Theoretical models for regulation of blood flow in the microcirculation

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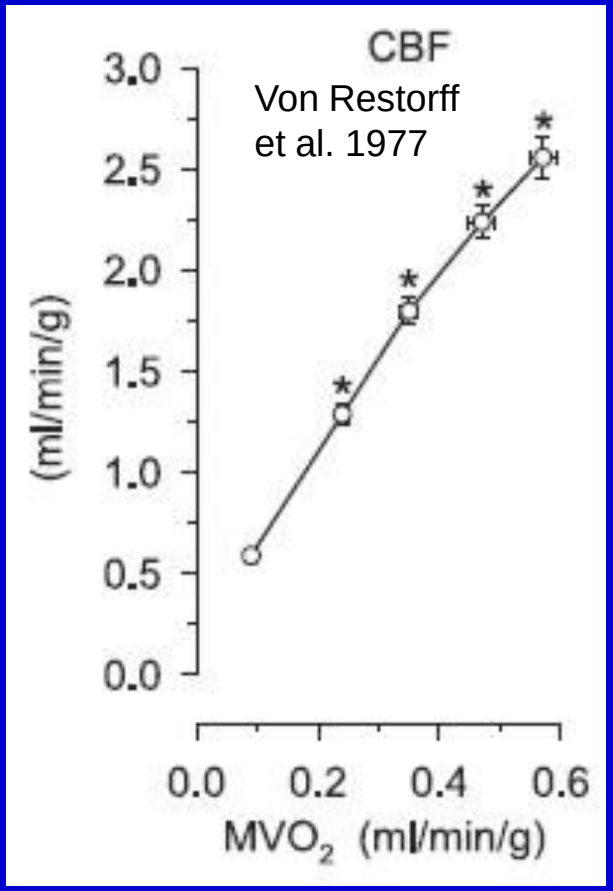
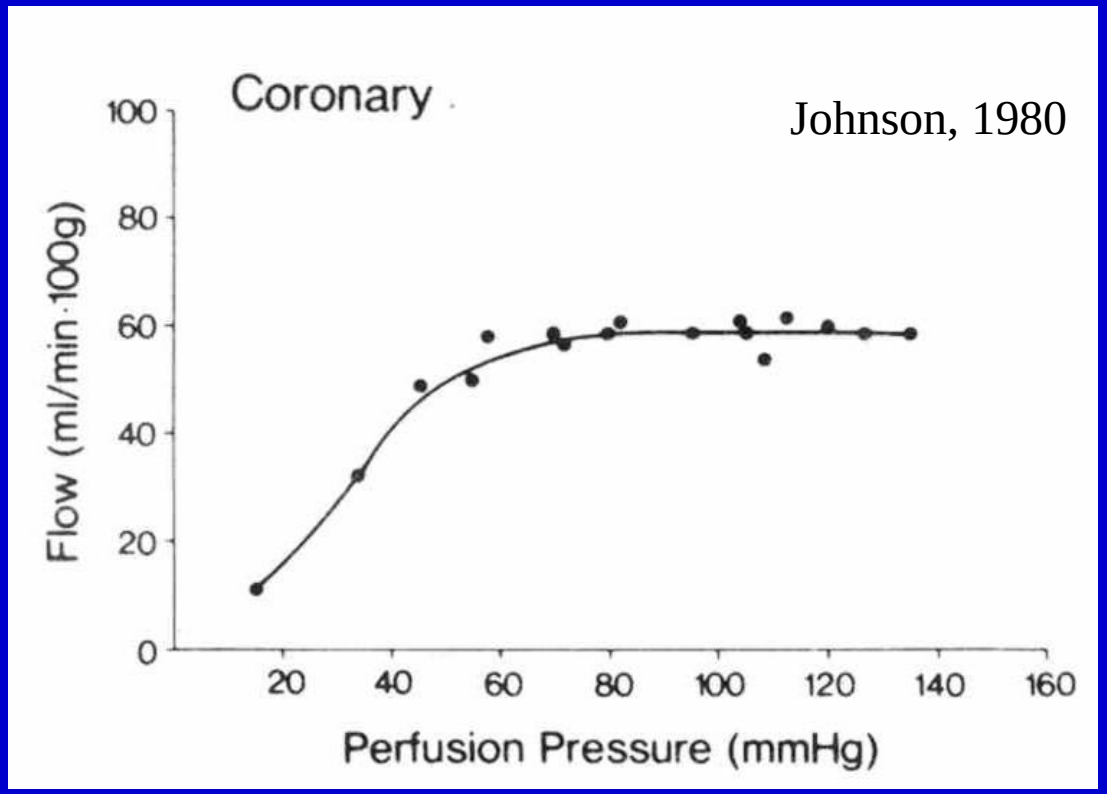
Regulation of coronary blood flow

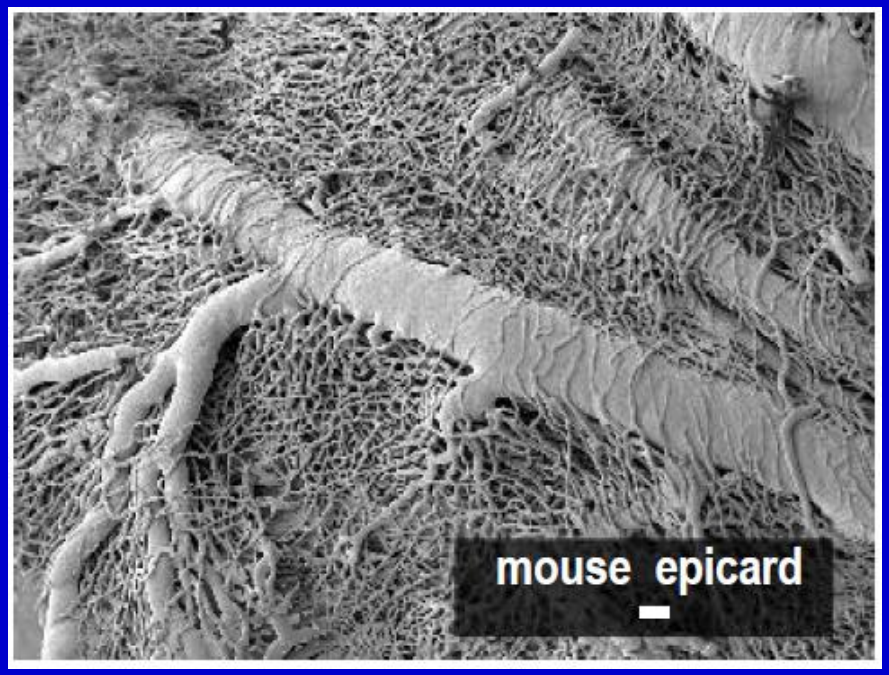
Metabolic regulation



Autoregulation

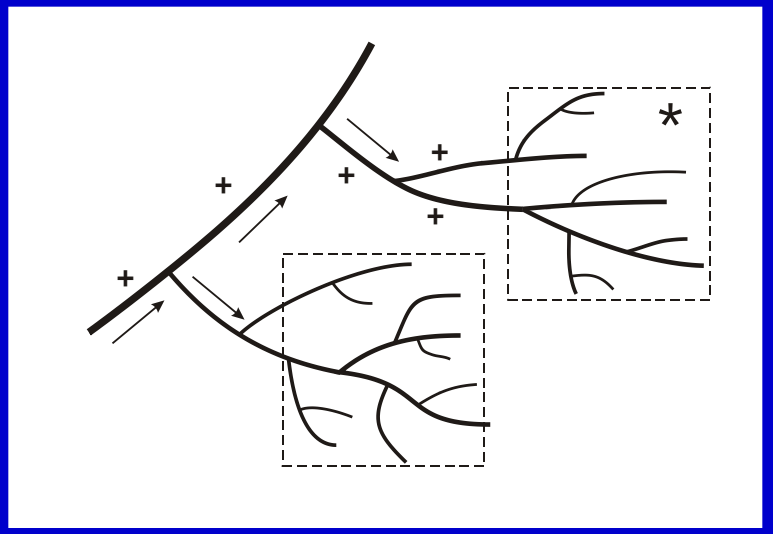


Mechanisms of local flow regulation

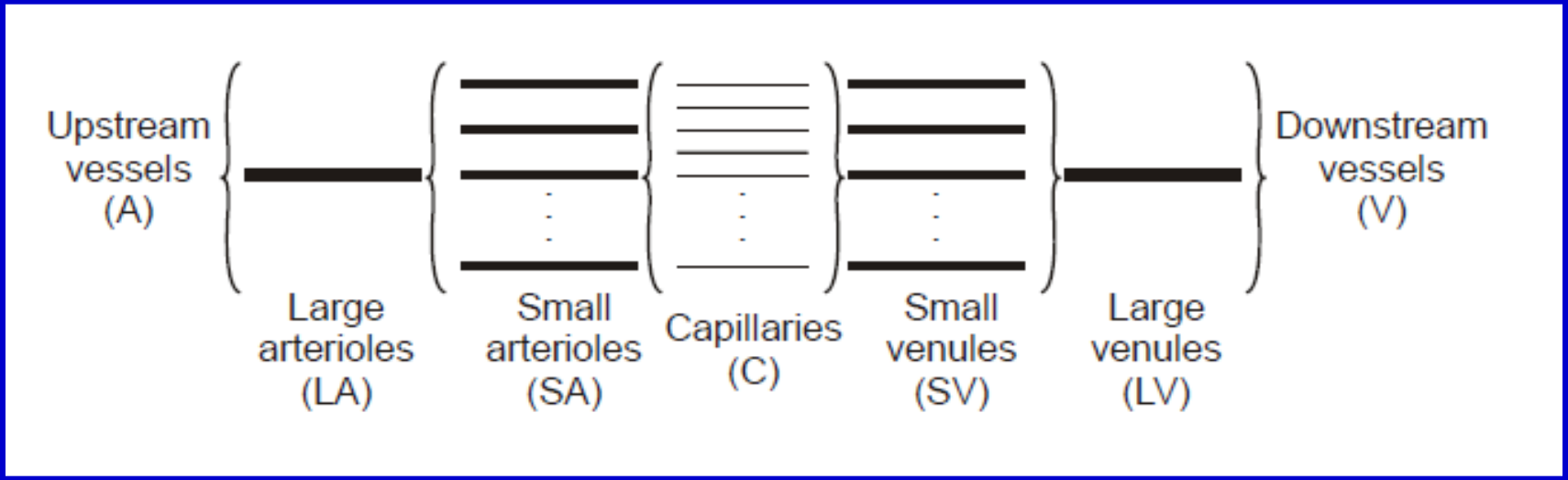


Pries and Secomb, 2008, Handbook of Physiology. Bar = 40 μm.

- Myogenic response
- Shear-dependent response
- Metabolic responses
- Conducted responses

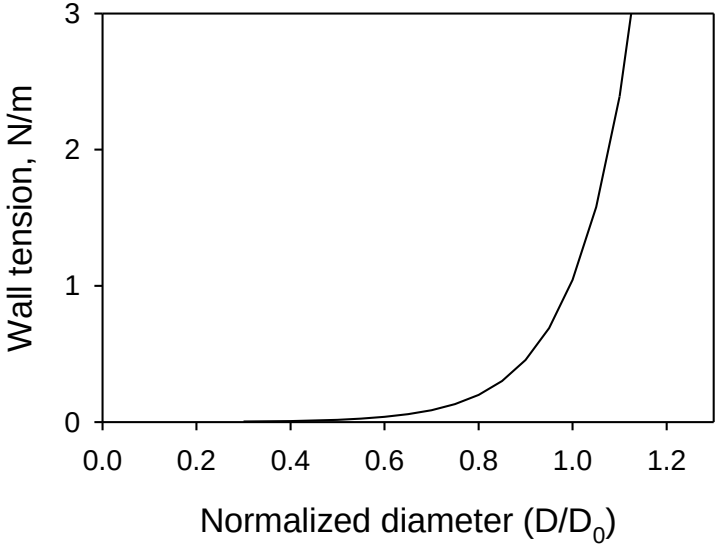


Representative segment network model

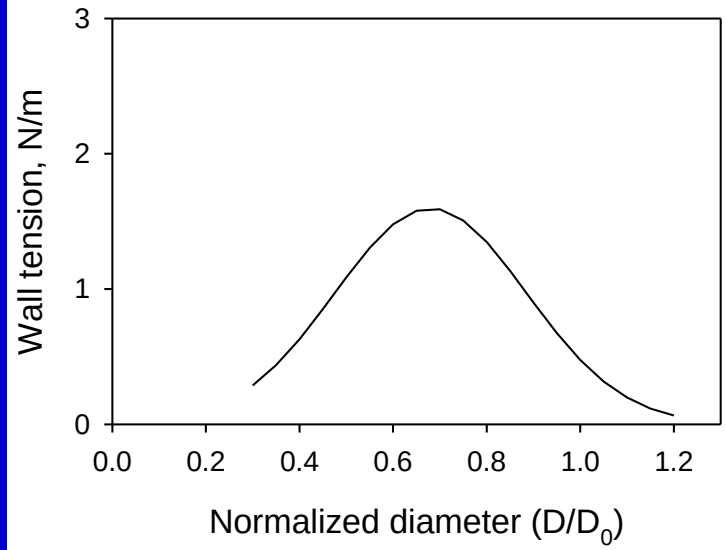


Arteriole mechanics: passive and active tension

$$T_{pass} = C_{pass} \exp[C'_{pass}(D/D_0 - 1)]$$

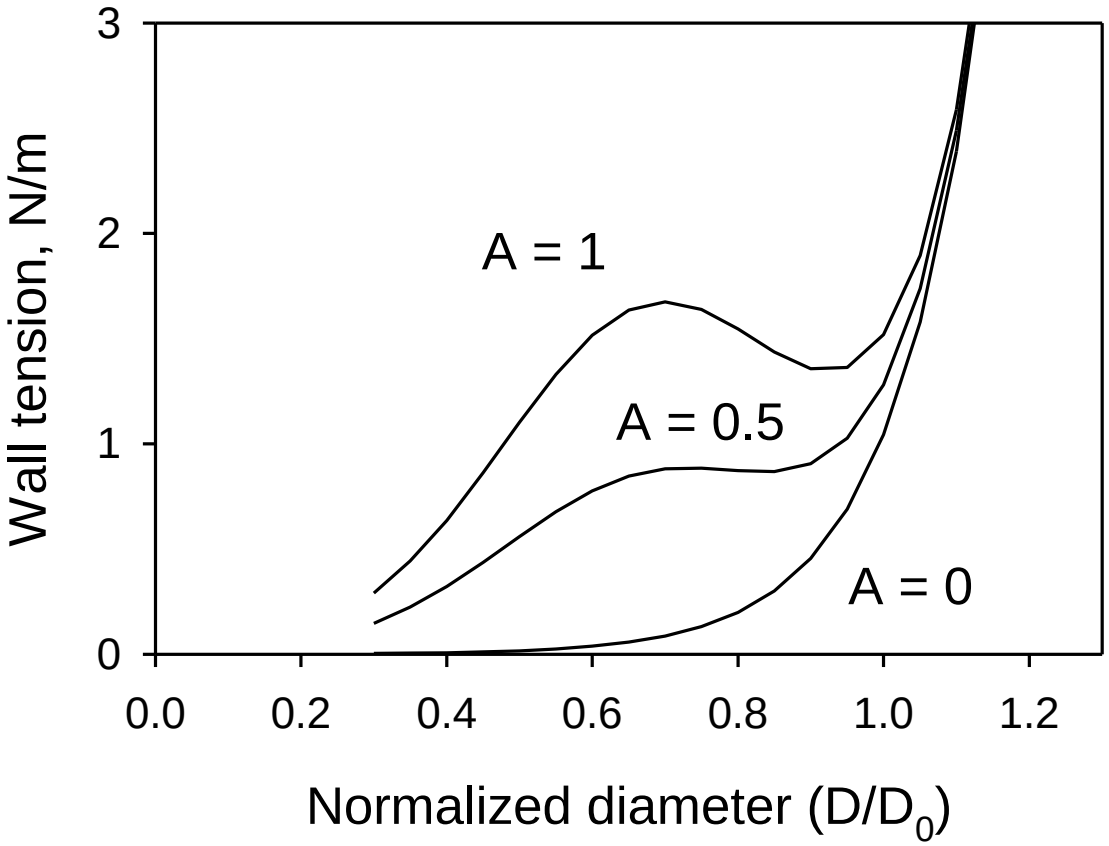


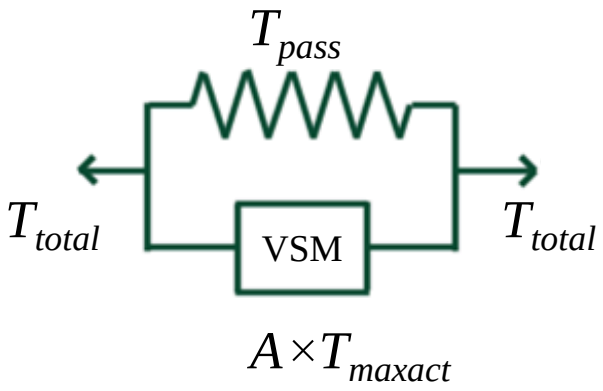
$$T_{maxact} = C_{act} \exp\left[-\left(\frac{D/D_0 - C'_{act}}{C''_{act}} \right)^2 \right]$$



Arteriole mechanics: total VSM tension

$$T_{total} = T_{pass} + A \times T_{maxact}$$





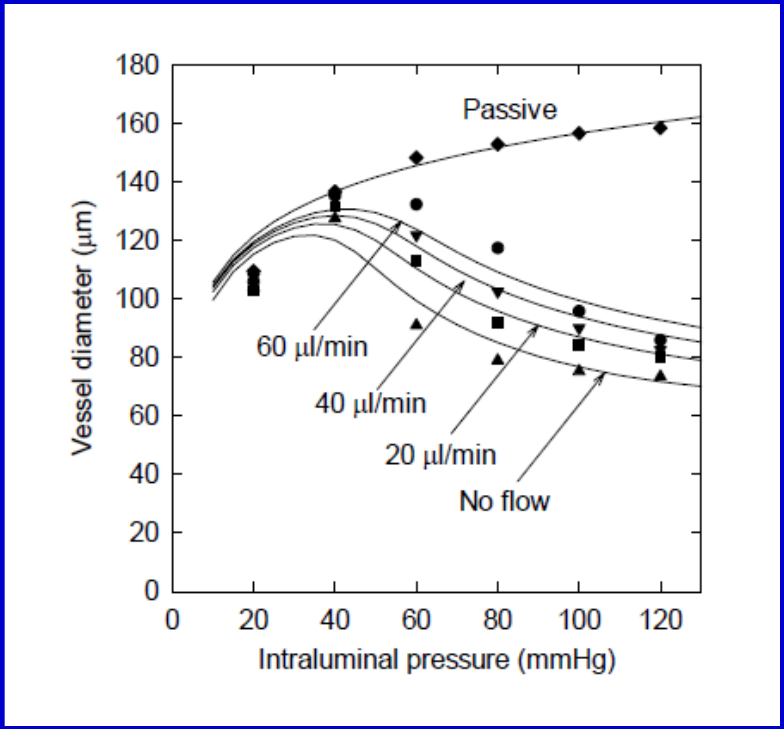
Control of activation

$$A = \frac{1}{1 + \exp(-S_{tone})}$$

where

$$S_{tone} = C_{myo}T - C_{shear}\tau_{wall}$$

$$- C_{meta}S_{CR} - C''_{tone}$$



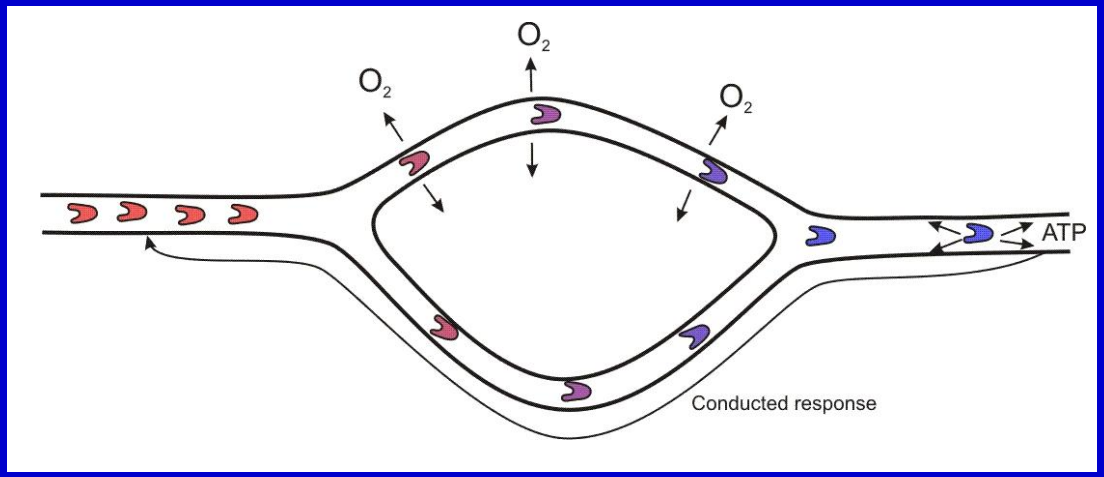
Carlson et al. 2008;
data from Sun et al. 1995

Wall tension $T \rightarrow$ Myogenic response

Wall shear stress $\tau_{wall} \rightarrow$ Shear-dependent response

Conducted metabolic signal $S_{CR} \rightarrow$ Metabolic response

Calculation of conducted response signal



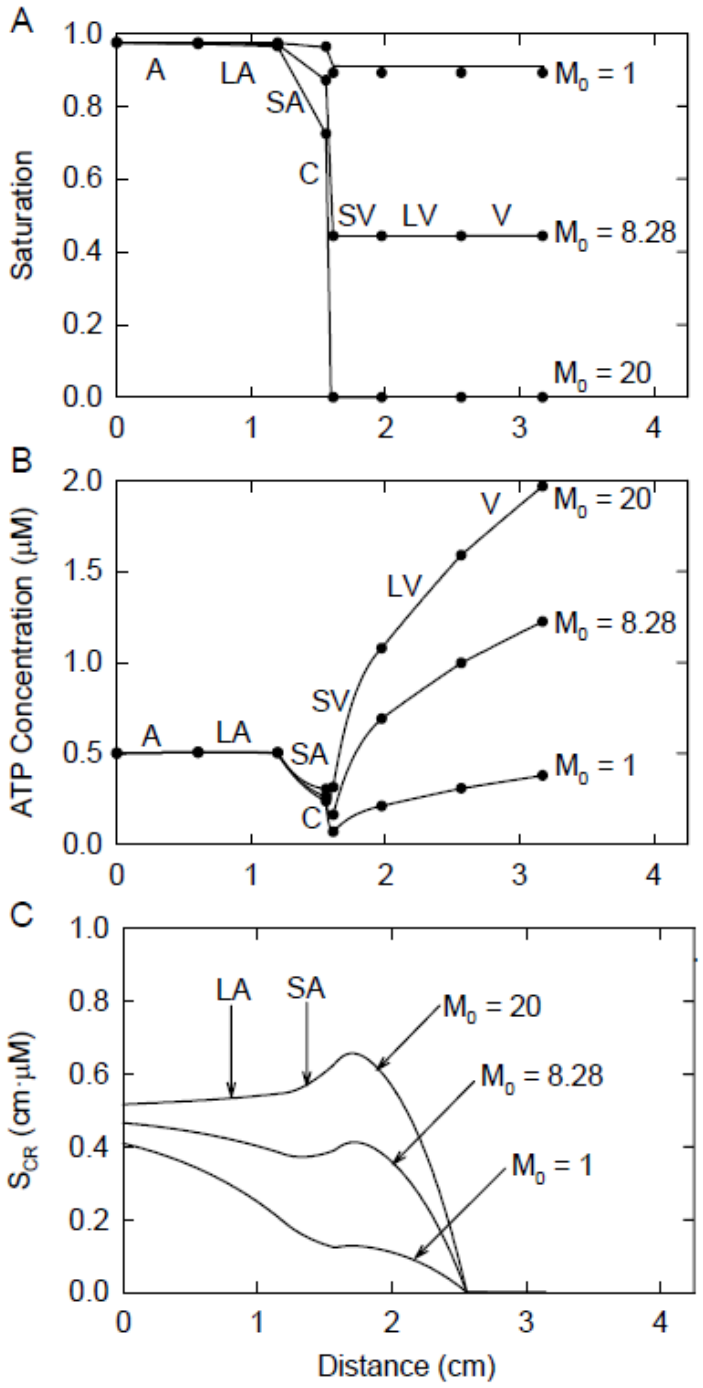
- Oxygen saturation decreases along flow pathway at rate proportional to tissue oxygen consumption
- ATP is released by red blood cells at a saturation-dependent rate, and degraded by endothelial cells
- A conducted signal is generated at each point in the vessel wall, in proportion to intravascular ATP level
- The signal is conducted upstream with exponential decay (length constant L_0 = 1 cm)

$$S_{CR}(x) = \int_{x}^{x_{end}} C_{ATP}(y) e^{-(y-x)/L_0} dy$$

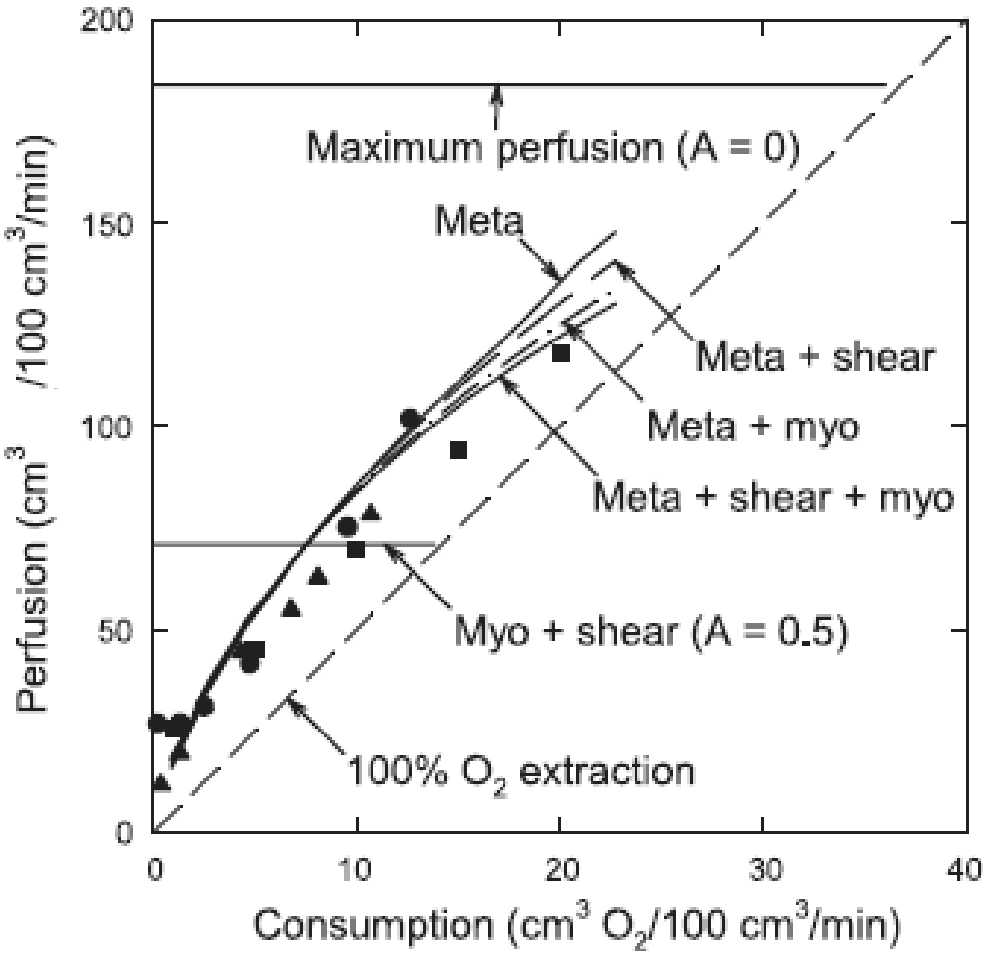
Variation of oxygen, ATP and conducted response along flow pathway

Results for fixed flow rate

M_0 = oxygen consumption rate in $cm^3O_2/100cm^3/min$

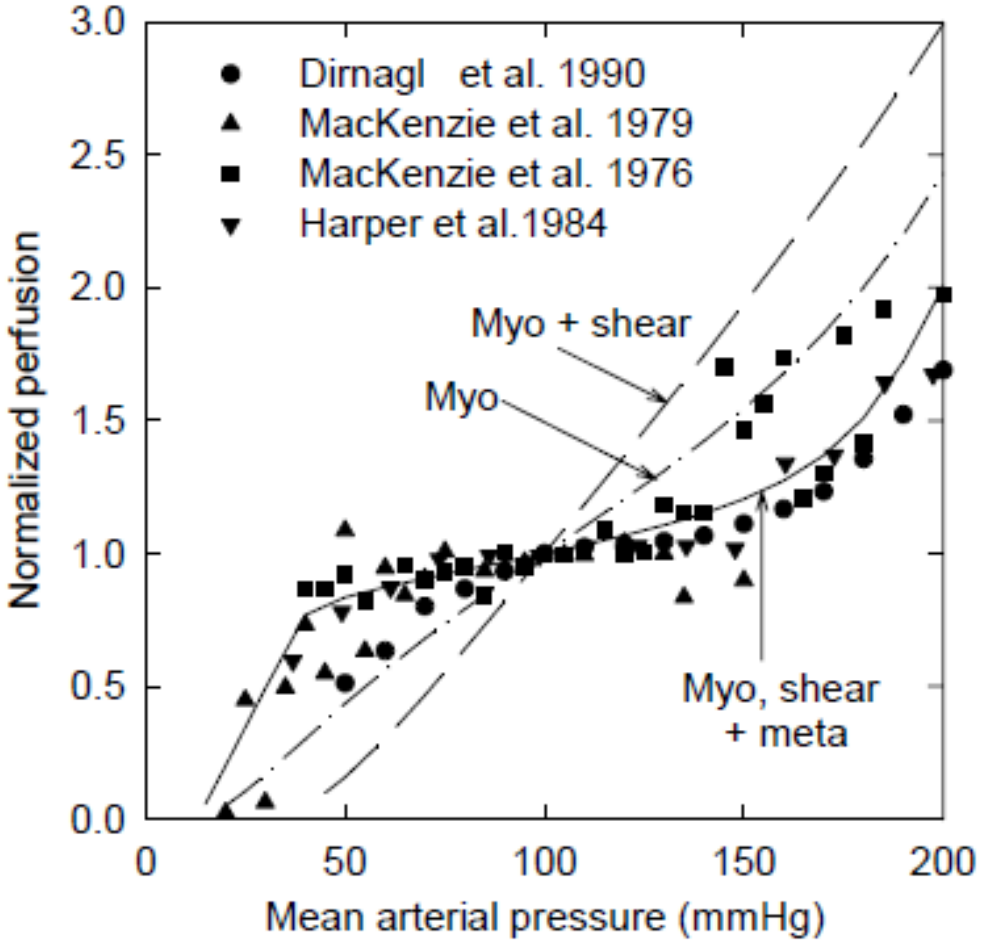


Metabolic regulation: model and experiments



Arciero et al. 2008; data of Horstman et al. 1976, Mohrman et al. 1988, Sparks 1980

Autoregulation: model and experiments



Carlson et al. 2008

Conclusions

- In the microcirculation, flow is modulated in response to changing needs (metabolic regulation), but maintained almost constant over a wide range of blood pressure (autoregulation).

- Autoregulation is achieved by the combined effects of metabolic and myogenic responses, which overcome the opposing effect of the shear-dependent response.

- Metabolic regulation is achieved by the metabolic response, which overcomes the slight opposing effects of myogenic and shear-dependent responses.

- Our theoretical models for these processes could be used in multi-scale simulations of cardiac function.