Developing Numerical Tools to Improve the Diagnosis of Peripheral Artery Disease

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1 Introduction

Peripheral artery disease (PAD) affects >10% of adults aged 65+ [1] and is caused by atherosclerotic narrowing of peripheral arteries, reducing muscle oxygen delivery and triggering exercise-induced pain [2]. PAD doubles cardiovascular event risk [3], yet traditional diagnostic methods often miss cases – particularly in patients with calcified arteries, dysfunction of the microcirculation, and other atypical presentations (more frequent in women), leading to delayed treatment and worse outcomes [4]. This project will explore the interaction of the key biological systems (blood delivery, vascular function, and oxygen uptake) degraded in PAD patients that are not captured in current diagnostic methods; therefore, making way for improved detection of PAD.

2 Model Overview

2.1 Microcirculation

At exercise onset, noradrenaline induces whole-body vascular constriction. This is opposed via two pathways [7]:

1. Rapid Onset Vasodilation (ROV), mediated by endothelial-derived hyperpolarisation conducted to the smooth muscle cells and upstream to the feed arteries (~1 s),
2. Slow Onset Vasodilation (SOV), mediated by metabolic signals in the micro-vessels and nitric oxide (NO) in the feed arteries (~15 s).

Vascular stiffness is modelled as a sigmoidal function of local NO and $\langle O_2 \rangle$.

Model Coupling:

Coupling to the terminal arterial model is done though wall shear stress (to inform NO production) and to the skeletal muscle by $\langle O_2 \rangle$ (to inform metabolic dilation).

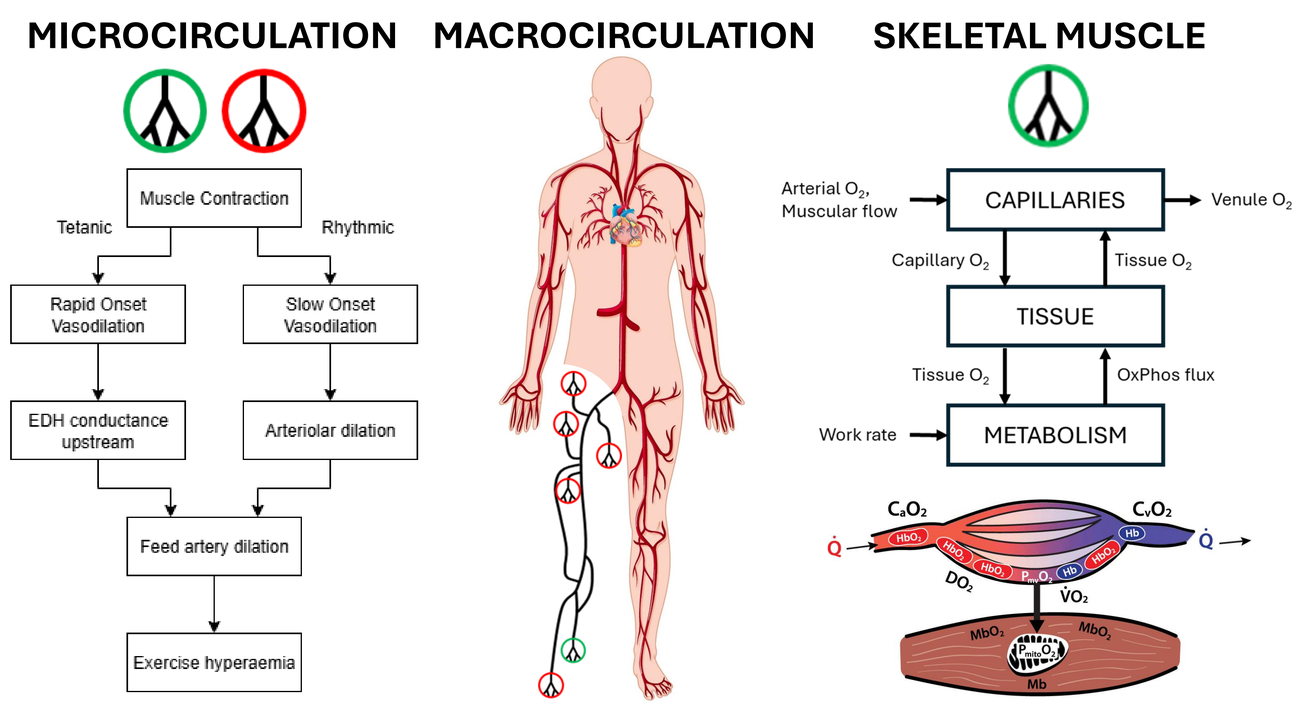


Figure 1: Schematics for each system included in the numerical model. (Left) A flow chart detailing the pathways to dilation of the feed artery [7]. (Middle) A diagram of an example arterial network for simulating leg blood flow. The terminal vessels are coupled to a lumped representation of the microcirculation. (Right) A component diagram for the skeletal muscle and matching illustration [10].

2.2 Macrocirculation

Blood flow in the macrocirculation is described using 1D Navier-Stokes for flow in compliant tubes [9], solved via finite element methods implemented in FEniCS [5]. Arterial plaque and hardening are captured by variable material properties and radii along the arterial length [8]. Arterial networks are portrayed as binary branching fractals.

Ultrasound-derived flow in the femoral artery acts as the root (i.e. inflow) condition. Conservation of mass, energy, and wave characteristics are enforced at junctions. Past the terminal arteries, peripheral resistance is described using Windkessel models [9].

2.3 Skeletal Muscle

Oxygen concentration $\langle O_2 \rangle$ in the muscle is transported via:

- advection (driven by blood flow),
- diffusion (within blood),
- perfusion (transfer into tissue).

$\langle O_2 \rangle$ utilisation in tissue is mediated by oxidative phosphorylation (OxPhos) to produce ATP in cellular metabolism, alongside the phosphagen system,

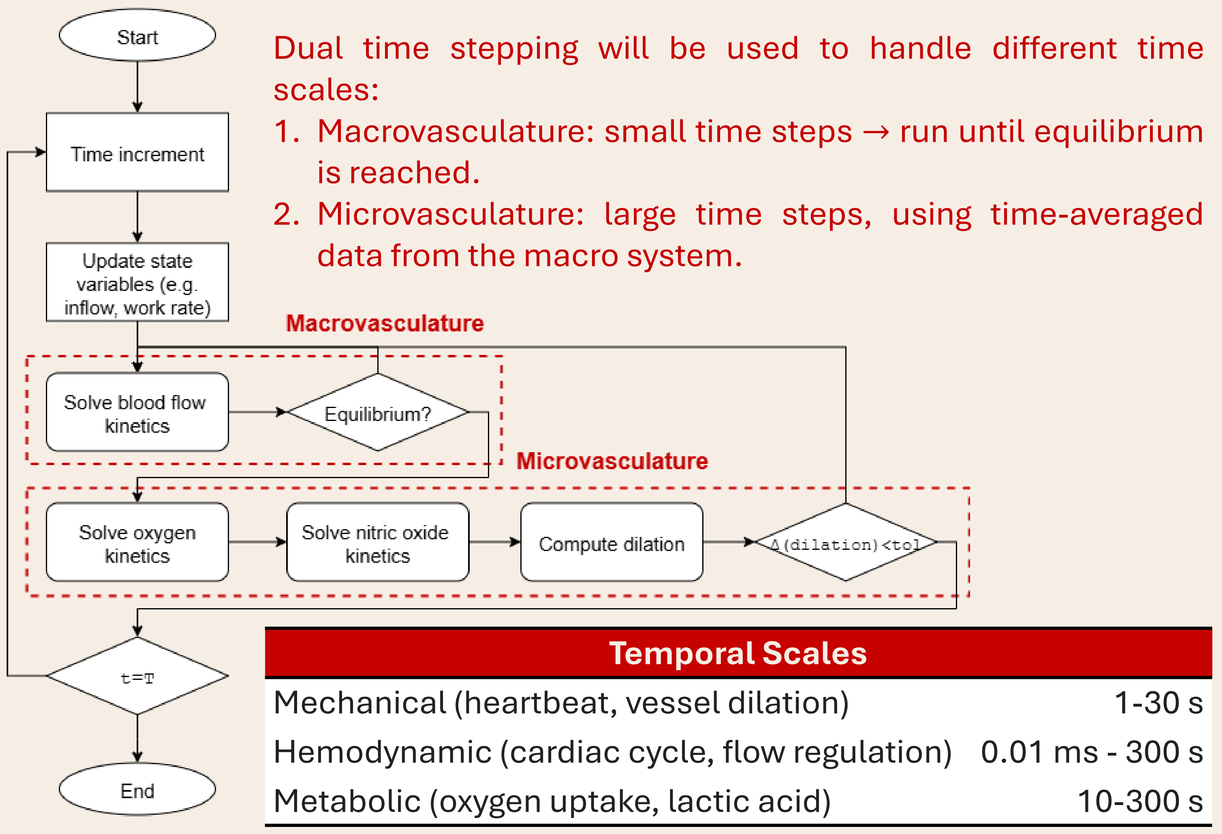
$$\mathrm{ATP} + \mathrm{Cr} \rightleftharpoons \mathrm{ADP} + \mathrm{PCr},$$

in the effort to meet the demand for energy production [6].

Model Coupling:

This model is coupled to the macrocirculation model via the blood flow leaving the large arteries. It is coupled to the microcirculation by feeding back the current $\langle O_2 \rangle$ to inform dilation.

3 Simulating Across Time Scales



Dual time stepping will be used to handle different time scales:

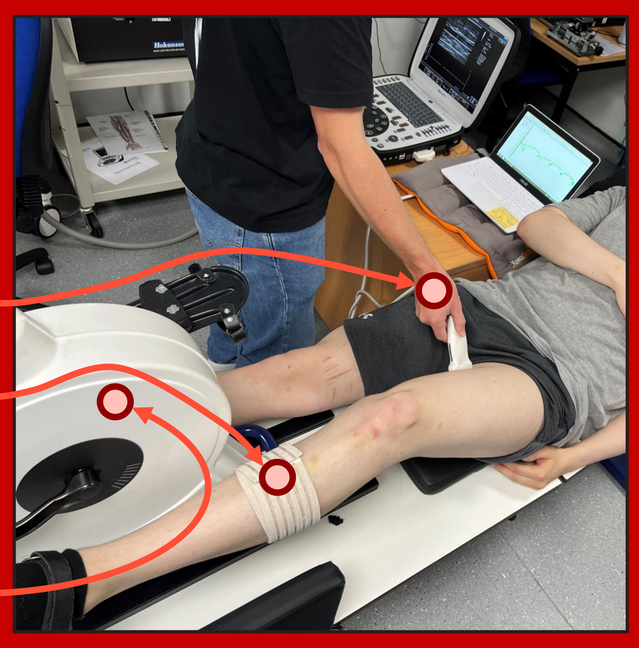
1. Macrovasculature: small time steps → run until equilibrium is reached.
2. Microvasculature: large time steps, using time-averaged data from the macro system.

Temporal Scales	
Mechanical (heartbeat, vessel dilation)	1-30 s
Hemodynamic (cardiac cycle, flow regulation)	0.01 ms - 300 s
Metabolic (oxygen uptake, lactic acid)	10-300 s

4 Experimental Work

The aim of the lab work will be for validation of and improving confidence in the numerical model.

Target Population
Healthy people & PAD patients
Male & female
With & without diabetes
Measurements
Ultrasound (flow, velocity, diameter)
NIRS (oxygen consumption)
Pulmonary oxygen uptake
Anthropometric data
Protocol
Recumbent cycling



Scan here to read more on GitHub!

5 Future Work

Code Development:

- Validation of individual models to literature and experimental results.
- Develop a new microcirculatory flow model to replace the Windkessel models.
- Implement the model coupling.
- Investigate how the degradation of each independent subsystem would affect patients and how each interact.

Experiments:

- Design an experiment that can be integrated into routine clinical practice.
- Exercise: recumbent cycling.
- Measures: ultrasound, NIRS, pulmonary oxygen uptake, heart rate, and anthropometric data.

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