Modeling Collapsible tube flow in vascular networks with Volume-based state variables

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Fluid flow and vascular transport within the circulation in tissues has been the subject of a large body of research, with the goals of understanding several important physiological reactions to mechanical factors and vasoactive drugs. The interaction between blood and associated fluid flow at a meso-scale (5 to 100 mm in size, roughly) and functional inputs has been studied in many modeling efforts with the aim to understand how perfusion can be affected by external pressure, muscular activity, and swelling, in addition to the known vasoactive drugs.

Mathematical modeling of the microcirculation encounters several well-known difficulties, and one addressed here is the nonlinear behavior of the vascular bed due to the collapsible nature of the veinous blood vessels. When a region of tissue is perfused, the key pressures to consider are the arterial supply pressure, the pressure in the veinous drainage, and the pressure in the tissue being perfused.

This tissue pressure can be difficult to define, since biological tissue is a mixture of several components intermingled at a molecular level. This is a well-known issue in the analysis of porous media, and three concepts are typically used to define a workable tissue pressure. First, the physical quantities are averaged on a small scale to develop a continuum-level index of quantities such as stress, deformation, chemical concentrations, and strain. This continuum approximation is occurs over several repeating small-level structures in the tissue. Pressure or stress at a point in a continuum-level analysis is actually an average over a few nearby components of the microstructure.

Second, the porous nature of biological tissues allows fluid in the extracellular space (lymphatic fluid, for example) to move within the tissue, so there is a potential defined that forces this fluid to move within the tissue. That potential is often defined as fluid pressure or pore pressure. If the microstructure of a material is well-defined, so that individual phases can be defined, then the pore pressure has a direct physical meaning. If the material is molecularly disperse, the potential that drives fluid movement within the tissue needs a more general definition.

Third, to address the second concept, a “reference medium” is typically defined which is a one-phase fluid medium that is in equilibrium with the tissue at a given physical state. That is, to define fluid pressure in a porous medium, one way is to use the thought experiment of excising a differential elements of the tissue and embedding it into a fluid medium which is in communication with the element across a semi-permeable membrane, The pressure and osmotic potentials in the reference medium that are needed to prevent fluid or solute flow across that membrane are taken as the fluid pressure and the osmotic potentials in the tissue. More detailed analyses, included charged solutes, can be found in work by Maroudas and Urban. With this concept, the fluid pressure in the tissue can be defined, along with the key osmotic potentials.

With the concept of fluid pressure defined, the relative role of solid components in biological tissues can be addressed. Solid components can be most directly defined as components that resist changes in shape at a constant volume. Solid components will also resist changes in volume, so there is some load sharing between fluid and solid components in bulk deformation. There are several concepts used to allocate the overall stress on solid and fluid components in soft tissues. There is a concept of “skeletal stiffness” which describes the material stiffness when the pore pressure is held constant.

One way to estimate the relative load sharing between fluid and solid components is to compare the tissue stiffness in shear (shape changes without volume changes) to bulk compression (volume changes without shape changes). In most biological tissues, at the loading frequency of a few hertz, the bulk modulus of hydrated tissues is in the range of 2 gigapascals whereas the shear modulus is in the range of 10 to 20 kilopascals – the solid “skeletal” modulus is roughly 105 times less than the bulk modulus of the overall tissue.

This discussion is meant to rationalize the use of the cerebrospinal fluid pressure as an approximation to the pressure on the outside of the blood vesssels in an analysis of the brain circulation. The argument is that the CSF is in contact with brain tissue, and that brain tissue is in contact with the external surface of the blood vessels (perhaps with a perivascular space as well). Based on the relative shear stiffness of the brain tissue and the bulk stiffness of the solid and fluid components, the overall pressure that the outside of blood vessels are exposed to will be very close to the mechanically defined pressure (i. e. the sum of the overall normal stress components).

This discussion also indicates that osmotic effects in tissues could be included in future studies, where the volume of swollen tissue could participate in the equilibrium of the circulation system.

For a given arterial input pressure, vascular drainage pressure, and tissue pressure, a model for aspects of the overall circulation can be defined using a 1-D flow path, shown below. The objective of this model is to develop numerical techniques that incorporate collapse of segments of the venous side of the circulation in static conditions and in some dynamic conditions. The nonlinear aspects of venous collapse are well known, and collapsed venous-side vessels are well-known in circulatory physiology, which has led to the concept of a “vascular waterfall” (references). Analysis of this phenomenon is difficult because of the nonlinear changes in both vessel resistance and vessel capacitance.

Typical flow analyses of microcirculation have used pressure within the vessels or transmural pressure as the state variables to describe the fluid flow network. The nonlinear nature of the vessel collapse phenomenon can make this approach difficult.



An approximate relationship between transmural pressure and the normalized diameter (the volume of a small segment) is shown in figure 1. As can be seen, stretching the vessel lumen (relative volume >1) results in an increased transmural pressure, resulting in a relatively stiff response, but decreasing the vessel area results in a substantial range where the vessel walls are essentially slack and the transmural pressure is very low. The approximation shown in figure 1 uses a dual exponential relationship which is

With X the Vessel area divided by the original vessel area.

To approximate the increase in resistance in the vessel as the area of the vessel is decreased in collapse, the vessel segment resistance was taken as

A simplified model to explore venous collapse in the cranial circulation is shown in figure 2.



**Pa**

**P1**

**P2**

**P3**

**P4**

**P5**

**P6**

**P7**

**P8**

**P9**

**P10**

**P11**

**P12**

**Pint**

**Va**

**Qcsf**

**Qcap**

**V1**

**Pv**

**V2**

**V3**

**V4**

**V5**

**V6**

**V7**

**V8**

**V9**

**Vc**

**Ra**

**Rca**

**Rra**

**R1**

**R2**

**R3**

**R4**

**R5**

**R6**

**R7**

**R8**

**R9**

**RD**

**Rc**

In this model, a single vessel is considered in which blood flows from left to right through resistors and into capacitors. The pressure in the cranium is represented by Pi. Fluid flow out of the vessel into the cranium is modeled by two flow variables Qcsf and Qcap, and flow from the cranium into the surrounding vasculature is modeled using a flow resistance Rc.

The arterial resistance is modeled by a constant resistance Ra, and the cerebral artery resistance is modeled by a constant resistance Rca. The capillary resistance vessels are modeled by a constant resistance Rra. The arterial capacitance relative to the cranium is modeled by a capacitor with volume Va and the capacitance of the cranium relative to the external region is modeled with a capacitor with volume Vc.

Nine vessel segments are modeled in series, with each of the capacitances using the pressure-volume characteristic as shown in figure 1. The flow resistances R1 through R9 use a resistance value from equation 2, with the corresponding capacitance value (i. e. R1 uses V1/V1o, etc).

Since the relationship between pressure and volume in the vein segments is highly nonlinear, using pressures within the vessels as a state variable for a time integration of the model is nearly impossible, so the approach taken was to use vessel volumes as a state variable. In the model below, if the pressures across all the capacitances in the model are defined, then the model state (pressures and flows) will be fully specified. Since the volumes of the vessel segments and the fluid volumes in the arterial and cranial capacitors specify these pressures, those volumes form a complete set of state variables.

The approach taken was therefore to use the conservation of mass equation as the primary equation for the simulation, and to integrate over time to run the dynamic simulations. MKS units (Pascal, meter, seconds) were used and double precision calculations were run using Jupyter Labs within an Ubuntu 24.04 operating system, using Anaconda.

The algorithm starts with an initial volume distribution, which is used to define pressures and flow resistances. The boundary conditions (arterial and venous pressures) and the pressures computed from the initial volume distribution are used to compute volume flows, and these volume flows are used in the conservation of mass equation to time integrate the model.

To set the initial conditions, an initial volume in the vein segments was used which was the volume at zero transmural pressure, multiplied by 1.2. This volume resulted in a transmural pressure of 2555 Pa, using the coefficients from Table 1. Using a nominal value of arterial pressure (10,000 Pa) the interstitial pressure was estimated at 7445 Pa, and this was used to set the initial pressures of the arterial and cranial capacitance elements. The initial volume for the arterial segment was estimated using a 10 cm long vessel with 3 mm diameter, and the cranial volume was estimated at 1500 cc.

Steady-state results

The model shown in figure 1 was time-stepped using the Euler forward method. Stable solutions resulted with a time step size of 10-6 to 10e-7, with steady state occurring at 5 or 10 seconds. With double-precision calculations, no significant round-off error was seen.

 



Segment volumes and transmural pressures with a 12 kPa inlet pressure. The top two plots show the results for a 10 kPa venous pressure, and the bottom two show results for a 6 kPa venoud pressure. Collapse of the most downstream (rightmost)segment is apparent.

The draining arterial pressure Pv was varied to simulate conditions where fully open veins are anticipated (that is, where both the arterial and venous pressures are above the interstitial tissue pressure) and conditions where collapse of the veinous components is likely (where venous pressure is below the interstitial pressure).

The results for veinous segment volumes were as expected for conditions where both the veinous pressures and the arterial pressures were above the interstitial pressure – an inflated vessel was apparent, with pressure and segment volume decreasing with distance from the arterial supply.

In conditions where the venous pressure was below the interstitial pressure, the collapse of the vessel to a small cross-sectional area occurred only in the venous segment closest to the outlet resistance (RD in figure 2). This is similar to physical results for collapsible tubes when the tubes are positioned within chambers that have a well-defined outlet to lower pressure. The spatial gradient in transmural pressure with distance at the exit corresponds to a focused narrowing of the collapsible tube adjacent to the outlet from the pressurized chamber used to apply external pressure. This is seen in many studies of collapsible tube behavior.



The overall dependence of flow on input and output pressures for a fixed internal pressure (7445 pa) shows an interesting result that in the range where the exit pressure is lower than the internal pressure, the flow through the vessel increases with increased exit pressure. The exit pressure appears to prop open the collapsed segment, reducing flow resistance.

Dynamic inputs (sinusoidally varying arterial pressure) around a steady state did not significantly change the volume response of the model when the narrowed exit segment existed.

 

The tube collapse adjacent to the outlet causes a local increase in flow resistance that elevates pressure within the tube adjacent to the collapsed area. This leads to an expanded tube upstream of the collapsed area, reducing the flow resistance. As a result, the collapsed region adjacent to the outlet is the only part of the tube that is collapsed in this steady-state solution.

To assess whether the focused area of collapse on the tube depended on the lumped-segment approximation being used, the number of veinous segments (Vi in figure 1) was doubled to 18. The results of the finer model (with a constant initial tube diameter) showed a similar focused area of collapse, with the segment adjacent to the exit resistance being the only collapsed segment.

 



Vessel transmural pressure and vessel segment volumes in the 18-component model for arterial pressure of 12000 Pa, with vascular pressures of 6500Pa (upper two plots) and 5000 Pa (lower two pots), with interior tissue pressure set at 7445 Pa.

To assess whether spatial variations in resting vessel diameter were involved in the localization of the collapsed areas, the veinous resting radius was varied from 1.5 mm (upstream) to 3 mm (downstream) over a 45 mm length. This had the effect of spreading the collapsed region over 3 to 4 segments, as shown in figure (<###>)(using the finer-scale model).

Linear variation in the resting tube diameter with position changed the response of the tube by spreading the collapsed region upstream in the flow.

 

 

Above are results for an exit vascular pressure of 6500 Pa. While the transmural pressures seem smooth, the vessel segment volumes changes substantially, as would be expected from the volume-pressure characteristic in figure 1. The tissue pressure was 7445 pa to start with and did not vary substantially during the 10 second run. (These are results from the last of 10 cycles. The pressure and volume results were stable after a few cycles.)

 

 

Above are results from a run similar to the previous case, but with the exit vascular pressure at 5000Pa. The pressure traces show some nonlinearities but the volume traces show even more.

Effect of cranial compartment stiffness:

In the models from figure 2, the fluid in the cranium interacts with the vessel volume, and the pressure in the cranium is related to the overall volume of the fluid in the cranium using a capacitance, and the volume of the cranium taken as Vc. The pressure-volume relationship for the cranium is linear, simply

The nonlinear relationships between pressure and blood vessel volume in figure 1 leads to a potential feedback loop where the increased vessel volume adds to the cranial volume, increasing the internal pressure in the cranium and influencing blood vessel segments. In the baseline model for this study, the cranial elastance (the inverse of the capacitance) was taken as 105 Pascals per cubic meter of fluid increase. In the initial sets of simulations meant to assess flows and collapsibility, the intracranial pressure varied by only a small amount. To assess the dynamic cranial pressure effect, the cranial Elastance (m^3/Pa) was set to 106, 2x106, 5x106 and 107 Pascals per cubic meter, and significant changes in flow patterns occurred. These cases used an input arterial pressure of 12,000 Pa, and a venous outflow pressure of 5,000 Pa (with the initial internal pressure set to 7445 Pa). a sinusoidal input of +/- 2000 Pa was superimposed on the steady input arterial pressure.

For a cranial stiffness of 106 pascals per cubic meter, the transluminal pressure in the vessel segments and the volume of the vessel segments smoothly vary, with collapse occurring in the downstream segments.





Increasing the elastance of the cranium to 4 x 106 led to some changes, where the most downstream segment is most compressed.





With a cranial elastance of 5 x 106 a two-state time behavior becomes apparent, where the end-vessel segment is compressed and the vessel becomes inflated.

 

 

With a cranial elastance of 107 Pa/m the two-state result seems more pronounced.





Observations:

Formulating the model in terms of vessel segment volumes seems like a promising way to develop a larger-scale model of a vascular system. The model was numerically stable in Euler forward time stepping so long as the time step was small enough. More complex time stepping methods (such as Euler backward) may be mode efficient.

The capacitance of the cranium was taken as large (the elastance was low) so the interaction of the expanding (or contracting) arteries was not very large. The effects on vascular segment volume were primarily due to relatively constant cranial pressure. Changing the cranial pressure or increasing the elastance of the outer constraint could be pursued to assess behavior in other tissues.

Formulating the circulation in terms of blood vessel volume distributions and time-stepping those volumes could be an advantage when linking or embedding a model for the vasculature.

**Appendix: Parameters**

The variables for simulations are defined as follows:

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters |  |  |  |
| vein segments |  |  |  |
| nominal radius | 1.5 mm |  |  |
| Length | 5 mm |  |  |
| Pressure-volume parameters |  |  |  |
|  | A1 | 1 |  |
|  | A2 | 0.2 |  |
|  | alpha | 15 |  |
|  | beta | 5 |  |
|  | K | 133 |  |
|  | Vmin(%) | 5 |  |
| blood viscosity | 0.004 | Pa-sec |  |
| Artery resistances |  |  |  |
| feed artery | Sca (1/R) | 1.00E-07 | pa/(m^3/sec) |
| resistance artery | Sra | 1.00E-07 |  |
| Supply artery |  |  |  |
| Base resistance | Ra | 2.00E+06 | (m^3/sec)/pa |
| Baseline Volume | Vao | 7.07E-07 | m^3 |
| Baseline Pressure | Pao | 2555 | pa |
| Artery Elastance | Ka | 9.43E+06 | m^3/pa |
|  |  |  |  |
| CSF flow | Qcsf | 7.45E-06 | m^3/sec |
| Capillary flow | Qcap | 0 |  |
|  |  |  |  |
| Drain Veins |  |  |  |
| Resistance of drain | SD | 1.00E-07 |  |
|  |  |  |  |
| Cranium Parameters |  |  |  |
| Baseline Volume | Vco | 0.0015 | M^3 |
| Baseline Pressure | Pinto | 7445 | pa |
| Elastance | Kc | 1.00E+05 | pa/m^3 |
|  |  |  |  |
| Cranial Conductance | Scr | 1.00E-09 | (m^3/sec)/pa |