Rayleigh-Plesset Equation with a Discontinuous Input Pressure

Qiyao Peng, Vivi Rottschäfer

Bachelor Seminar 2024

1 Introduction and Preliminaries

Many existing drugs are aimed at targets present in the brain. However, the blood-brain barrier (BBB) is a major barrier protecting the brain; it limits the transport of drugs from the blood into the brain. The BBB consists of endothelial cells that are connected by tight junctions between the neighboring cells. To increase the permeability of the BBB, and hence, drug delivery into the brain, it is known that inserting microbubbles (MBs) into the bloodstream and applying focused ultrasound (FUS) shows great potential. MBs are microspheres filled with gas which is surrounded by a lipid, protein or polymer shell, or so-called coat. Under the impact of FUS, the MBs start to oscillate. If the input pressure of the FUS is in a proper range, then the MBs perform a stable, periodic growth and compression, such that pores are formed on the membrane of the coat to release the drug molecules.

From the mathematical perspective, the Rayleigh-Plesset (RP) equation is often utilized to describe the radius change of the MBs. However, most work (e.g. [1]) assumed that (1) the MB is a sphere and (2) the FUS is continuously applied. Actually, neither of the assumptions is realistic in clinical practice. In this BSc project, we will focus on the second assumption. According to [2], the FUS therapy switches on the FUS for few seconds, then pauses for some time and this "on and off" process repeats several times. In other words, the FUS is applied discontinuously in a periodic manner, which of course will influence the behavior of the RP equation. The time range when the FUS is on, is called a *pulse*.

There are many versions of the RP equation, and one of the simple versions of the RP equation was developed by de Jong et al. [1], which reads

$$\rho\left(R\ddot{R}+\frac{3}{2}\dot{R}^2\right)=\left(p_0+\frac{2\sigma(R_0)}{R_0}\right)\left(\frac{R}{R_0}\right)^{-3\kappa}\left(1-\frac{3\kappa}{c}\dot{R}\right)-\frac{2\sigma(R)}{R}-\frac{4\mu\dot{R}}{R}-p_0-p_A(t). \quad (1.1)$$

This describes the change of the radius of the MB. Here, R represents the radius, the dot represents differentiation with respect to time so that $\dot{R}$ and $\ddot{R}$ represent the velocity and acceleration of the microbubble wall. Moreover, R_0 is the initial radius of the microbubble, ρ is the fluid density, p_0 is the ambient pressure, $\sigma(R)$ is the surface tension, κ is the polytropic gas exponent, μ is the fluid dynamical viscosity, c is the speed of the sound, and $p_A(t)$ is the applied pressure of FUS. The surface tension σ depends on the radius of the MB and the material of the coat. In deriving Equation (1.1), the thermal effect caused by the oscillation of the MBs and the tension on the MB surface is neglected, and the blood is assumed to be an incompressible viscoelastic fluid.

Suppose the input pressure is expressed by

$$p_A(t)=C_0+C_1\sin(2\pi t),\ \ C_0,C_1>0,$$

and when the FUS is continuously on, then the radius oscillation is shown in Figure 1.1 for $C_0 = 0kPa$ (in red) and $C_0 = 110kPa$ (in blue) for $C_1 = 110kPa$, which shows the existence of a new average radius when FUS is applied.

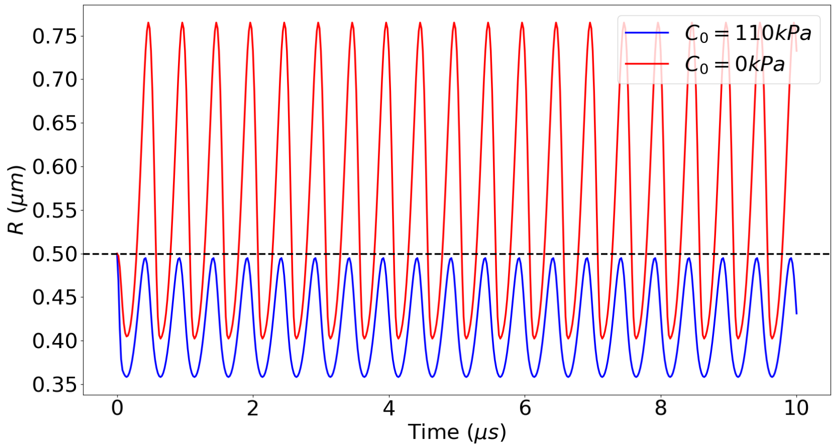

Figure 1.1: The solution of Equation* (1.1) *given for* $C_0 = 0kPa$ *(in red) and* $C_0 = 110kPa$ *(in blue) where in both cases* $C_1 = 110kPa$*,* $R(0) = 1/2$ *and* $\dot{R}(0) = 0$*.

2 Research Questions and Methodology

In this project, you will study the RP equation in (1.1) in case the FUS, $p_A(t)$ is turned on and off at certain time points. The approach you take will be by combining analysis of the equation with numerical simulations. Moreover, a literature study of RP equations is expected to be done. Naturally, possible research questions are

(1) How do the characteristics of the FUS influence the solution R?

(2) How will the radius of the MB change with the input pressure of FUS? Is the average radius the same as using the continuous input pressure?

References

[1] N. de Jong, M. Emmer, A. van Wamel, and M. Versluis. Ultrasonic characterization of ultrasound contrast agents. Medical & Biological Engineering & Computing, 47(8): 861–873, may 2009. doi: 10.1007/s11517-009-0497-1. URL `https://doi.org/10.1007%2Fs11517-009-0497-1`.

[2] W. Tzu-Yin, K. E. Wilson, S. Machtaler, and J. K. Willmann. Ultrasound and microbubble guided drug delivery: mechanistic understanding and clinical implications. Curr. Pharm. Biotechnol., 14(8):743–752, 2013. doi: 10.2174/1389201014666131226114611.