2025\_06\_22

**The parameters in the stress component are adjusted to fit the coupled model to Experiment 5 (Reynold& Murphy (1988))**

**Stress Index Dynamics with k7 Introduced as a Function in the Parameter Settings from Wang et al. (2008)**

We define the k7 function as follows:

where .

In the following slides, we present parameterisation while we defined k7 as the above function, where the model results show a pattern more closely aligned with the experimental data.

2025\_02\_20

**Coupled Endothelial and Smooth Muscle Cell Model**

This computational model simulates shear-induced NO signalling in endothelial (EC) and smooth muscle cells (SMC) to study arterial behaviour. The SMC model includes actin-myosin cycling, intracellular Ca²⁺, and NO signalling, while the EC model captures shear stress-induced NO production. Coupling these models predicts SMC contraction under varying shear stress. Implemented in CellML, the model provides insights into arterial function and vascular regulation.

* All codes have been edited and validated.
* The EC component (4) and SMC components (1,2,3) are coupled.
* **The involved and edited CellML Models:**

1. Main\_Coupled\_SMC\_Model.cellml
2. Intracellular\_Calcium\_SMC.cellml
3. NO\_cGMP\_Signalling\_SMC.cellml
4. Coupled\_Main\_EC\_Model.cellml
5. EC\_SMC\_Units.cellml

* The main file is “**Main\_Coupled\_SMC\_Model.cellml**”.

A diagram of a cell structure

Description automatically generated

**Figure 3.** Arrangement of the model showing in CellML scripts involved.

Note. Parameters values were changed from the airway setting to lung arteriole setting from Table 1 in [4].

References:

1. Hai, C. M., & Murphy, R. A. (1988). Cross-bridge phosphorylation and regulation of latch state in smooth muscle. *American Journal of Physiology-Cell Physiology*, *254*(1), C99-C106.
2. Sriram, K., Laughlin, J. G., Rangamani, P., & Tartakovsky, D. M. (2016). Shear-induced nitric oxide production by endothelial cells. *Biophysical journal*, *111*(1), 208-221.
3. Wang, I. Y., Bai, Y., Sanderson, M. J., & Sneyd, J. (2010). A mathematical analysis of agonist-and KCl-induced Ca2+ oscillations in mouse airway smooth muscle cells. *Biophysical journal*, *98*(7), 1170-1181.
4. Wang, I., Politi, A. Z., Tania, N., Bai, Y., Sanderson, M. J., & Sneyd, J. (2008). A mathematical model of airway and pulmonary arteriole smooth muscle. *Biophysical journal*, *94*(6), 2053-2064.
5. Yang, J., Clark, J. W., Bryan, R. M., & Robertson, C. S. (2005). Mathematical modeling of the nitric oxide/cGMP pathway in the vascular smooth muscle cell. American Journal of Physiology-Heart and Circulatory Physiology, 289(2), H886-H897.

Note. The reason of choosing k7 as a function in the stress component of the SMC Mode (2025\_06\_22)l:  
The literature indicates that the level of **latch-bridge formation depends on** the activation levels of MLCP, specifically occurring **when activated MLCK is low and activated MLCP is significantly higher.** This is reflected in a low MLCK/MLCP ratio (~k1/k2), which is much lower in tonic smooth muscles compared to phasic smooth muscles, explaining the higher occurrence of latch-bridges in tonic muscles.

In the Wang model, k1 and k2 (representing the effects of activated MLCK and MLCP) are not constant, so the MLCK/MLCP ratio (~**k1/k2) varies**. However, we have kept the rate constant associated with latch-bridge formation (k7 = 0.03) fixed. I suggest redefining k7 as a function of k1/k2. While more experimental data are needed to establish a precise relationship, we can currently apply a simple function that aligns with our experimental observations.