IMPLEMENTATION OF EXPERIMENTAL UNCERTAINTY TO IMPROVE HEMOLYSIS MODELING IN CARDIOVASCULAR DEVICES

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Introduction

Despite the widespread use of numerical hemolysis models in biomedical engineering, these models fail to account for the inherent uncertainty in their underlying experimental data. However, uncertainty quantification is of paramount importance in computational modeling of medical devices as emphasized by recent guidance document of the US Food & Drug Administration [1]. The current gold standard for hemolysis modeling is to conduct an experiment of controlled exposure time and shear stress at different operating points and to record the resultant hemolysis index (HI). To build a numerical model, a power law (equation 1) is fitted through all data points.

$$HI = C * ShearStress^{\beta} * Time^{\alpha} \qquad (1)$$

In this process all information of the underlying experimental variability gets lost and the resulting hemolysis model only represents a mean state of hemolysis. This study proposes a universally applicable method to implement variation of experimental data into numerical models of hemolysis through the Markov Chain Monte Carlo (MCMC) method.

Methods

We applied the MCMC method to an experimental hemolysis data set [2], conducting 50,000 samples across four chains to derive stochastical distributions for the fitting parameters C, α, and β. These distributions were then utilized in a non-intrusive polynomial chaos expansion to create a reduced order model for hemolysis calculation in the FDA pump benchmark simulation [3]. This approach allowed for fast sampling from MCMC posterior distributions to estimate hemolysis variability across different operating points of the FDA blood pump. We then compared model predictions to published multi-laboratory data of hemolysis in the FDA pump [4].

Results

The analysis exposed the non-uniqueness of traditional model fitting, identifying multiple local minima in the sum of squared errors from least squares fitting. MCMC results yielded a constant, optimal C=3.515e-5 and approximately normally distributed α and β with means of approximately 0.49 and 1.55, respectively. With this, the MCMC model closely matched mean and variance of experimental data [4] in most of the conditions, particularly when comparing relative performance across different operating conditions of the pump (Figure 1). In contrast to this, the conventional approach (deterministic Zhang in Figure 1) does not allow to compute the variation of hemolysis in the FDA pump.

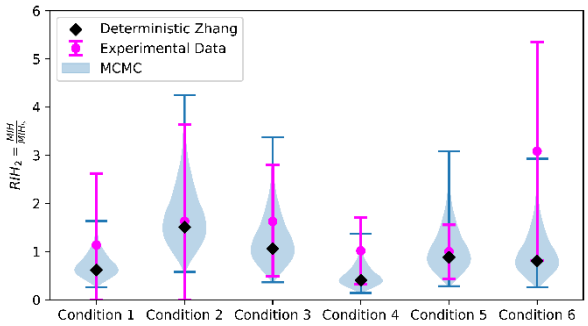

Figure 1: Experimental hemolysis results of [4] in magenta, with numerical prediction of original, deterministic Zhang et al. [2] model (black) and probabilistic MCMC predictions in form of a violine plot (blue).

Discussion

This study successfully demonstrates how the inherent uncertainty in hemolysis experiments can be captured and implemented into numerical blood damage models. It further shows that incorporating fitting parameter variability through MCMC substantially enhance the robustness of hemolysis model prediction. The current gold standard of relative comparisons is strengthened by incorporating the variance of the underlying experiments, providing a stronger foundation for comparing simulated hemolysis outcomes with in-vivo experiments. The developed method can easily incorporate further experimental datasets encompassing various stress types, donor species, and a higher number of repetitions. Such an approach has the potential to set a new standard of predictive accuracy in hemolysis modeling.

References

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