Agent-Based Modelling of the vibration-induced arterial growth

Maha Reda*+, Christophe Noël*, Emmanuelle Jacquet+

* Institut National de Recherche et de Sécurité, Vandoeuvre-Lès-Nancy, France
+ Univ. Bourgogne Franche-Comté – Department of Applied Mechanics, Besançon, France

Background

- In France, **11% of workers** are exposed to **Hand-Arm transmitted Vibrations (HAV)**
  - **8%** have an exposure time ≥ 20 hours / week

- A sustained exposure to HAV can perturb some mechanical quantities inside the digital artery:
  - **Wall Shear Stress (WSS) values (the mechanical shear stress exerted by the blood on the arterial wall)**
  - Dynamic stress and deformation fields.

- On the long term, these perturbations may lead to various vascular pathologies and disorders such as:

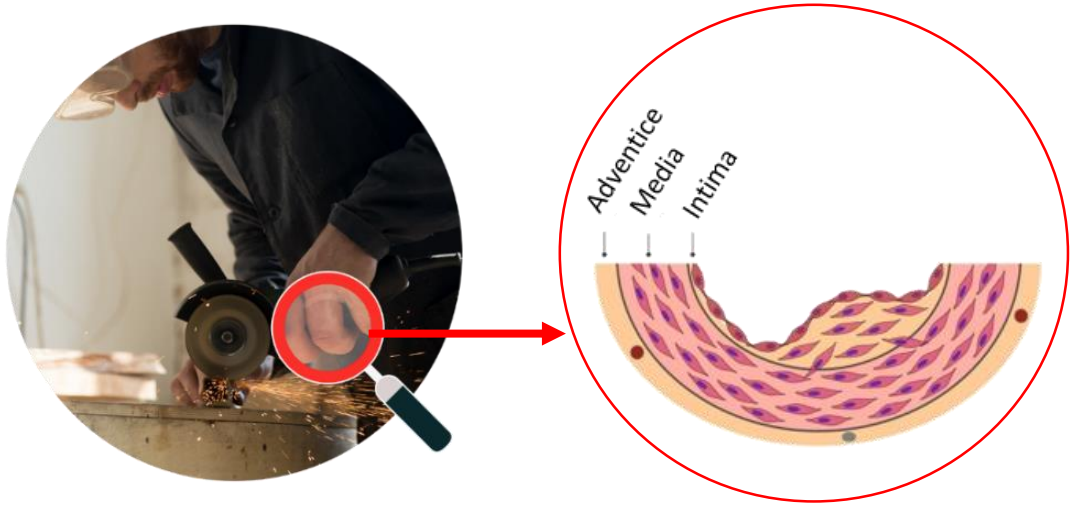
The **vibration-induced Raynaud's syndrome** i.e.

Vibration White Finger (VWF).

Vibration White Finger

Background

- Raynaud's syndrome: a vascular disorder that causes vasospasms in the body extremities (fingers and toes), often triggered by cold or emotional stress**.**
- It is characterized by an **arterial growth and remodeling** potentially induced by an **intimal hyperplasia** phenomenon.



Thickening of the intima due to:

- Presence of Smooth Muscle Cells (SMCs) in intima instead of in media only.
- Pathological proliferation of SMCs + SMCs synthesis of ExtraCellular Matrix inside the intima.

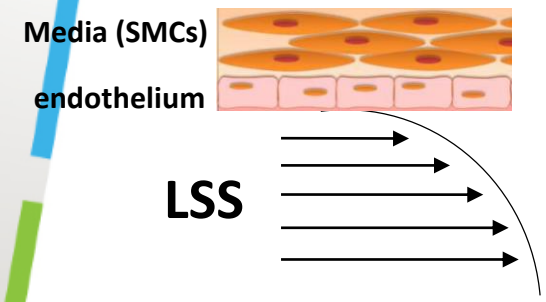
- Our goal is to develop a model of the intimal hyperplasia that can predict the degree of arterial growth upon exposure to vibration.

Methods

- Vibration can reduce the WSS values between the blood and the endothelium and causes a Low Shear Stress (LSS) flow inside the digital artery (Noël and Settembre, 2017).

- The LSS can alter some endothelium functions
  - the Endothelial Cells (EC) secretion of Growth Factors (GF).

- These Growth Factors control the Smooth Muscle Cells (SMCs) proliferation and migration.



GF secretion → SMCs Proliferation and Migration

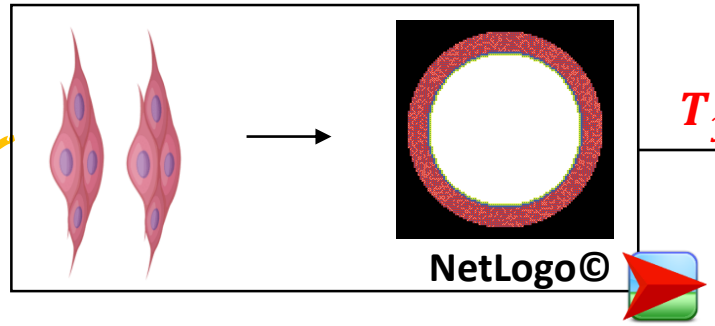
*Keystone of **intimal hyperplasia** phenomenon*

Methods

$T_{seconds}$

Vibration-induced LSS

Lattice Agent-Based Model



T_{years}

Arterial growth as a function of WSS

- GF secretion: $m_{GF} = \mathrm{f_{gf}}(\mathrm{WSS})$ / cell / time

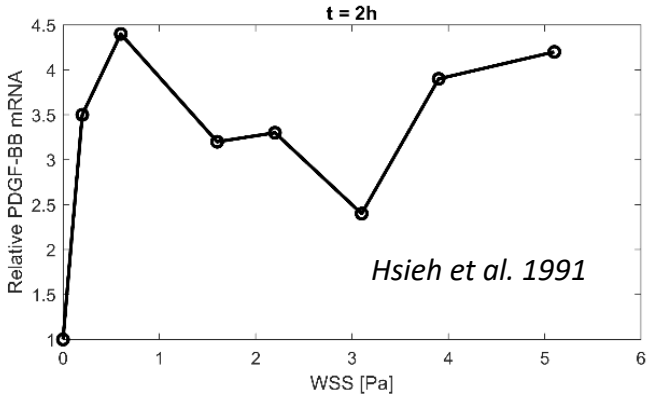
- SMCs proliferation/apoptosis: $\mathrm{P_{SMC}} = f_{SMC}(m_{GF})$

- ECMs synthesis/degradation: $\mathrm{P_{ECM}} = f_{ECM}(m_{GF})$

-SMCs migration: $M = f_{mig}(m_{GF})$

Growth factors considered in our model: PDGF-BB

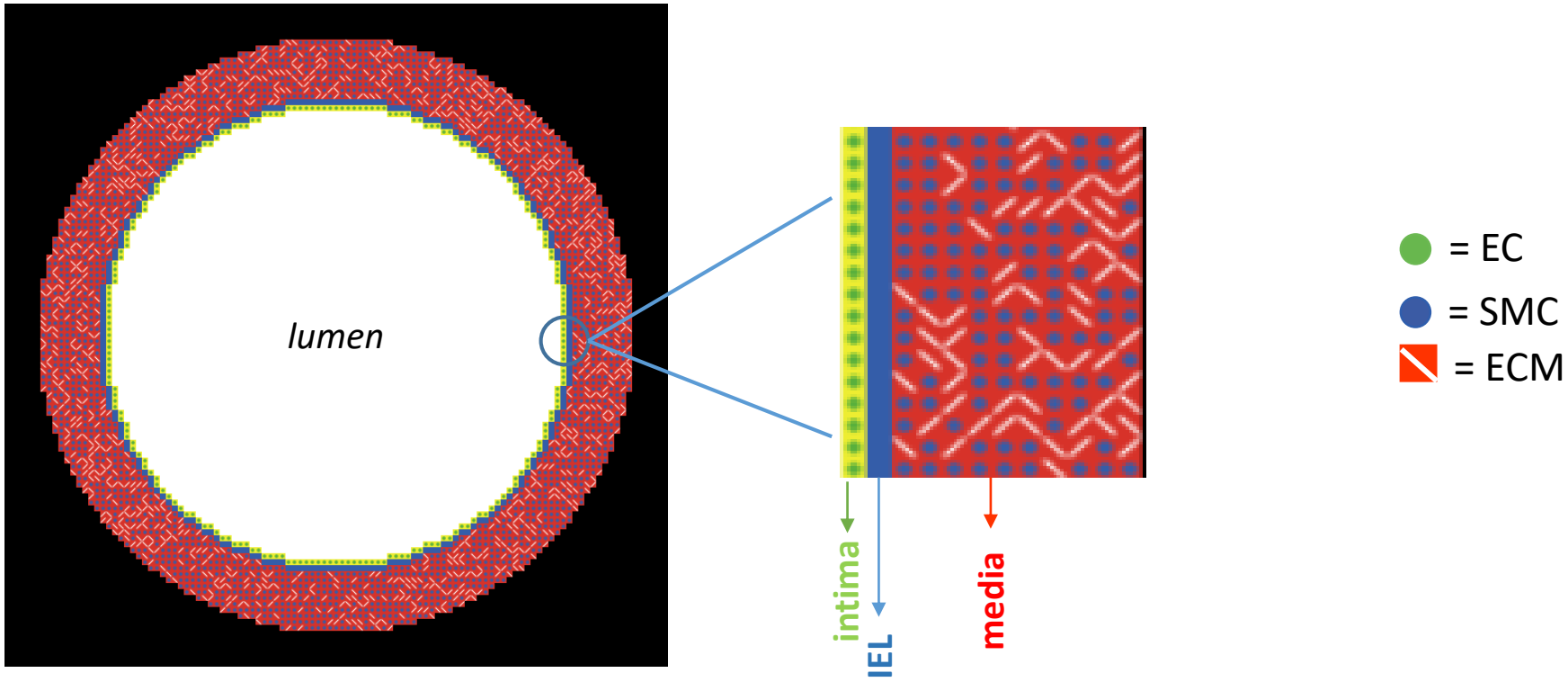
Example :



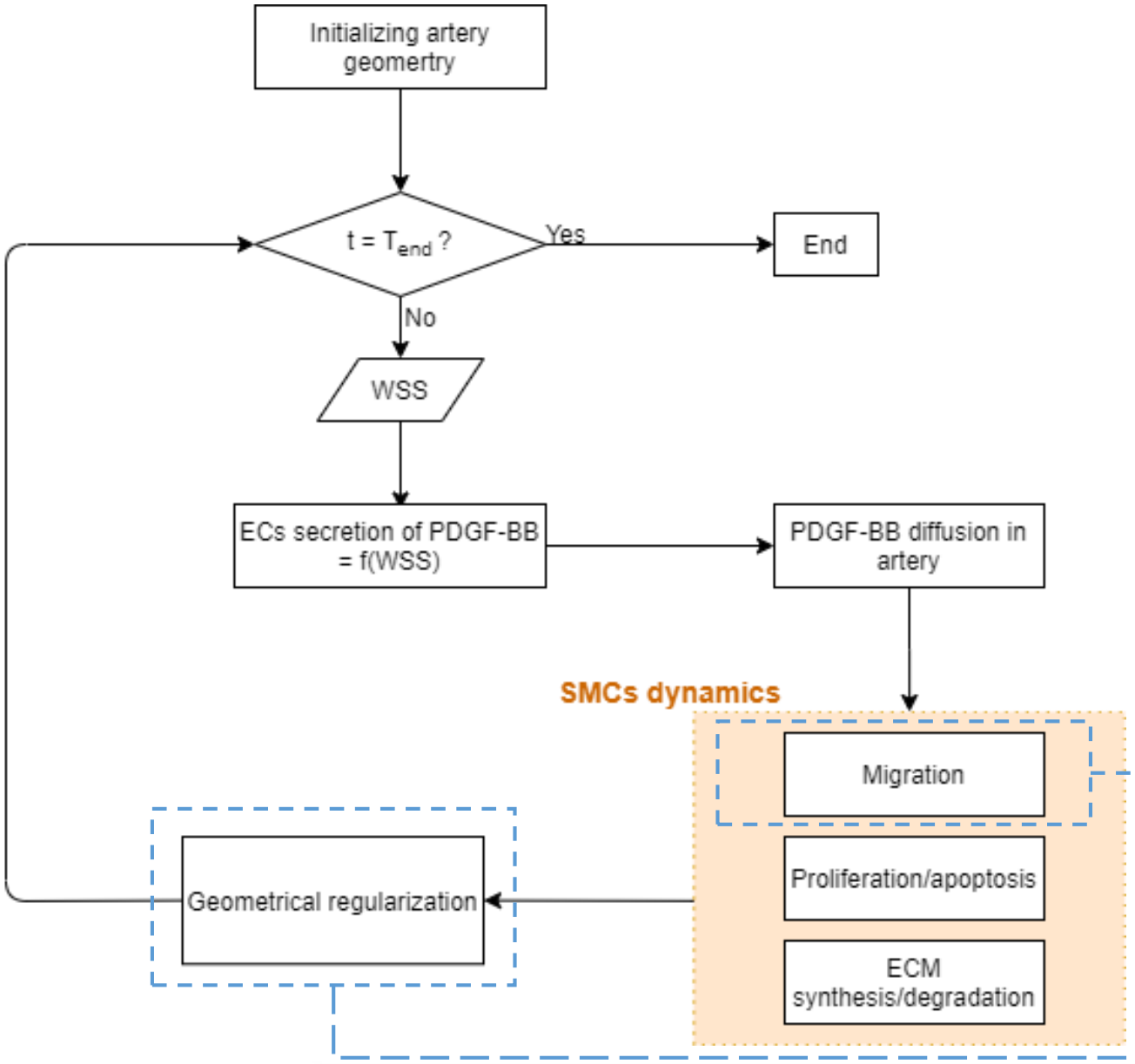
\+ Parameters identification

Methods

- 2 layers of a muscular artery are modelled, separated by the Internal Elastic Lamellae (IEL):
  - Intima: Endothelial Cells (ECs)
  - Media: Smooth Muscle Cells (SMCs) + ExtraCellular Matrix (ECM) (collagen and elastin fibers)



Methods



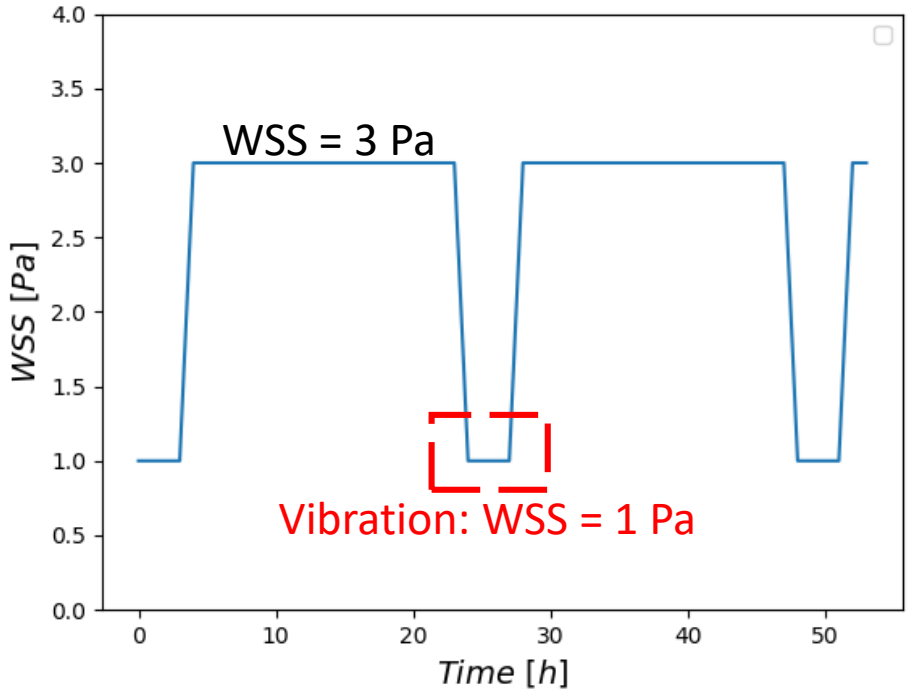
A regularization method
to ensure isotropic movement of the cells
while migrating

Rearrangement of cells following the
minimum energy principle

Results

- Physiological state: no exposure to vibration ➔ WSS = 3 Pa

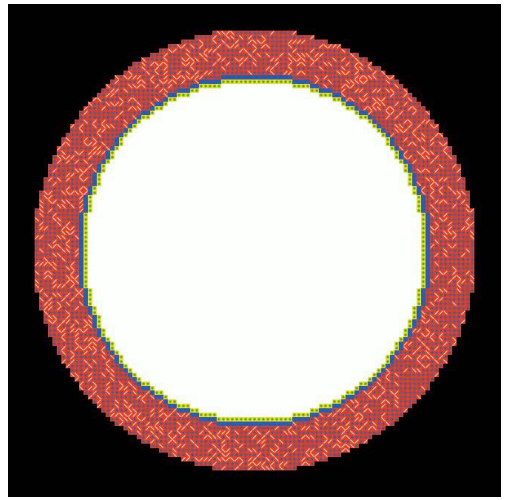
- Working conditions: exposure to vibration ➔ WSS = 1 Pa
  - 4h / day
  - 1h / day

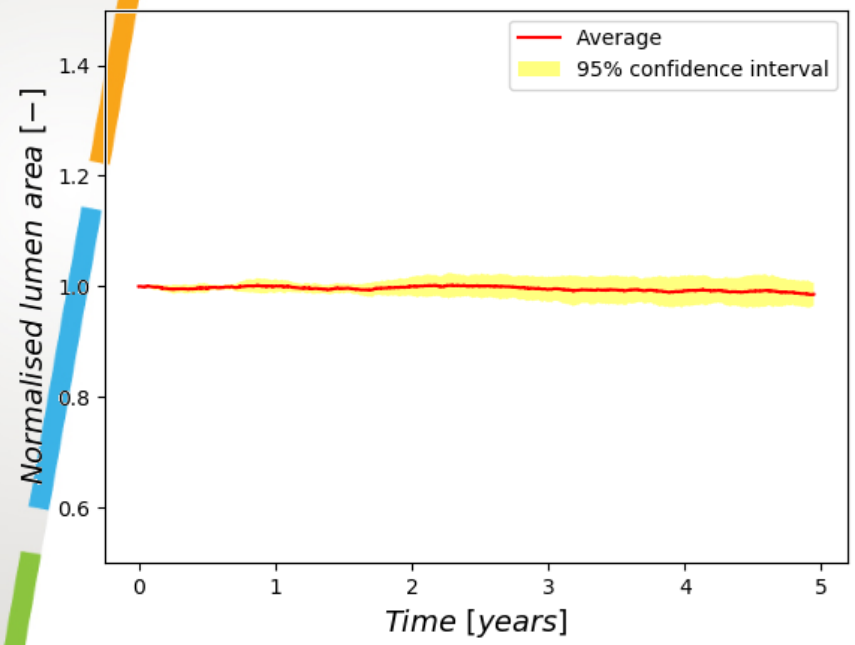


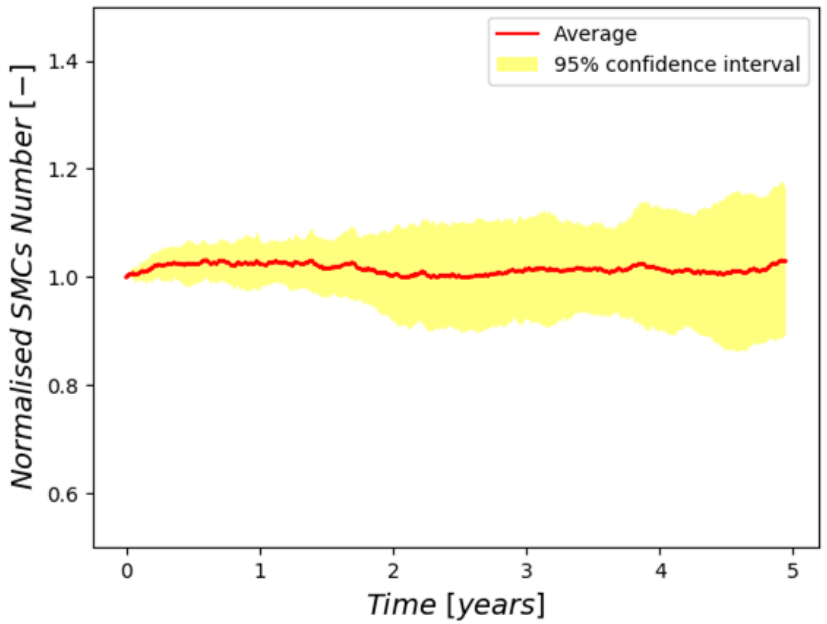
Results

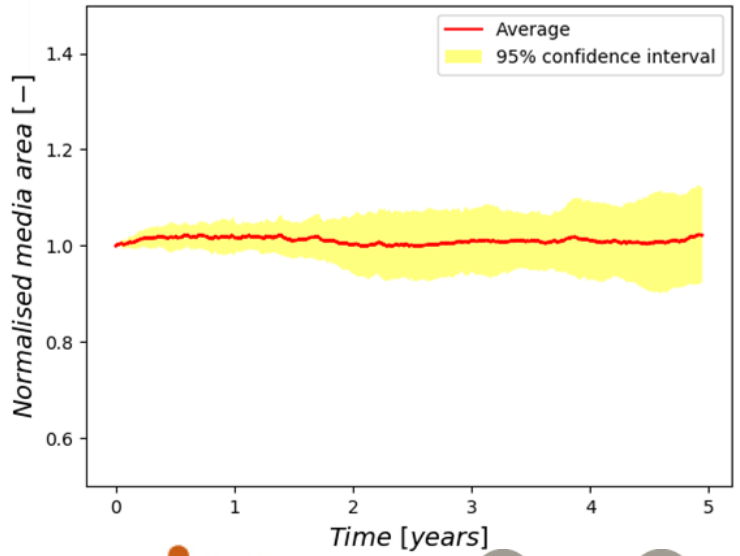
- Simulating the physiological equilibrium (in the absence of vibration)

$$P_{proliferation} = P_{apoptosis}$$
$$P_{synthesis} = P_{degradation}$$





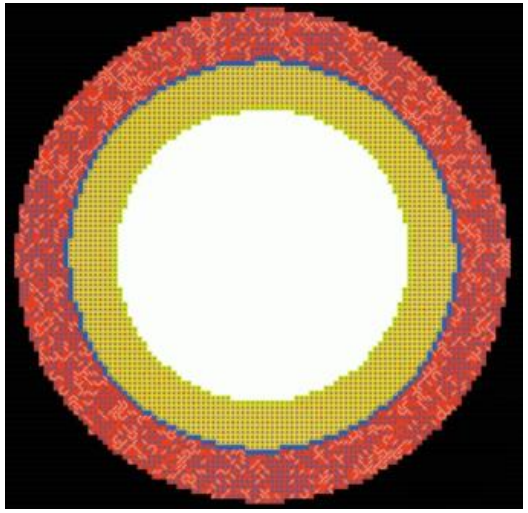


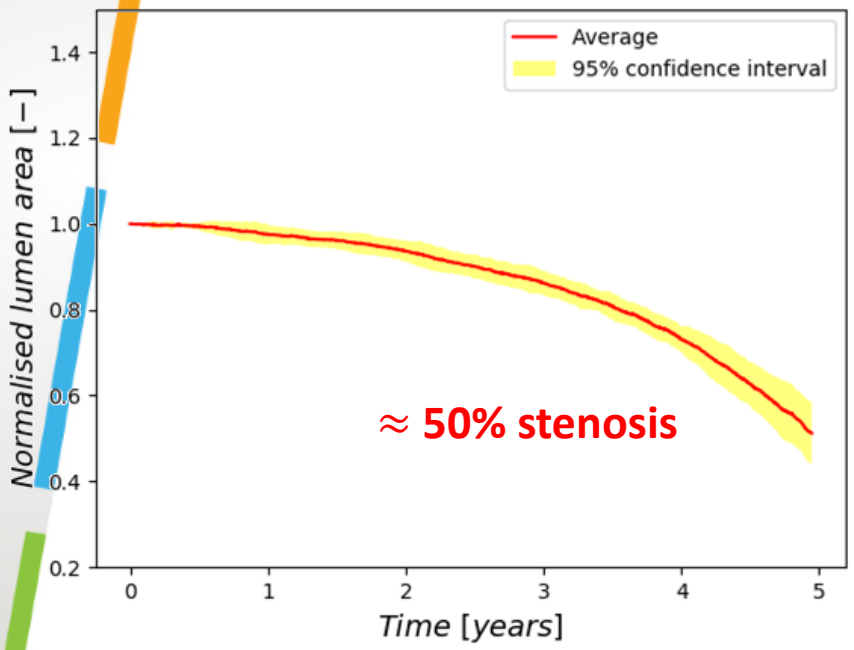


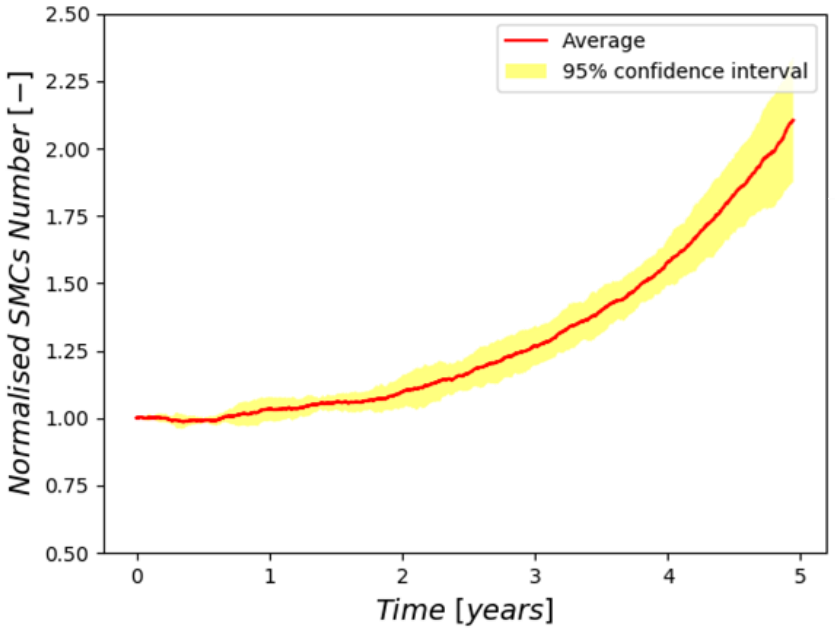
Results

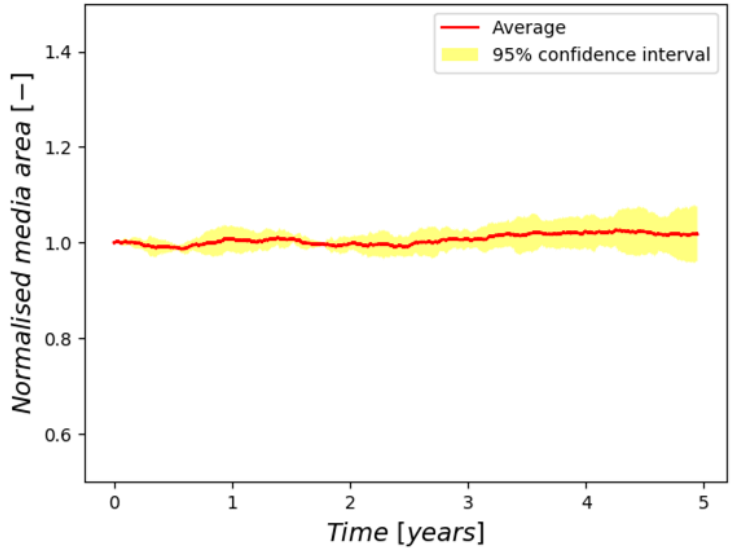
- Simulating the intimal hyperplasia

Working condition: 4 h of exposure / day for 5 years





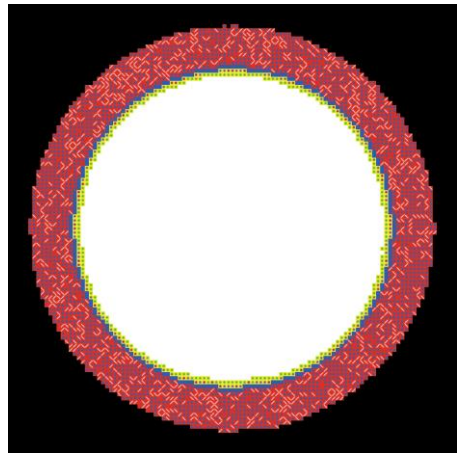


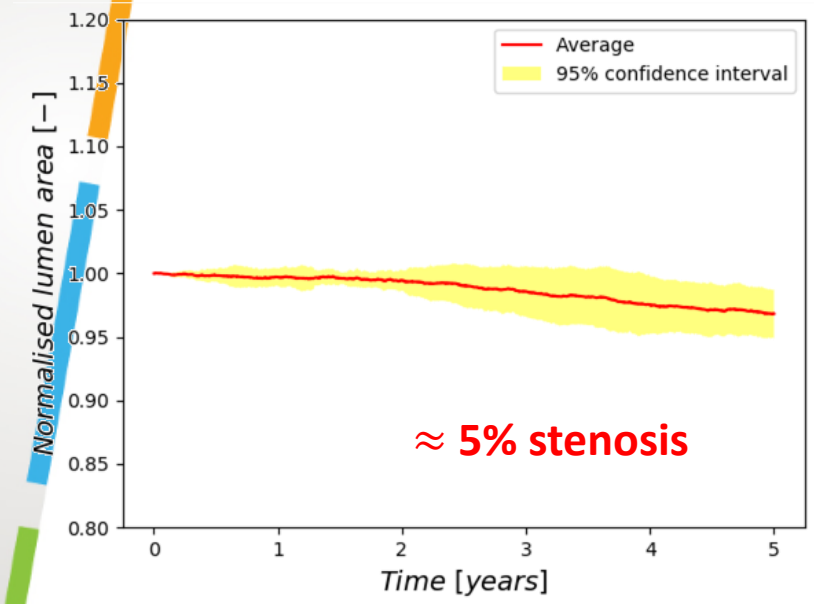


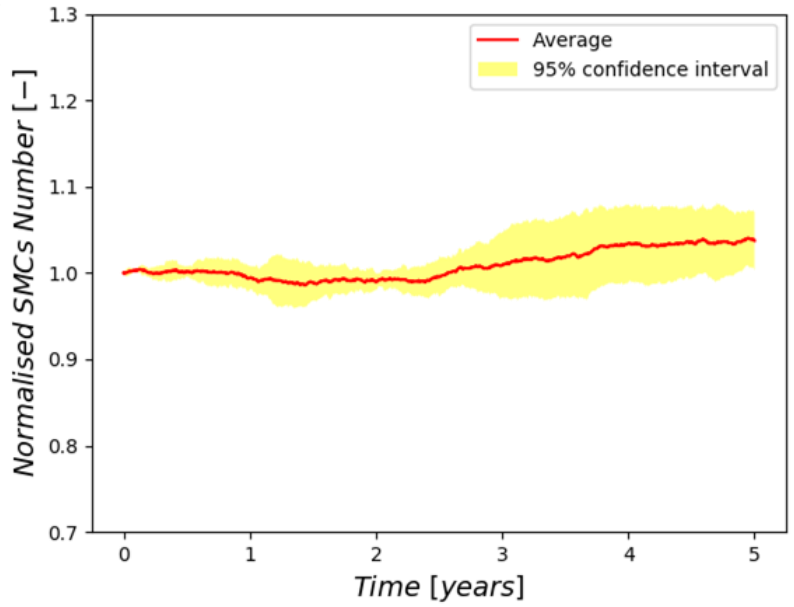
Results

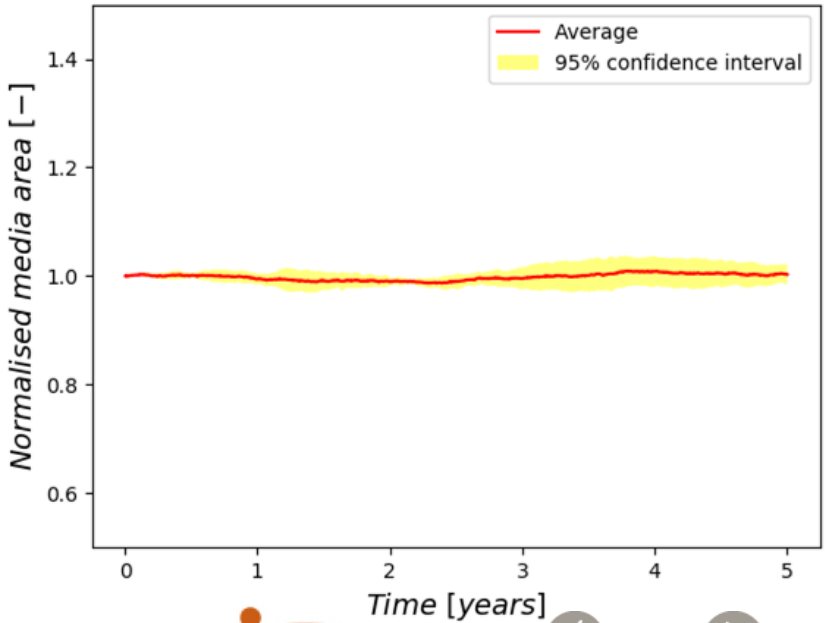
- Simulating the intimal hyperplasia

Working condition: 1 h of exposure / day for 5 years









Conclusion

- Implementation of a lattice agent-based model of the vibration-induced intimal hyperplasia in NetLogo.
- The model can describe the physiological state and predict the isotropic arterial growth as a function of exposure time to vibration.
- It can simulate different working conditions and predict the resulting degree of arterial growth specific to each condition.
- The model has the ability to include more agents and to study different and more complex cellular phenomena.

Outlook

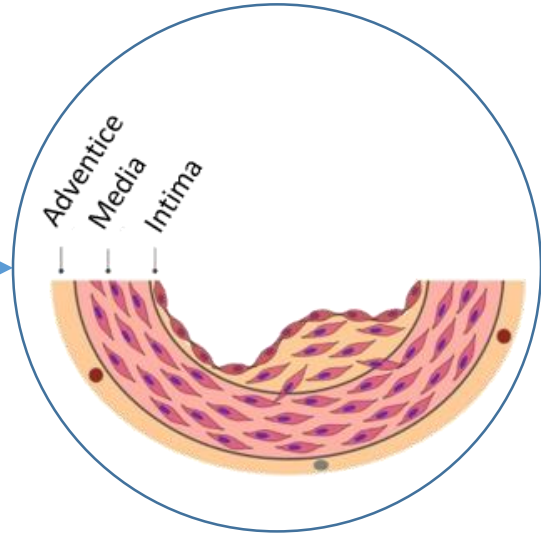
WSS

Agent-based Model
- Proliferation, migration, apoptosis…

Geometry, anisotropy..

Finite element method

Stress, deformation..



Time

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