value in this point is set to 0.5. The occupation value of the remaining points that are neither axons part nor myelin is set to 0. The combined 3D NumPy arrays (occupation of RVEs) would embody the input of training data for CNN (**Figure 5**). The output is the anisotropic material properties of RVEs (stiffness tensor of 72 constants).

3. RESULTS AND DISCUSSION

In the first step, 927 FE RVE models are created. During the FE analysis, each RVE model is subject to six loading tests (one in each direction as described in Figs 4 and 7) to determine the stiffness tensors of 72 constants (**Figure 7**) for the output data of CNN.



Real part stiffness tensor of RVE

51.2603	46.9232	47.4527	1.30016	1.6237	0.4676
49.3719	48.594	47.3477	1.2747	1.55549	0.426518
49.3799	46.8518	49.1081	1.24919	1.58754	0.446288
0.051059	0.028111	0.002908	0.936006	0.015672	0.00965
0.058731	0.023084	0.06006	0.016339	0.962514	0.026492
-0.01814	-0.00292	0.006712	0.003229	0.01183	0.893384

Imaginary part stiffness tensor of RVE

0.588205	-0.29058	-0.1526	0.050418	0.128437	0.06339
-0.08247	0.302588	-0.19093	0.037226	0.099464	0.045219
-0.08032	-0.3107	0.431111	0.030198	0.112135	0.054449
0.019878	0.007888	0.001927	0.334907	0.006874	0.004648
0.021951	0.004889	0.026724	0.007516	0.348829	0.013226
-0.0089	0.000954	0.00523	0.001634	0.00545	0.316166

Figure 7. Example of an RVE sample subjected to six(6) different loading conditions (left) and the resulting RVE stiffness tensor (right) .

High density voxelization can better capture the intrinsic geometric details of the composite architecture of the RVEs. When the density of voxelization increases, the number of occupation values (n×n×n) increases in a particular RVE. The larger number of occupation values in an RVE, the more information is contained in the 3D NumPy arrays. The latter leads to increased accuracy and completeness of the RVE geometrical description. However, using a large number of occupation values will sharply increase the input dimensions of the CNN, resulting in higher computational cost. Here, a balance between the geometric expressiveness and the computational cost was achieved by selecting a 30×30×30 dimensional occupation for voxelization. That is, the voxelization method will generate a 30×30×30 dimension 3D NumPy arrays as the input data of CNN. The architecture of 3D CNN is illustrated in **Figure 8**.

The full dataset (927 samples) was separated as the training dataset (881 samples) and the testing dataset (46 samples). During the training process, the occupation data of 3D NumPy arrays generated from 3D RVEs are the input training data of CNN. The output training data of the CNN, i.e., an RVE's stiffness tensor, is generated from the FE model. The training data will go through the architecture of the CNN and obtain the output in the final stage in **Figure 8**. Then this output will be used to calculate Mean Square Errors (MSE) based on the output of the FE model. After that, the optimization process will be used to update the CNN model. Those processes are called forward propagation and backward propagation in neural network training. The validation set was split as 10% of the training set.

In Figure 8, each convolution layer has convolution filters and an activation function. A convolution filter passes over all the voxels of the 3D NumPy array to produce voxels to assess the convolved output in the current layer. The activation function employed in this paper is the Rectified Linear Unit (ReLU), which is used to introduce the nonlinear relationship between inputs and outputs. ReLU activation function can be defined as $y = \max(0, x)$, where x is the input value, and y is the output value. The max-pooling layer partitions the input 3D NumPy array into non-overlapping sub-regions, and for each such sub-region outputs the maximum value. After the final convolution layer, 3D NumPy array is flattened into a 1D NumPy array (fully connected layers). The fully connected layers are gradually reduced dimension to 72 by the dense layer.

The trained CNN can generate the stiffness tensor based on the input of 3D voxelization of the geometrical structure of the RVEs. As is described **in Figure 5**, based on new tissue samples, the new 3D geometrical reconstruction process can offer new 3D models. The new 3D models will act as the input of the voxelization process and record the occupation data of the 3D NumPy arrays. In turn, the 3D NumPy arrays will be integrated into the trained CNN, and the CNN will output the stiffness tensors. During this scheme, the FE analysis can be omitted, and the on-time result of RVEs' anisotropic material properties will be derived directly from the CNN.

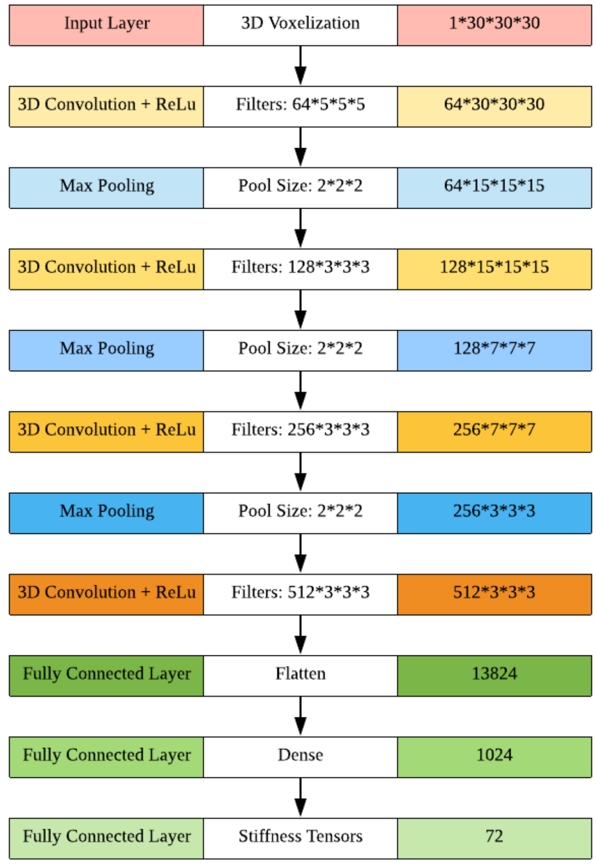


Figure 8. The architecture of the 3D CNN used in this study. The left column is the name of the layer and the activation function of CNN. The middle column is the filter size and input/output data. The right column is the feature tensor size output of each layer. ReLu activation function was used for the convolution layer. The max-pooling layer was applied between each convolution layer.

The validation set was split as 10% of the training set. The training history is shown in **Figure 9**. The results indicate that the MSE (the difference between expectation output and training output in each epoch) is decreased based on the training process. An epoch is one cycle through the full training dataset. In this training history, it is clear that the model is continuously decreasing the bias at each epoch. Moreover, the 3D CNN model has comparable performance on both training and validation datasets. The final validation MSE value is 0.0051, and the final training MSE value is 0.0038. The prediction of the testing dataset based on the trained CNN results in a coefficient of determination of R^2=0.8225. The coefficient of determination ranges from 0 (poor fit) to 1 (perfect fit) and it provides a measure of how well the test outcomes can be explained by the model. The above results illustrate that the training process is successful based on the current 3D CNN architecture. Furthermore, with careful design of architecture and tuning of the hyperparameters (voxelization size, pool numbers, pooling dimensions, filters number/dimensions, as described in **Figure 8**), the deep learning approach (3D CNN) has a high potential to produce a reliable and robust prediction of the anisotropic material properties of RVEs with given geometrical information.

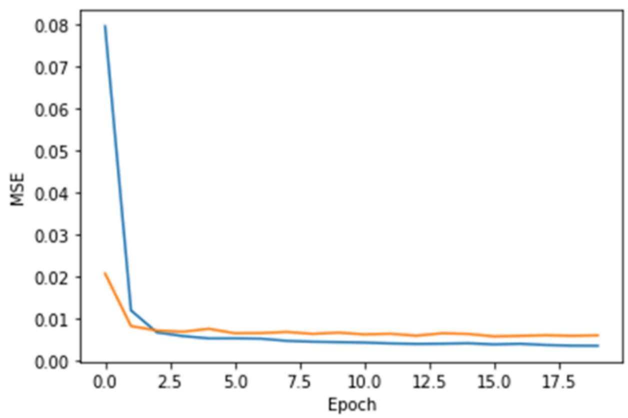


Figure 9. The plot of the 3D CNN model loss on training and validation datasets. The loss function used in the training procedure is MSE. The blue line is the MSE of training datasets. The orange line is the MSE of validation datasets.

4. CONCLUSIONS

The use of FE techniques to construct brain white matter (BWM) RVEs with anisotropic frequency domain viscoelastic material is computationally expensive. Different methodologies are sought in order to reduce the computational cost and avoid computational mesh failure while maintaining the intricate architectural information of the different phases present in the BMW. A 3D convolution neural network (CNN) model that exploits the voxelized geometric information encoded in distinct locations is employed while it cross-references the RVEs' material properties. In effect, we demonstrated the acumen of utilizing 3D CNN techniques for solving the prediction problem of anisotropic material properties of RVEs. The results showcase the high accuracy and learning capability of the CNN-RVE method to predict the anisotropic BWM material properties. The RVE models in this paper is a triphasic one (includes axons, myelin, and glia) and its scaling up is very demanding computationally. In addition, the RVEs' complicated internal structures make the FE model failure-prone during the FE meshing procedure. This novel combination of the CNN-RVE method achieved a dramatic reduction in the computational time compared to FE methods currently presented in the literature. Furthermore, the proposed method effectively solves the RVEs modeling problem by reducing the computational cost and avoiding FE mesh failure. Although the designed 3D CNN architecture successfully achieved the goal of this study, there are still additional possibilities to further improve the model performance by implementing some advanced techniques.

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