ANALYSIS OF SPONTANEOUS DIAMETER OSCILLATIONS IN BLOOD VESSELS

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INTRODUCTION

What is vasomotion?

- Spontaneous, rhythmic oscillations in vessel diameter, typically observed in small arteries and arterioles
- Frequency of oscillations: 3-30 min^{-1}
- Amplitude of oscillations: 50-100% of vessel diameter

Hypothesized roles of vasomotion:

- Reduces average flow resistance
- Increases oxygen transport to tissues or capillary bed
- Maintains fluid balance between vessels and tissues
- Supplies oxygen to tissues in cases of reduced perfusion
- Promotes functional recruitment of previously inactive microvascular units

Proposed mechanism of vasomotion:

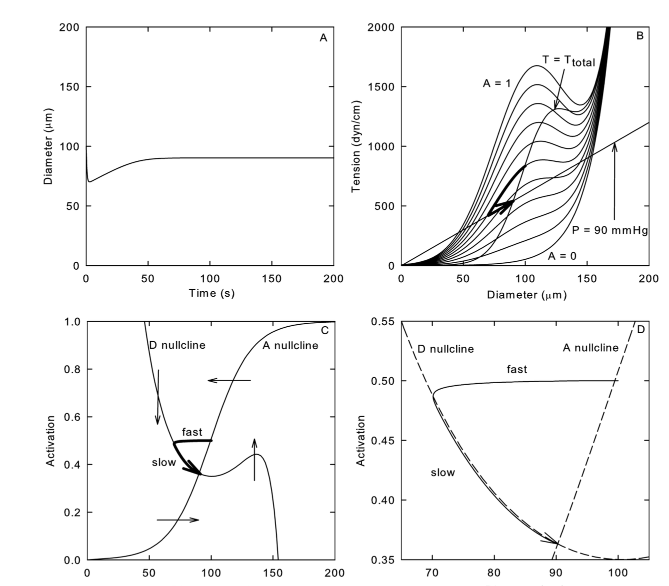
- Oscillations result from interactions between
  - nonlinear mechanics of the vessel wall
  - active contraction of smooth muscle cells
- Oscillations appear and disappear abruptly with changes in wall shear stress or pressure

RESULTS

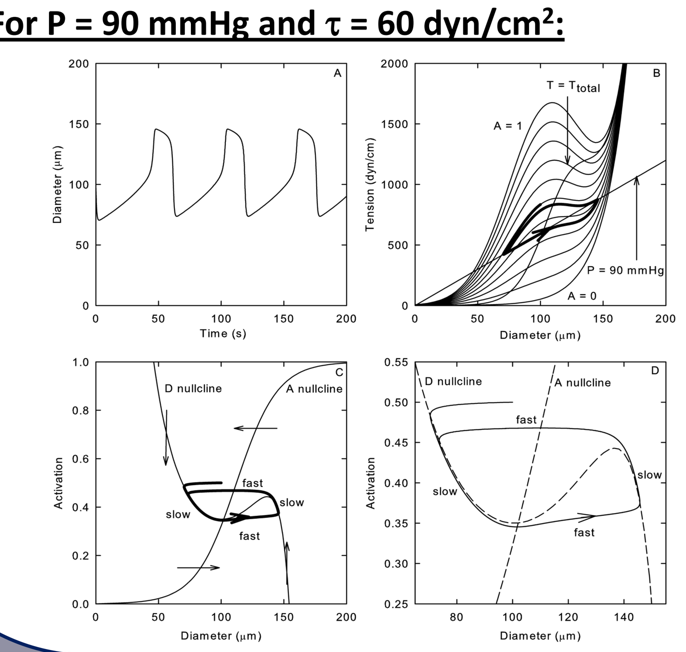
Network 1

In a single vessel, for fixed pressure and two different values of fixed shear stress, there is a change in stability as shear stress (τ) is increased

For P = 90 mmHg and τ = 30 dyn/cm²:

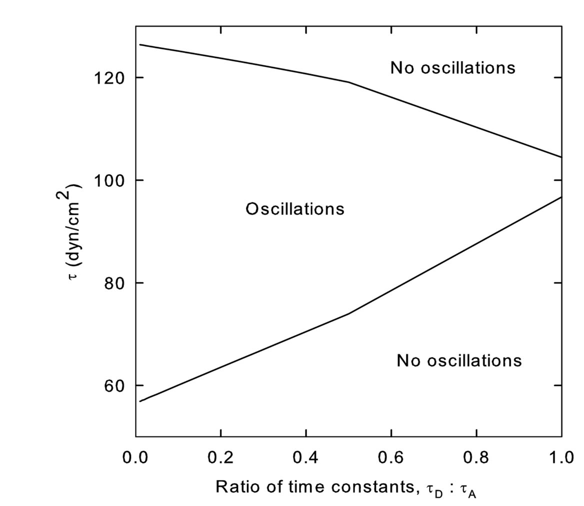


For P = 90 mmHg and τ = 60 dyn/cm²:

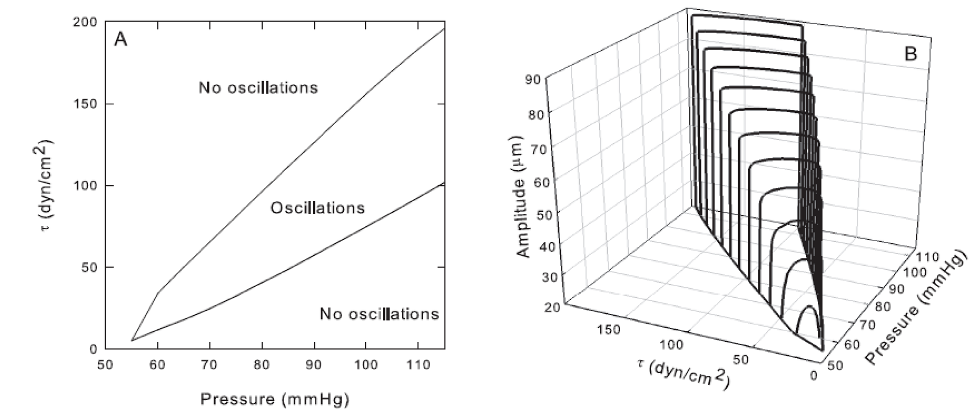


Loss of stability is shown to depend on the ratio of time constants τ_D:τ_A. As the ratio of time constants is increased, the range of shear stress values at which oscillations arise is greater

For P = 90 mmHg:

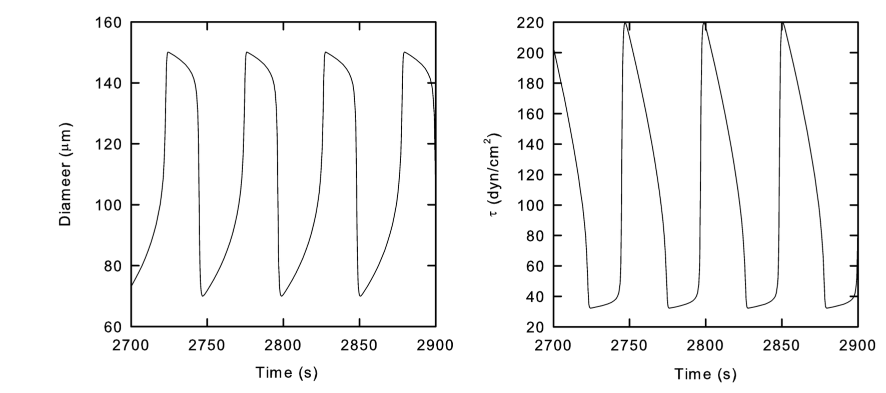


Panel A shows the values of pressure and shear stress that give rise to oscillations. The amplitudes of these oscillations increase dramatically with pressure (panel B). Note that vasomotion is predicted to be absent for P < 55 mmHg



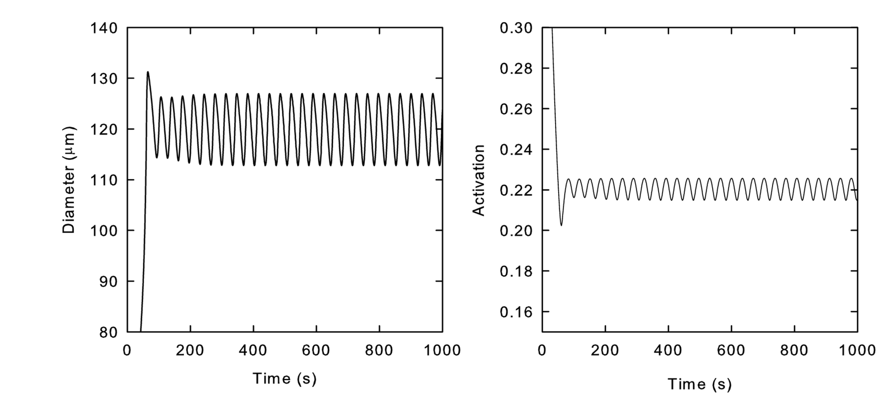
Network 2

Vasomotion is also predicted according to this mechanism in a simple network setting. The predicted period and amplitude of oscillation are comparable to those predicted in an isolated segment



Network 3

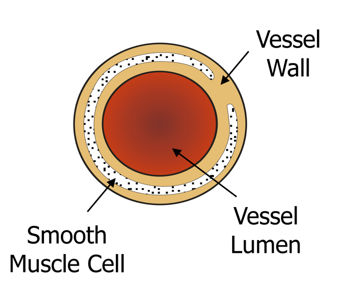
Oscillations are predicted in a more realistic network setting for limited parameter ranges. In particular, oscillations are observed for high values of oxygen demand



MODEL FORMULATION

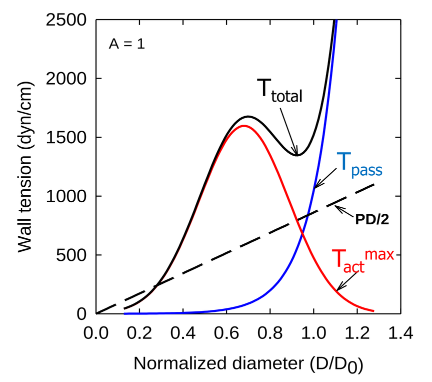
Vessel wall mechanics

- Tension (T) generated in the vessel wall is represented as the sum of a passive and active component:

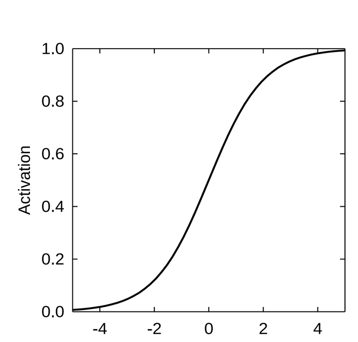


$$T_{total} = T_{pass} + A T_{act}^{max}$$

Passive tension — Active tension



- Activation (A) represents the level of vascular smooth muscle tone and varies between 0 and 1. At steady state, A is assumed to equal A_{total}, which depends on a stimulus, S_{tone}. This stimulus represents the combined effects of multiple response mechanisms:



$$A_{total} = \frac{1}{1+\exp\{-S_{tone}\}}$$

$$S_{tone} = c_{myo}T - c_{shear}\tau - c_{meta}S_{CR} + c''_{tone}$$

Myogenic response — Shear response — Metabolic response

METHODS

Determining diameter and activation

- Single vessel dynamics are governed by myogenic and shear-dependent responses (metabolic response is assumed constant)
- Time constant for diameter (τ_D) is assumed to be less than the time constant for activation (τ_A)

$$\frac{dD}{dt} = \frac{1}{\tau_d}\frac{2}{P_c}\left(T - T_{total}\right)$$

$$\frac{dA}{dt} = \frac{1}{\tau_a}\left(A_{total} - A\right)$$

$$\downarrow$$

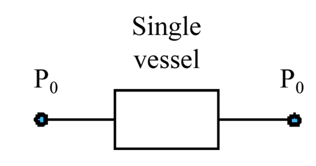
$$\frac{dD}{dt} = \frac{1}{\tau_d}\frac{2}{P_c}\left(T - (T_{pass} + A T_{act}^{max})\right)$$

$$\frac{dA}{dt} = \frac{1}{\tau_a}\left(\frac{1}{\exp(-S_{tone})} - A\right)$$

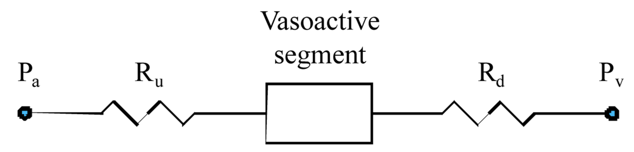
- Numerical and theoretical analysis are used to examine the sensitivity of oscillations to model parameters
- Oscillations are predicted for certain pressure and shear stress values

Three vessel configurations

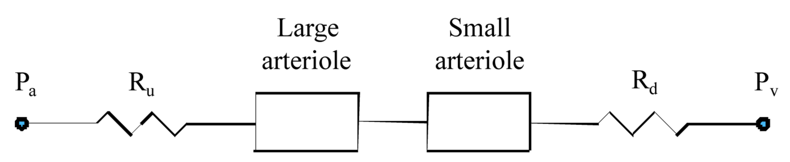
Network 1: isolated vessel



Network 2: simple network (one vasoactive segment)



Network 3: seven compartment network (two vasoactive segments)



DISCUSSION

- In a previous theoretical model of blood flow regulation (Arciero et al., 2008), smooth muscle tone is assumed to depend on myogenic, shear-dependent, and metabolic responses. This model is used to predict changes in vessel diameter and activation in three vascular networks (Networks 1-3)
- For certain parameter ranges, model equations do not have a steady state solution but instead give rise to oscillations in diameter and activation, demonstrating a novel potential mechanism for vasomotion involving the interaction between:
  - tone generation in smooth muscle
  - nonlinear viscoelastic properties of the vessel wall
- **In a single vessel:**
  - Oscillations abruptly appear and disappear with small changes in pressure or shear stress
  - Amplitudes of oscillations vary rapidly over narrow parameter regimes
- **In larger networks:**
  - Oscillations occur for high pressure or high oxygen demand
  - Network effects may have a stabilizing effect on the system