

A computational framework to predict the spreading of Alzheimer's disease: COMSOL implementation

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Abstract

Documentation that accompanies the COMSOL Multiphysics implementation of a three dimensional, bio-chemo-mechanical finite element framework for the prediction of Alzheimer's disease progression. The model couples the propagation of toxic tau and amyloid- β proteins, described by Fisher–Kolmogorov-type reaction–diffusion equations, with a finite-strain hyperelastic description of atrophy-driven brain tissue shrinkage.

The theoretical formulation of the model is provided in the original paper [1] while this document provides instructions for its implementation in the finite element software COMSOL Multiphysics. Subject-specific brain geometries and axonal orientation fields are obtained through an automated medical image processing pipeline (BrainImage2Mesh). The code can be downloaded from <https://mechmat.web.ox.ac.uk/codes>. If using these codes for research or industrial purposes, please cite the following article:

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1. COMSOL implementation

We proceed to describe the implementation in the finite element package COMSOL Multiphysics [2] of the continuum models for protein spreading and cerebral atrophy. The primal fields and nodal degrees-of-freedom (DOFs) are the toxic tau relative concentration \bar{c}_{tau} , the toxic A β relative concentration $\bar{c}_{\text{A}\beta}$, and the displacement components \mathbf{u} . The cerebral atrophy measure ϑ is also solved for, as an internal DOF.

1.1. Files inputs

1.1.1. Mesh

Open the COMSOL Model Wizard and select 3D as the space dimension. Use the Import node with file type Nastran and select the file `<subject>_mesh.bdf` produced by BrainImage2Mesh. Upon import (see Fig. 1), COMSOL preserves the 12 anatomical subdomains as distinct domain selections, identified by their integer labels. These selections are then renamed as shown in Fig. 2.

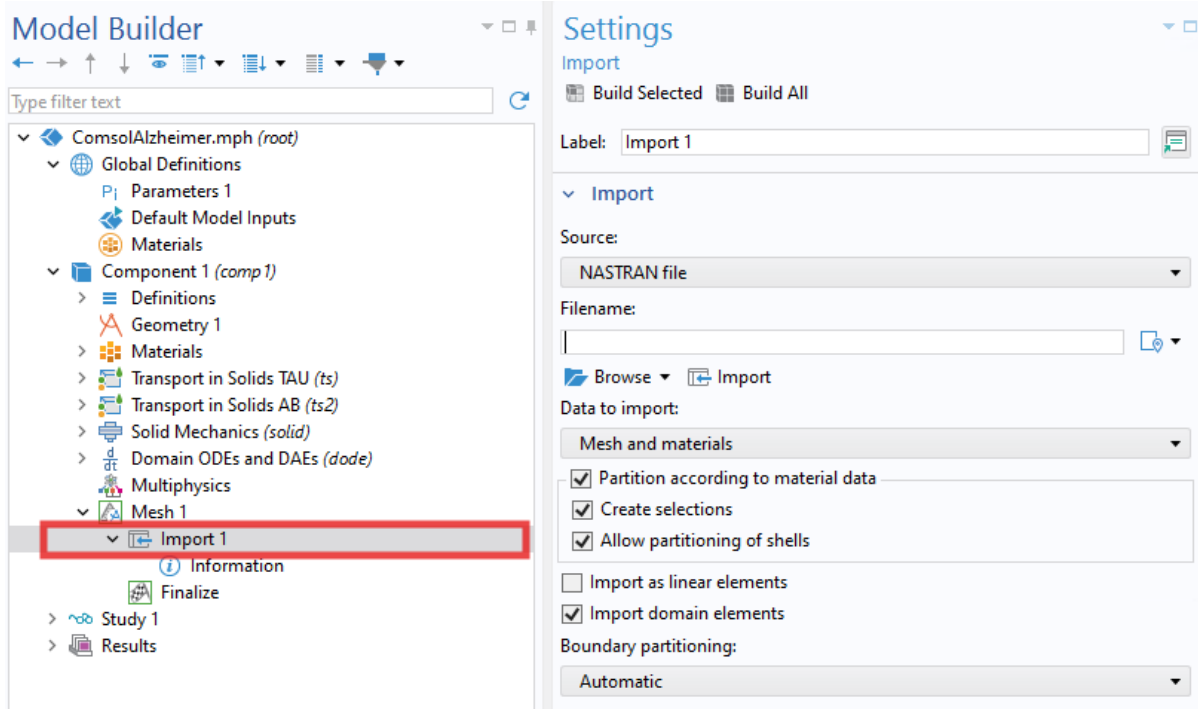


Figure 1: Mesh import.

Domain Selections	
Name	Source in file
Ventricles	PID 1
White matter	PID 2
Cerebral cortex	PID 3
Entorhinal cortex	PID 4
Hippocampus	PID 5
Brainstem	PID 6
Cerebellum cortex	PID 7
Cerebellum white matter	PID 8
Thalamus	PID 9
CSF	PID 10
Amygdala	PID 11
Corpus callosum	PID 12

Figure 2: Mesh domains.

Material properties are assigned to each domain in the Materials node (see Fig. 3).

The screenshot shows the COMSOL Model Builder interface. On the left, the 'Materials' node is selected under 'Component 1 (comp1)'. The right pane displays the 'Materials' settings, showing a table of material assignments for various domains.

Material	Selection
CSF (mat3)	Domains 2, 8, 15–17, 19–27, 31, 33, 35, 37, 42, 46–47, 50, 52, 55–59
Ventricles (mat11)	Domain 6
Amygdala (mat1)	Domains 10, 44
Cerebellum Cortex (mat4)	Domains 4, 53
Cerebral Cortex (mat6)	Domains 1, 12, 14, 30, 34, 39, 43, 54
Entorhinal cortex (mat8)	Domains 9, 11, 45, 48–49, 51
Hippocampus (mat9)	Domains 7, 41
Thalamus (mat10)	Domains 13, 36
Brainstem (mat2)	Domain 18
Cerebellum white matter (mat5)	Domain 5
Corpus callosum (mat7)	Domain 29
White matter (mat12)	Domains 3, 28, 32, 38, 40

Figure 3: Materials node.

1.1.2. Axonal vector field

The file `vector_field.txt`, produced by `BrainImage2Mesh`, contains the axonal unit vectors. It is loaded under the `Definitions` node as an `Interpolation` (see Fig. 4). Three interpolation functions are created, one per vector component (V_x0 , V_y0 , V_z0), using columns 1–3 of the file as spatial coordinates. This interpolated field defines the initial axonal unit vectors, denoted as \mathbf{a} , used in the tau diffusion tensor \mathbf{d}_{tau} .

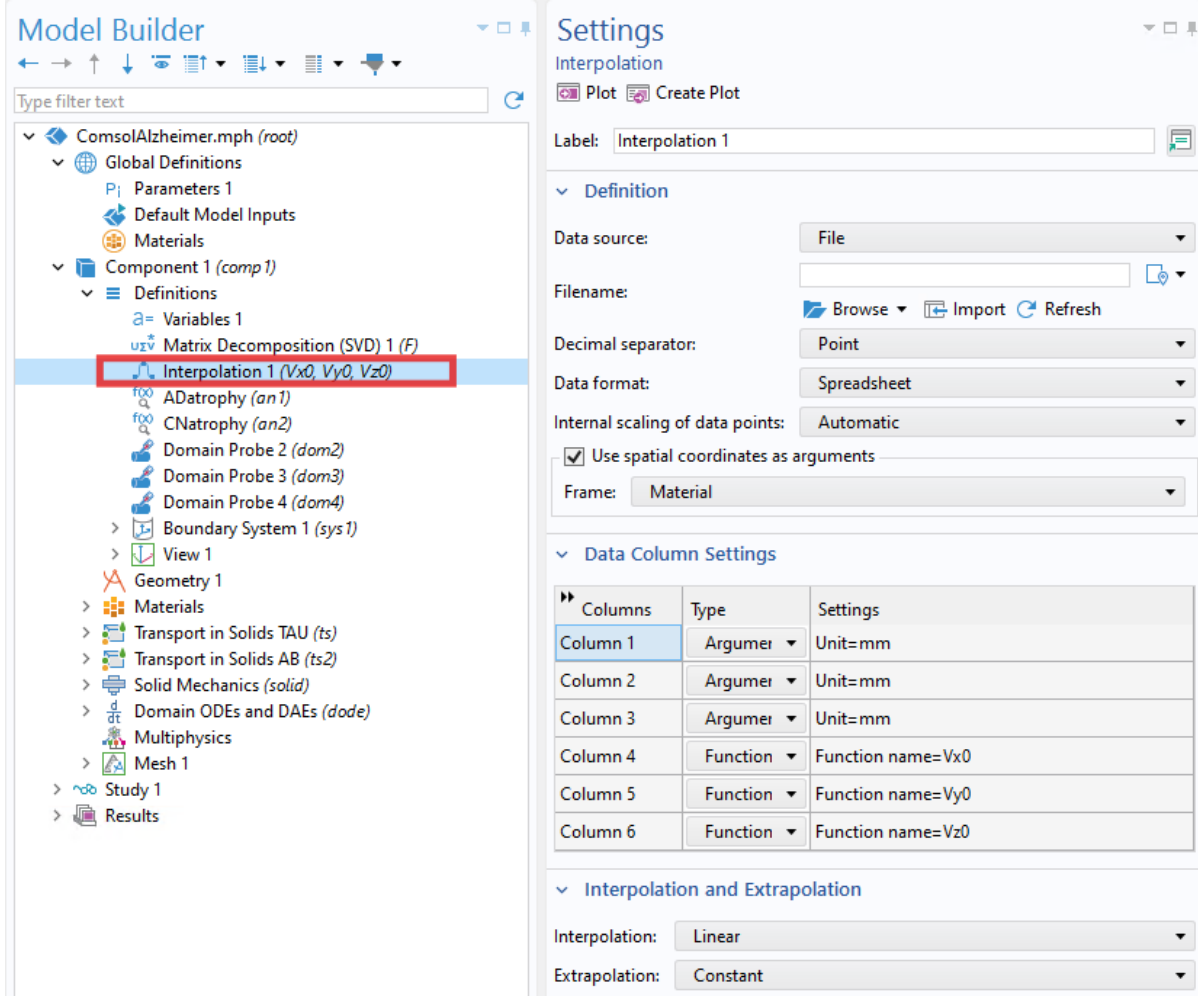


Figure 4: Axonal vector field import.

1.2. Physics

As described below, three physics interfaces are used in the implementation, two in-built ones (Solid Mechanics and Transport in Solids), and one user-defined domain ODE, implemented using the Mathematics module. Details can be found in the COMSOL documentation.

1.3. Protein spread implementation

1.3.1. Built-in Transport Modelling

We implement the spreading of toxic proteins using the `Transport in Solids` interface, which is part of the `Chemical Species Transport` module. Diffusion is considered to be the main transport mechanisms, and therefore convection is deactivated. We particularise the implementation to two species (`Dependent Variables`) with concentrations \bar{c}_{tau} and $\bar{c}_{A\beta}$. The transport equations are formulated in the spatial frame, which is explicitly selected in the interface settings. With this choice, the governing equation solved by COMSOL reads

$$\frac{\partial c_i}{\partial t} + \nabla \cdot \mathbf{\Gamma}_i = J s_i, \quad (1)$$

with the diffusive flux given by

$$\mathbf{\Gamma}_i = - \left(J \mathbf{F}^{-1} \mathbf{d}_i \mathbf{F}^{-T} \right) \nabla c_i. \quad (2)$$

Separate diffusion tensors are defined for tau and A β denoted d_{tau} and $d_{A\beta}$, as seen in Fig. 5 and Fig. 6, following the expressions provided in the original paper.

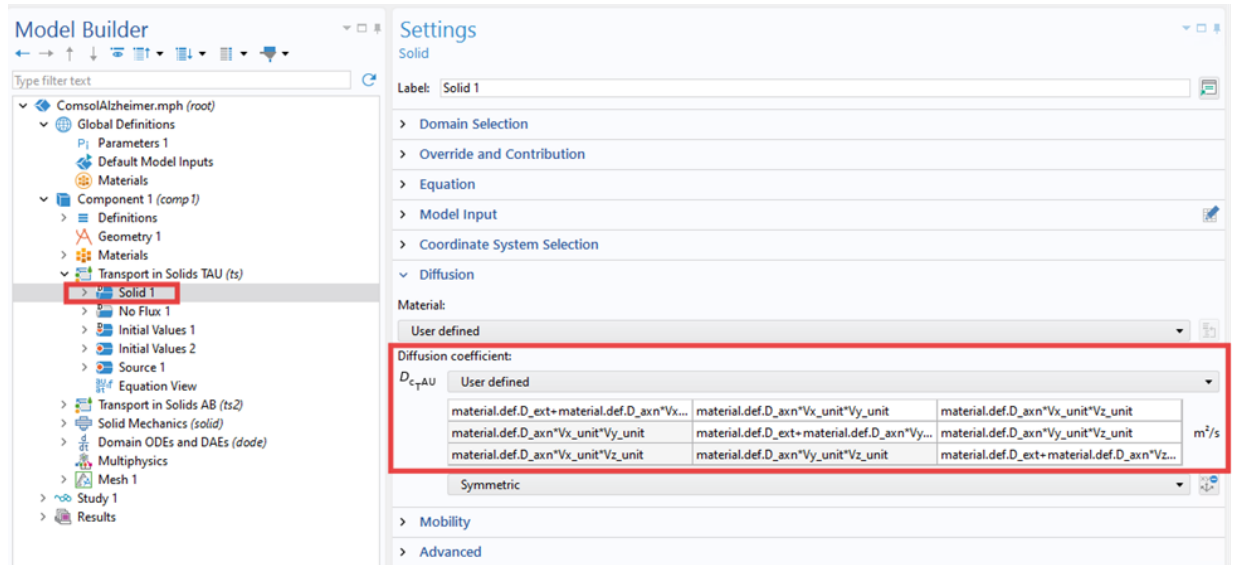


Figure 5: Diffusion tensor for tau transport.

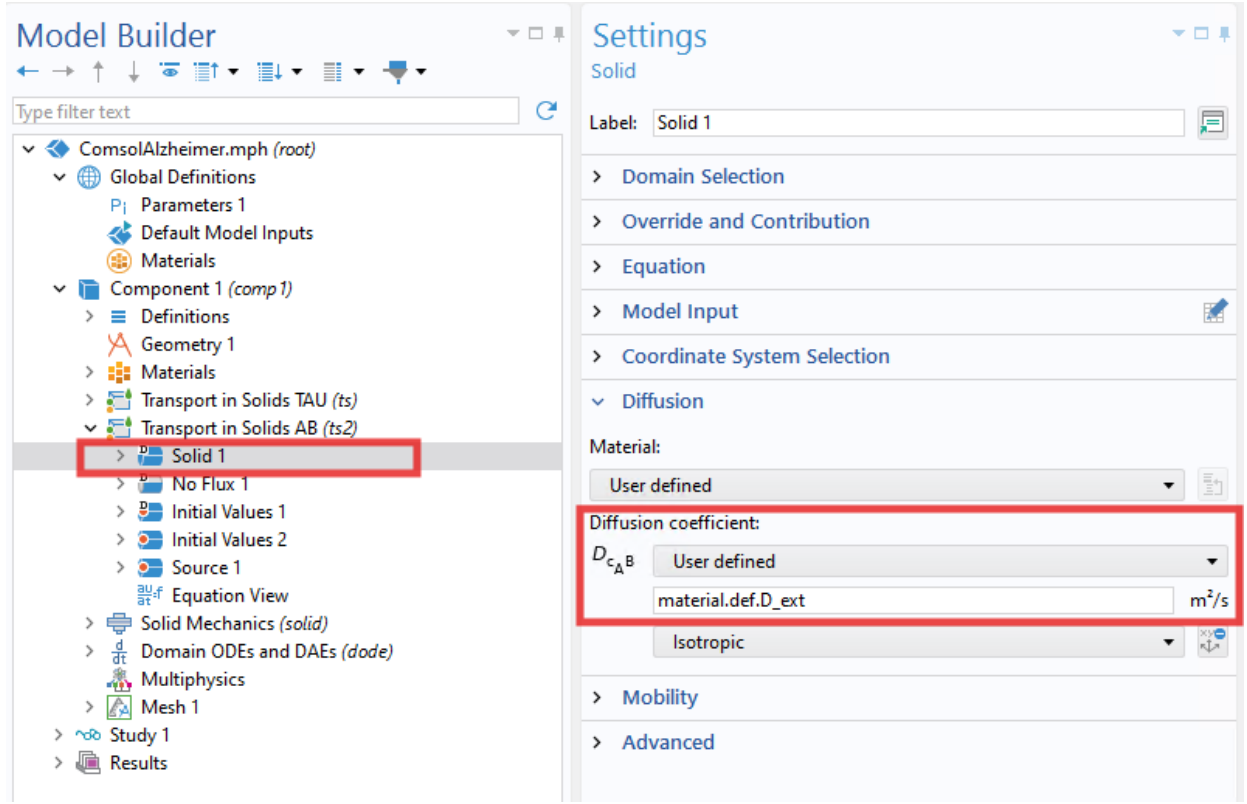


Figure 6: Diffusion tensor for $A\beta$ transport.

Reaction terms are implemented by adding a *Source* node for each species. In the source expressions s_{tau} and $s_{A\beta}$, we define the reaction terms corresponding to the model expressions R_{tau} and $R_{A\beta}$.

Zero-flux boundary conditions are enforced by selecting the default *No Flux* condition on the external boundary of the brain matter. Initial conditions are defined by prescribing a non-zero concentration seed for each protein species within selected brain regions and setting the concentration to zero in the remaining domains.

The values of this protein seed are found in the *Variables* nodes (see Fig. 7), and can therefore be changed there if desired.

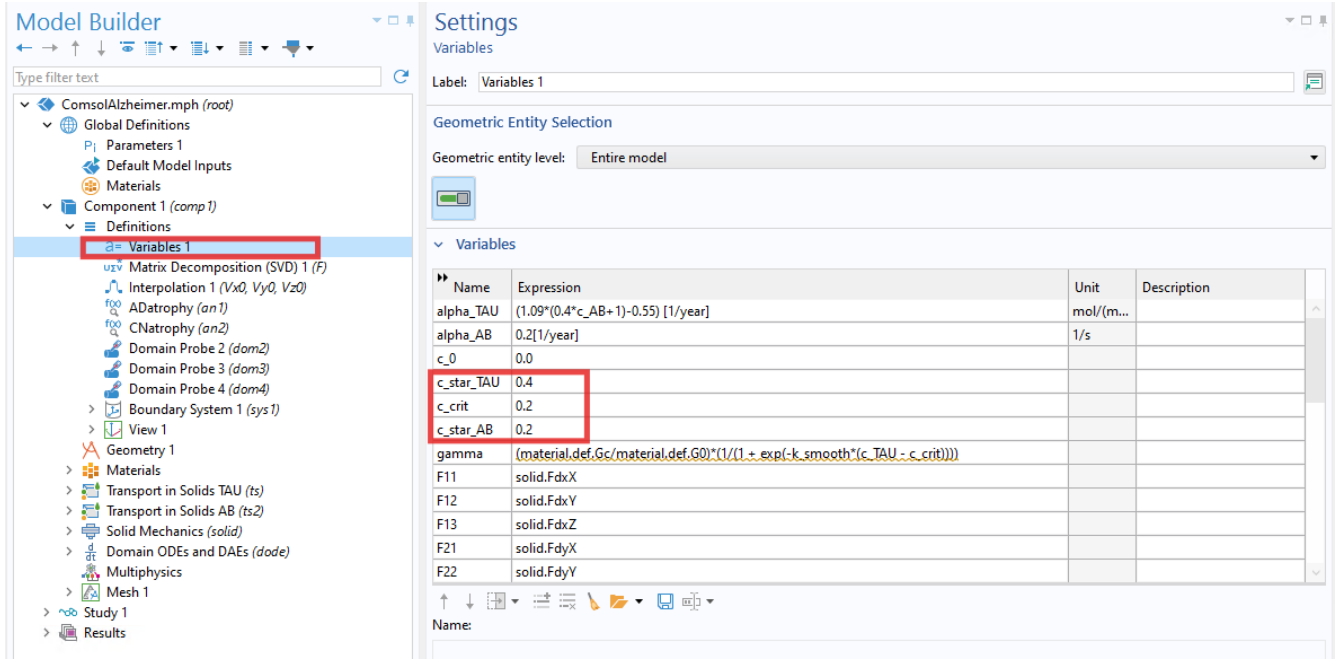


Figure 7: Variables node.

1.4. Cerebral atrophy implementation

1.4.1. User-defined Domain ODE

The cerebral atrophy measure ϑ is implemented using the Domain ODEs and DAEs interface from the Mathematics module. The time evolution of ϑ is introduced through the damping term of the interface, as seen in Fig. 8, with the damping coefficient set to unity.

$$\underbrace{\frac{\dot{\vartheta}}{d_a \frac{\partial \vartheta}{\partial t}}}_{\text{Source term } f} = \left(1 + \frac{G_c}{G_0} \frac{1}{1 + \exp[-10^2 (c_{\text{tau}} - c_{\text{tau}}^{\text{crit}})]} \right) G_0. \quad (3)$$

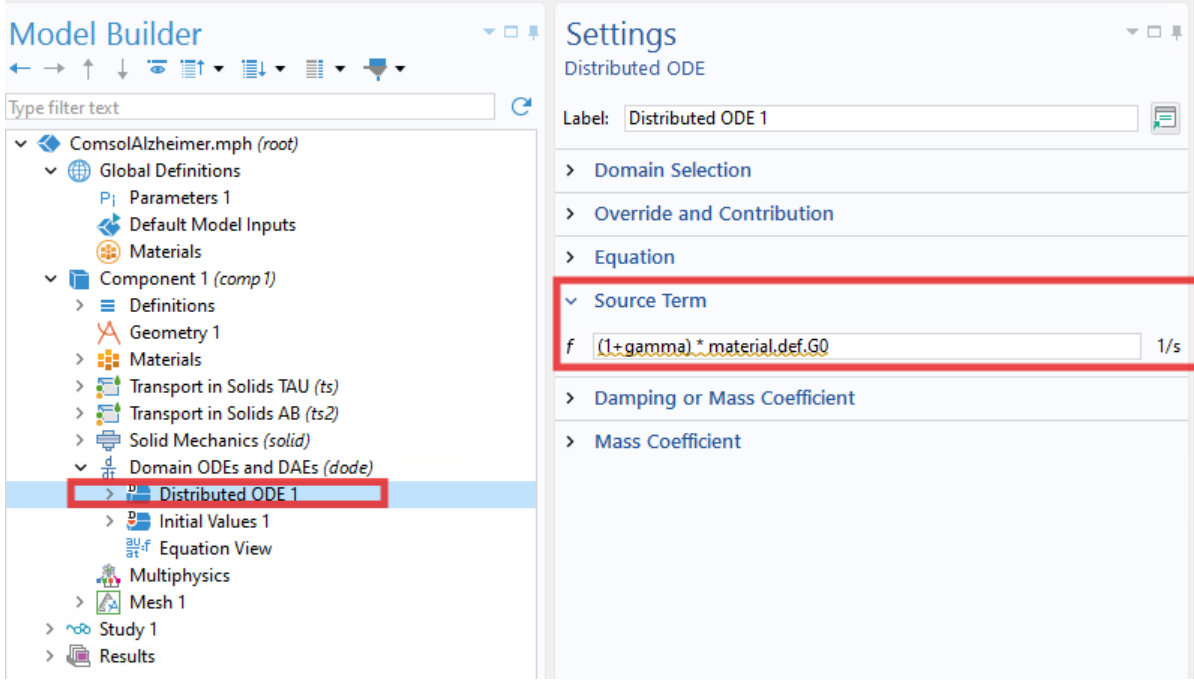


Figure 8: ODE source term.

The atrophy measure ϑ is initialized to represent a healthy state at the beginning of the simulation. Accordingly, the following initial conditions are imposed:

$$\vartheta(\mathbf{X}, 0) = 1, \quad \partial_t \vartheta|_{t=0} = G_0. \quad (4)$$

1.4.2. Built-in solid mechanics modelling

The mechanical response of the brain tissue is implemented using the `Solid Mechanics` interface from the `Structural Mechanics` module. The displacement field \mathbf{u} is defined as the dependent variable. A quasi-static formulation is selected by disabling inertial effects. With these settings, the balance of linear momentum solved by COMSOL reads

$$\nabla \cdot (\mathbf{FS})^T = \mathbf{0}, \quad (5)$$

where \mathbf{S} denotes the second Piola–Kirchhoff stress tensor.

A `Hyperelastic Material` node is added, and a compressible neo-Hookean formulation with a simplified volumetric strain energy (Simo–Pister) is selected. With this configuration, the strain energy density reads

$$W_s = \frac{G}{2} (tr(\mathbf{C}) - 3) - G \ln(J_e) + \frac{\lambda}{2} (\ln(J_e))^2. \quad (6)$$

where $\mathbf{C} = \mathbf{F}^\top \mathbf{F}$ is the right Cauchy-Green deformation tensor.

The neo-Hookean model is specified by two material parameters, namely the Lamé parameters λ and G . The corresponding energy density function W_s is equivalent to the pristine elastic strain free energy density ψ_0^e in our formulation. To recover the atrophy-weighted elastic strain free energy density ψ^e , the Lamé parameters λ and G are multiplied by the atrophy measure ϑ . Since these parameters appear linearly in each term of the strain energy function, this modification results in $W_s = \vartheta \cdot \psi_0^e$, as seen in Fig. 9

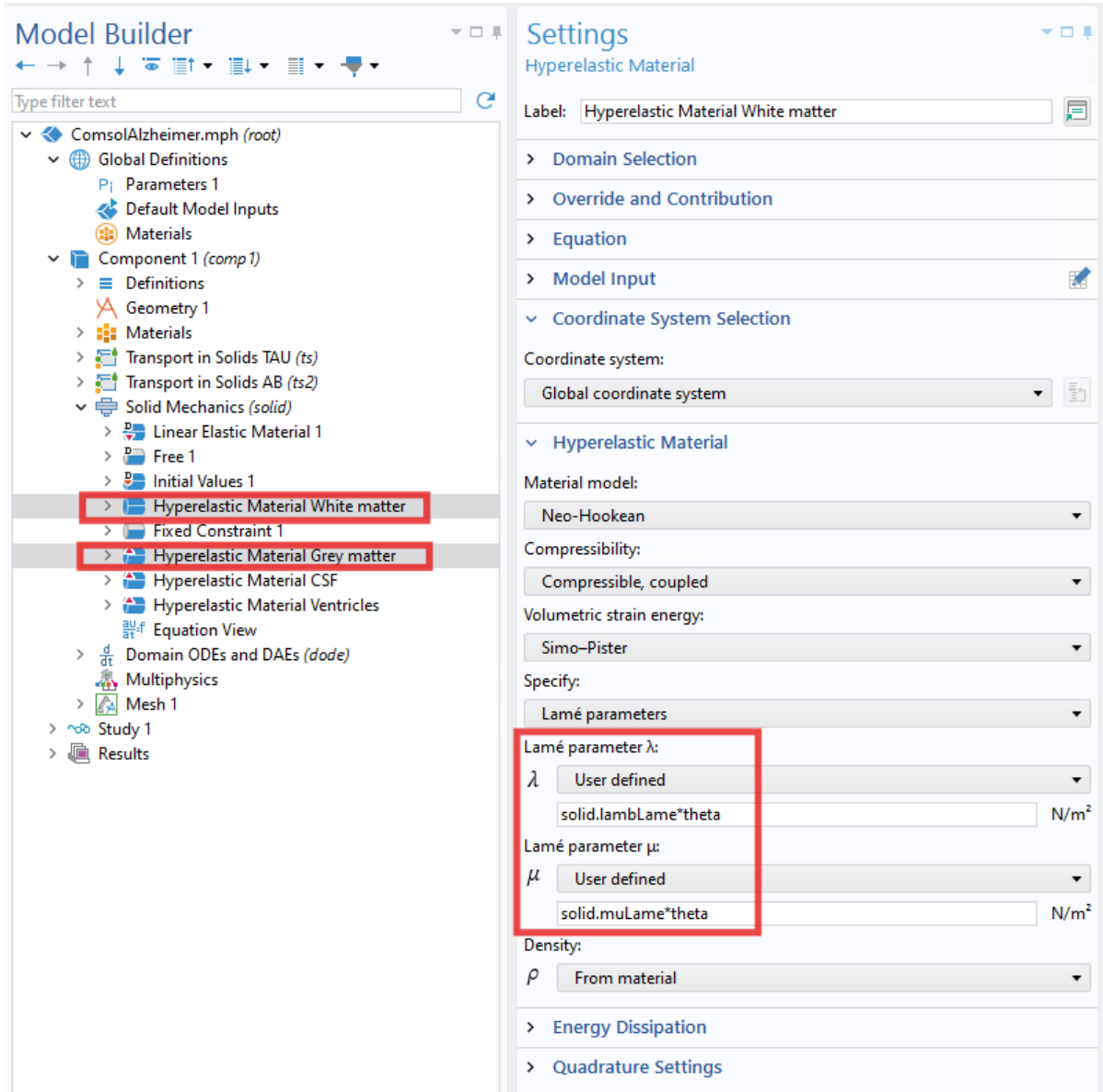


Figure 9: Setup of the Hyperelastic Material node.

Atrophy-induced deformation is introduced using the `External Strain` feature within the

Hyperelastic Material node (see Fig. 10 and Fig. 11), where the atrophy deformation gradient \mathbf{F}^a is prescribed.

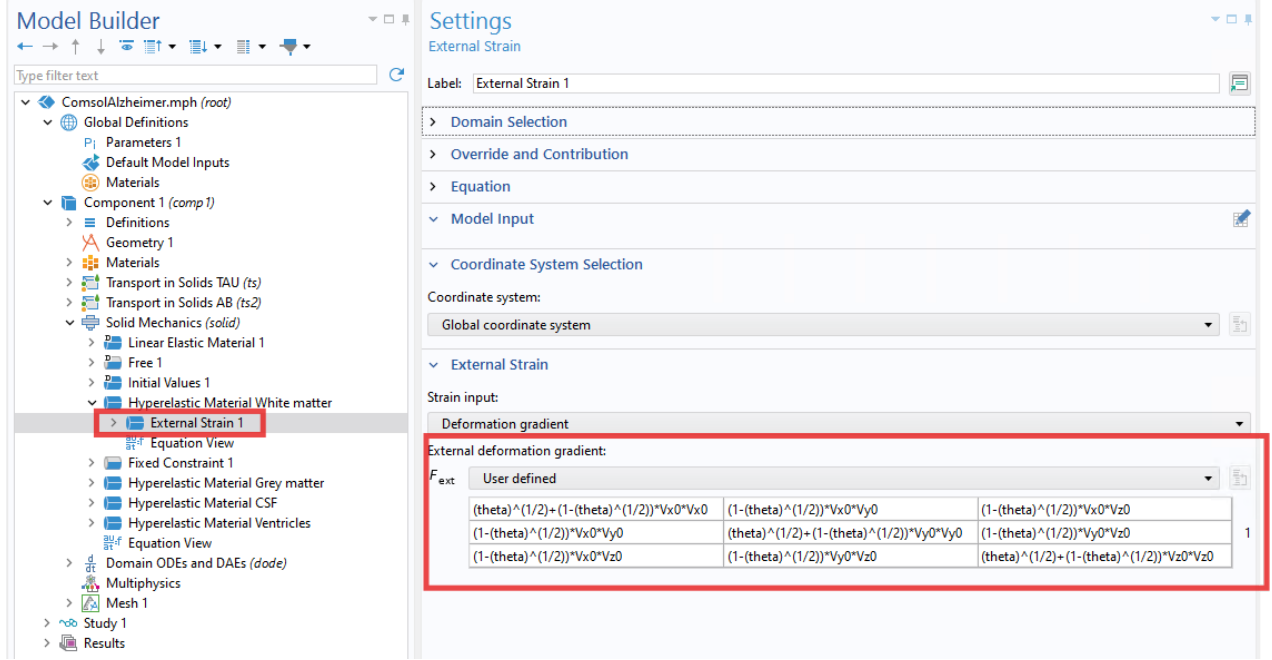


Figure 10: White matter atrophy deformation gradient

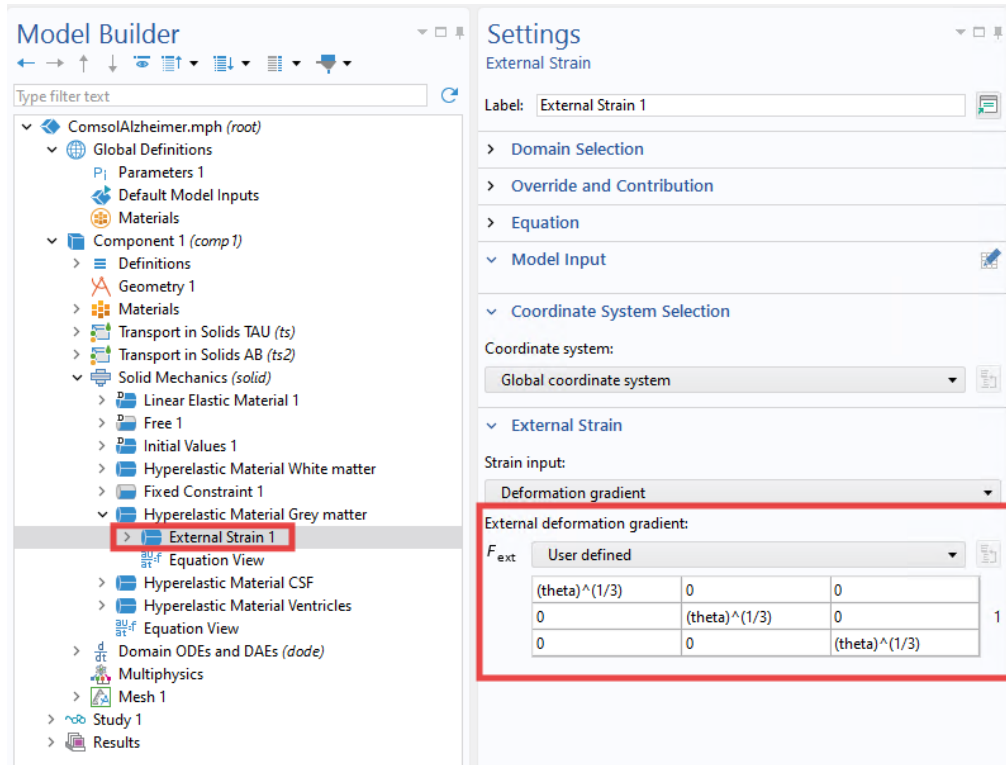


Figure 11: Grey matter atrophy deformation gradient

Rigid body motion is prevented by applying a fixed constraint on the cerebrospinal fluid (CSF) domain. The displacement field is initialized by setting $\mathbf{u} = \mathbf{0}$ at the beginning of the simulation.

1.5. Domain assignment

Each physics interface acts only on the anatomical domains where it is physically meaningful. Fig. 12 shows the assignments used in this implementation:

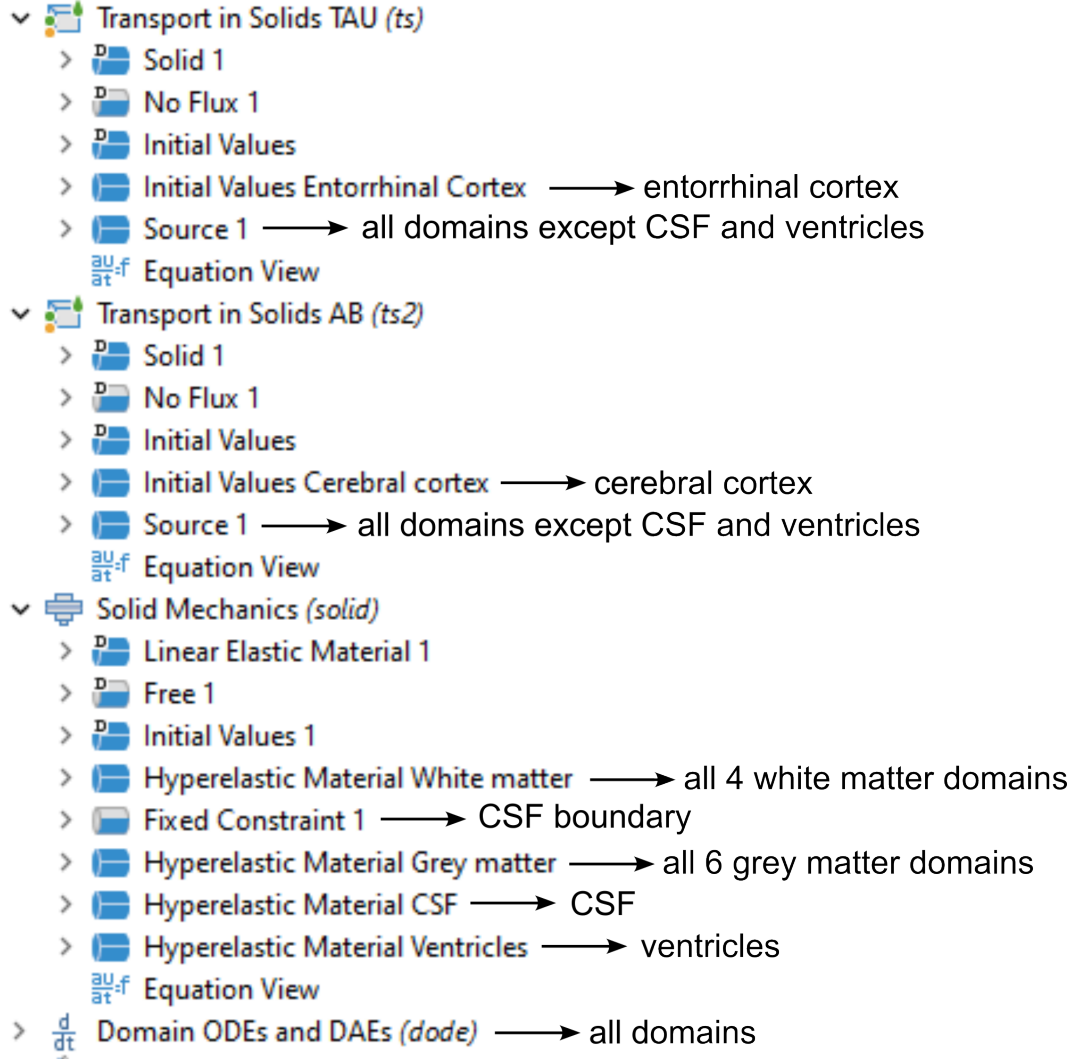


Figure 12: Domain assignment.

1.6. Case studies: Healthy brain

When simulating a healthy brain as a control case, three modifications to the model are required. First, the atrophy tensor is set to be identical for grey and white matter, as seen in Fig. 13. Second, only age related (natural) atrophy is considered. Therefore the accelerated atrophy rate

associated with toxic protein accumulation is set to zero (Fig. 14). Third, the Transport in Solids interfaces for tau and $A\beta$ are deactivated, since no toxic protein propagation is simulated.

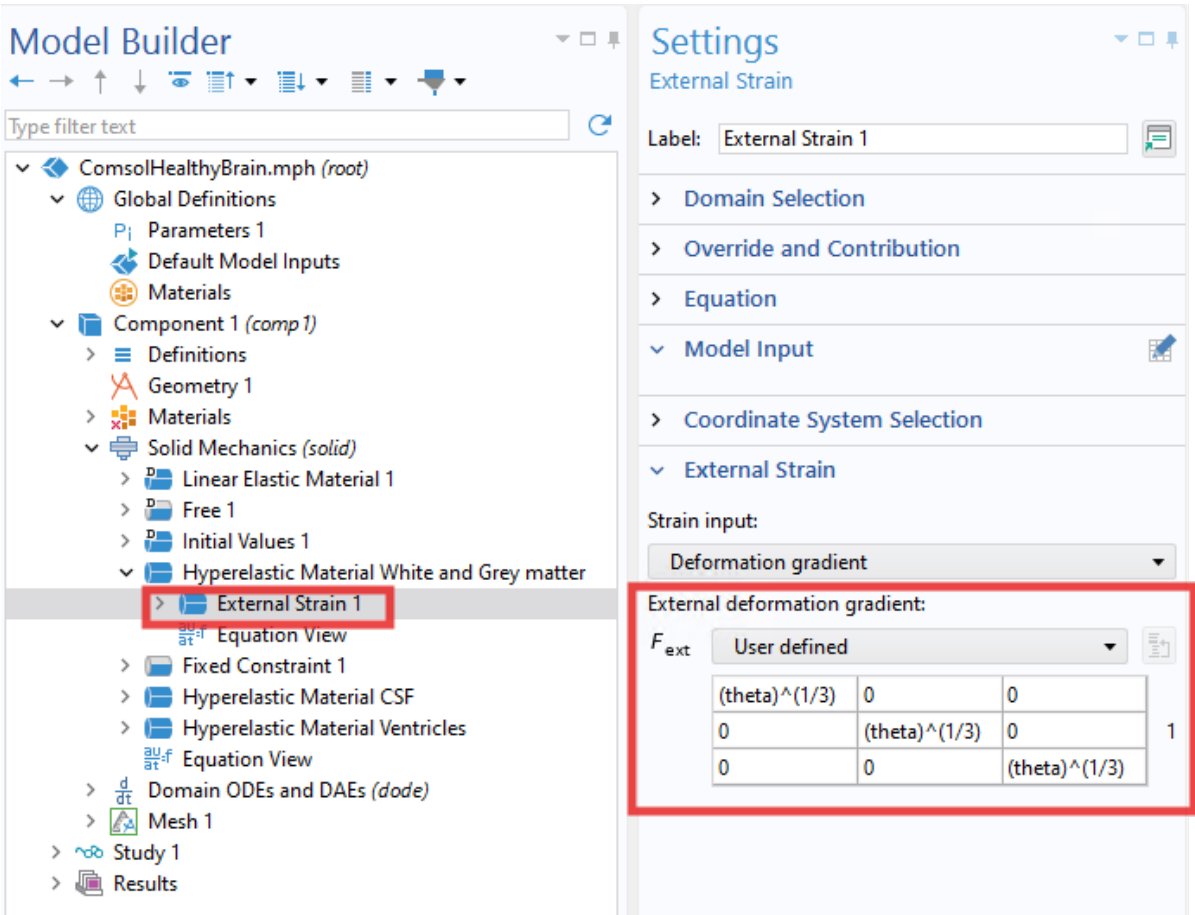


Figure 13: Atrophy deformation gradient in healthy brain.

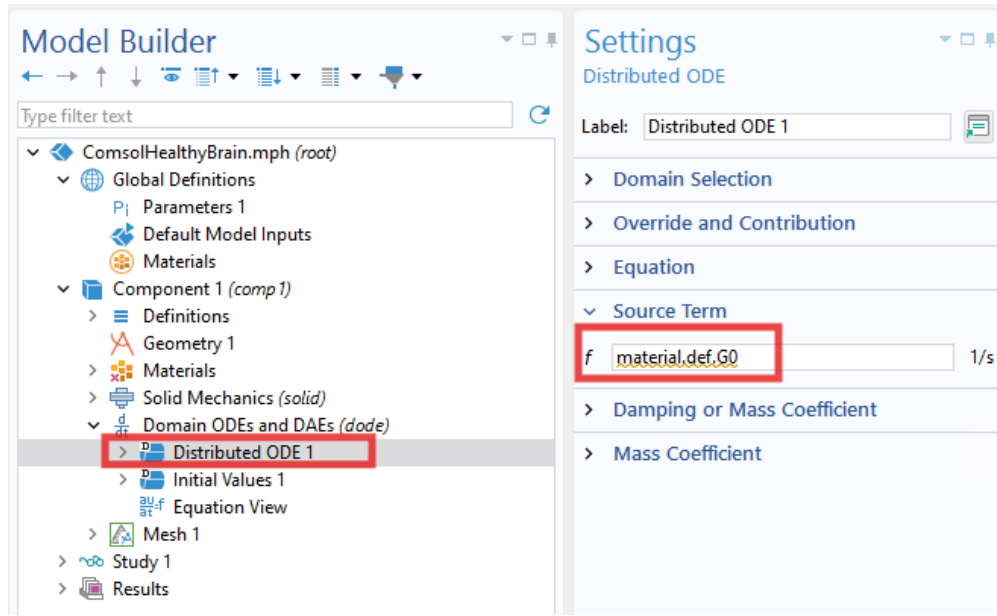


Figure 14: ODE source term in healthy brain

2. Conclusions

A finite element implementation of the coupled bio-chemo-mechanical model for predicting the spreading of Alzheimer's disease is presented. The present document provides details of the model implementation in the software package COMSOL Multiphysics. The code developed is freely available at <https://mechmat.web.ox.ac.uk/codes>.

References

- [1] A. Vazquez-Palomo, C. Betegón, J. Weickenmeier, E. Martínez-Pañeda, A computational framework to predict the spreading of alzheimer's disease, *Engineering with Computers* 42 (78) (2026). doi:10.1007/s00366-026-02313-5.
- [2] COMSOL Multiphysics v. 6.0, <https://www.comsol.com>, COMSOL AB, Stockholm, Sweden.