# Estimation of hemolysis in centrifugal blood pumps using morphology tensor approach

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**Abstract**

Implantable ventricular assist devices are an effective temporary solution to heart failure, especially in the context of long wait times for heart transplants. With further progress, these devices may provide a permanent clinical cure for end-stage heart disease. Traditionally, device designers have relied on experimental analysis, and it is only recently that computational fluid dynamics has emerged as a cost-effective and reliable design tool. We present here a model for hemolysis prediction, designed to be used with computational fluid dynamics analysis of any blood-handling device. The model is based on experimentally measured physical properties of human blood cells, and hemolysis measurements in simple shear flows. An implementation of the model and numerical predictions of hemolysis are presented in the context of an on-going computational analysis of the GYRO blood pump being developed at Baylor College of Medicine. The numerically predicted hemolysis index matches well with experimentally measured values.

*Keywords:* Blood flow; Hemolysis; Morphology tensor

## 1. Introduction

Each year, approximately 50,000 end-stage heart disease patients wait for heart transplants in the US, while only 2400 donor hearts are available. Such statistics provide enormous impetus for research efforts into development of efficient, anti-traumatic, anti-thrombotic and totally-implantable blood pumps. These devices are already being used successfully as medium-term bridge-to-transplant or recovery, and the current research is focused on ensuring a more reliable long-term usage.

As with any other blood-handling device, the blood pumps are traditionally designed based on insights from Newtonian fluid mechanics, and adapted for blood through *in vivo* animal experiments. This process is both time-consuming and expensive. With recent advances in computational resources and robust numerical schemes, computational fluid dynamics (CFD) has emerged as a reliable design tool for hydraulic design of blood pumps.

While the hydraulic design of the pump delivers appropriate flux against given pressure head, the hemolytic design of the pump is equally important. Blood damage (hemolysis) and blood coagulation (thrombosis) are two important features of the hemolytic design. A clear understanding of these processes in complex flows in blood handling devices is yet to be formed. In absence of an exact behavior, several models have been proposed in the literature that relate the blood damage to the local shear rates in the flow. These models are based on the simple shear flow experiments that measure the time dependent hemolysis at steady shear [1,2]. Giersiepen et al. [3] developed a correlation for steady-shear hemolysis in short time scales relevant to flow in a blood pump based on experimental results by Wurzinger et al. [4]. The correlation is:

$$\frac{\Delta \mathrm{Hb}}{\mathrm{Hb}} = 3.62 \times 10^{-7} \sigma^{2.416} \Delta t^{0.785}, \tag{1}$$

where $\Delta$Hb/Hb is the ratio of plasma free hemoglobin to the total hemoglobin in the sample, $\sigma$ is the shear stress (Pa) and $\Delta t$ is exposure time (s).

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Recently, we proposed a tensor-based model for hemolysis that is based on an analogy between blood cells and fluid droplets [5]. In this model, the instantaneous shape of an individual red blood cell (RBC) is tracked as it flows through the device. The parameters in the model are based on physical properties of the RBCs and experimentally observed phenomena. A three-dimensional implementation of the model is presented here for the first time, where the hemolysis is estimated for an accurate representation of a centrifugal blood pump, using a sample of particle traces obtained by CFD analysis.

In the following section, we present the construction of the tensor-based blood damage model and relate it to the empirical blood damage correlation of Eq. (1). In Section 3, the model is applied to the results of a three-dimensional CFD analysis of the GYRO centrifugal blood pump. Finally, we end with a discussion of the results and summary of the work.

## 2. Morphology tensor approach

When at rest, a mammalian red blood cell has bi-concave disc shape; it has a viscoelastic membrane that encapsulates Newtonian liquid (hemoglobin), and the cell is suspended in a Newtonian medium (plasma). When blood is at rest, the RBCs form coin-stack shaped structures (roleaux); these structures break and blood cells are individually suspended when blood is set into motion. Owing to its biconcave shape, an RBC has 40% excess surface area compared to a sphere of the same volume. The excess surface area enables RBCs to undergo both volume- and surface-area-preserving deformations. It is observed that RBCs assume an ellipsoidal shape and remain oriented along the flow direction in a simple shear flow. This behavior of RBCs is very similar to that of fluid droplets neutrally suspended in another immiscible fluid. As the shear rate increases, the RBCs become highly stretched and develop pores through which hemoglobin oozes into plasma, resulting in hemolysis. Barring catastrophic hemolysis, which occurs at shear rates above $42{,}000\,\mathrm{s}^{-1}$, the RBCs gradually return to their original shape as the shear rate of the flow is decreased. It is also observed that the RBCs show a tank-treading phenomenon under the influence of shear flow, where the viscoelastic membrane of the cell starts to revolve around the enclosed fluid, while the cell remains aligned with the flow.

We employ the analogy between RBCs and fluid droplets to construct the blood damage model. The shape of the droplets is represented by a morphology tensor $\mathbf{S}$. A deformation equation for fluid droplets was proposed by Maffetone and Minale [6], and we modify it here to account for the tank-treading motion shown by the RBCs. Thus, the morphology $\mathbf{S}$ of the RBCs at any instant can be expressed as:

$$\mathbf{S}^{\circ} = -f_1\left[\mathbf{S} - g(\mathbf{S})\mathbf{I}\right] + f_2\left[\tilde{\mathbf{E}}\cdot\mathbf{S} + \mathbf{S}\cdot\tilde{\mathbf{E}}\right] + f_3\left[\tilde{\mathbf{W}}\cdot\mathbf{S} - \mathbf{S}\cdot\tilde{\mathbf{W}}\right] \quad (2)$$

where:

$$\mathbf{S}^{\circ} = \frac{d\mathbf{S}}{dt} - \left[\mathbf{\Omega}\cdot\mathbf{S} - \mathbf{S}\cdot\mathbf{\Omega}\right] \quad (3)$$

$$g(\mathbf{S}) = \frac{3\,III}{II} \quad (4)$$

and $II$ and $III$ are the second and third invariants of $\mathbf{S}$, respectively:

$$II = \frac{1}{2}\left(\mathrm{tr}(\mathbf{S})^2 - \mathrm{tr}(\mathbf{S}^2)\right); \quad III = \det(\mathbf{S}) \quad (5)$$

To account for the instantaneous rotation of the tank-treading cell, we consider the rotating reference frame defined by the unit eigenvectors $\tilde{\mathbf{e}}_i$ of $\mathbf{S}$; the rotation tensor $\mathbf{\Omega}$ is hence computed as:

$$\mathbf{\Omega} = \tilde{\mathbf{e}}_i\frac{d\tilde{\mathbf{e}}_i}{dt} = \tilde{\mathbf{e}}_i\left(\frac{\partial\tilde{\mathbf{e}}_i}{\partial t} + \mathbf{u}\cdot\nabla\tilde{\mathbf{e}}_i\right) \quad (6)$$

Therefore, $\mathbf{S}^{\circ}$ is the frame-invariant time derivative of the droplet morphology tensor, and $\tilde{\mathbf{E}}$ and $\tilde{\mathbf{W}}$ are the rate of strain and vorticity tensors in the rotating reference frame. Equation (2) preserves the volume of the droplet (i.e. $\frac{\mathrm{dIII}}{\mathrm{dt}} = 0$). The first term on the right hand side of Eq. (2) recovers the shape of the droplet in the absence of shear flow. The second term represents the non-affine deformation of the droplet. The third term captures the tank-treading motion which reduces the relative vorticity seen by the droplet. Equation (2) is an implicit equation in $\mathbf{S}$ because the rotation rate $\mathbf{\Omega}$ depends on $\mathbf{S}$ (unless the flow is steady, where $\frac{\mathrm{dS}}{\mathrm{dt}} = 0$ and $\mathbf{\Omega} = \mathbf{0}$). The droplet is spherical at zero shear ($\mathbf{S} = \mathbf{I}$), and becomes ellipsoidal as the shear increases. The ellipsoidal shape and orientation is identified by the eigenvalues of $\mathbf{S}$.

Equation (2) is applicable for computing any micro-capsule deformation, and is made specific for capturing RBC deformation by setting its parameters $f_1$, $f_2$ and $f_3$. Experimental observations reported in the literature are used to choose the appropriate values of these parameters. The relaxation time of RBCs is approximately 200 ms; thus, we set $f_1 = 5.0\,\mathrm{s}^{-1}$ so that the relaxation time of the droplet matches that of an RBC in the context of small-deformation approximation. In a steady shear flow of intensity $G$, the droplet remains at fixed orientation to the flow ($\mathbf{\Omega} = \mathbf{0}$), and with $f_2 = f_3$

[5], the steady-state droplet deformation equation becomes:

$$f_1\,(\mathbf{S} - g(\mathbf{S})\mathbf{I}) \;=\; f_2\,(\nabla\mathbf{u}\cdot\mathbf{S} \;+\mathbf{S}\cdot\nabla\mathbf{u}^T) \tag{7}$$

The eigenvalues $\lambda_1$, $\lambda_2$ and $\lambda_3$ of $\mathbf{S}$ are computed from Eq. (7):

$$W^2 = \lambda_1 \quad = \quad \left(\frac{f_1^2}{f_1^2 + f_2^2 G^2}\right)^{1/3} \tag{8}$$

$$L^2 = \lambda_2 \quad = \quad \left(\frac{f_1^2}{f_1^2 + f_2^2 G^2}\right)^{1/3} \left[\frac{(f_1^2 + f_2^2 G^2) + G f_2\sqrt{f_1^2 + f_2^2 G^2}}{f_1^2}\right] \tag{9}$$

$$B^2 = \lambda_3 \quad = \quad \left(\frac{f_1^2}{f_1^2 + f_2^2 G^2}\right)^{1/3} \left[\frac{(f_1^2 + f_2^2 G^2) - G f_2\sqrt{f_1^2 + f_2^2 G^2}}{f_1^2}\right] \tag{10}$$

where $L$, $B$ and $W$ are three semi axial lengths of the droplet. An RBC undergoes 6% areal strain before hemolyzing; therefore, an RBC should stretch to $1.40 \times 1.06$ times its original surface area at catastrophic hemolysis. Matching the droplet area with hemolyzing RBC area gives:

$$f_2 = f_3 = 1.25 \;\times\; 10^{-3} \tag{11}$$

The three parameters $f_1$, $f_2$ and $f_3$ together incorporate relaxation time, tank-treading, and critical areal strain limit into the hemolysis model.

The instantaneous shape of the droplet, obtained from Eq. (2) in a general flow, is used to compute instantaneous shape distortion $D = (L - B)\,/\,(L + B)$. In a steady shear flow, the distortion and the shear flow intensity $G_{\text{eff}}$, and the corresponding steady shear stress $\sigma_{\text{eff}}$ are related as:

$$G_{\text{eff}} = \sqrt{\frac{f_1^2 D^2}{(1 - D^2)\, f_2^2}}, \qquad \sigma_{\text{eff}} = \mu_{\text{blood}} G_{\text{eff}} \tag{12}$$

where $\mu_{\text{blood}}$ is the blood viscosity, taken as 3.5 cP. Because in steady shear there is a one-to-one correspondence of shear stress and distortion, we construct a strain-based hemolysis model by requiring that the strain-based and stress-based models yield the same results in steady shearing; using Eq. (1) yields a strain-based relationship:

$$\frac{\Delta \text{Hb}}{\text{Hb}} = 3.62 \;\times\; 10^{-7}\left(\mu_{\text{blood}}\sqrt{\frac{f_1^2 D^2}{(1 - D^2)\, f_2^2}}\right)^{2.416} t^{0.785} \tag{13}$$

## 3. Numerical example

In our previous work we reported on the hydraulic design of the GYRO Centrifugal blood pump [7], under development at the Baylor College of Medicine. We employ the deformable-spatial-domain/stabilized space-time (DSD/SST) finite element method. The moving boundaries are handled with shear-slip mesh update method (SSMUM). A complete description of SSMUM and DSD/SST for three-dimensional analysis of the GYRO centrifugal blood pump has been previously reported [8].

The RBC deformation computations presented here are completely uncoupled from flow solution. The velocity data obtained from the flow simulations is used to trace pathlines, and velocity gradient is interpolated along the pathlines. This enables Lagrangian computation of RBC morphology given by Eq. (2). The coordinates of pathlines are computed using forward Euler integration:

$$\mathrm{x}_{n+1} \quad = \quad \mathrm{x}_n + \mathbf{u}_n \Delta t, \tag{14}$$

where $n$ is the number of trace point, and $\mathrm{x}_n$ and $\mathrm{x}_{n+1}$ are positions of trace point at time $t_n$ and $t_{n+1} = t_n + \Delta t$, respectively. The droplet morphology is also obtained using forward Euler integration along a pathline:

$$\mathbf{S}_{n+1} \quad = \quad \mathbf{S}_n + \Delta\mathbf{S}_n, \tag{15}$$

$$\Delta\mathbf{S}_n \quad = \quad \Big(-f_1\,[\mathbf{S}_n - g(\mathbf{S}_n)\mathbf{I}] \;+\; f_2\left[\tilde{\mathbf{E}}_n\cdot\mathbf{S}_n + \mathbf{S}_n\cdot\tilde{\mathbf{E}}_n\right] + f_3\left[\tilde{\mathbf{W}}_n\cdot\mathbf{S}_n - \mathbf{S}_n\cdot\tilde{\mathbf{W}}_n\right] + [\mathbf{\Omega}_n\cdot\mathbf{S}_n - \mathbf{S}_n\cdot\mathbf{\Omega}_n]\Big)\Delta t. \tag{16}$$

Unlike rate of strain and vorticity tensor, the rotation rate tensor $\mathbf{\Omega}_n$ is computed with the information from the step $n - 1$:

$$\mathbf{\Omega}_n = (\mathbf{e}_i)_n \frac{(\mathbf{e}_i)_n - (\mathbf{e}_i)_{n-1}}{\Delta t}, \tag{17}$$

where $(\mathbf{e}_i)_n$ and $(\mathbf{e}_i)_{n-1}$ are eigenvectors of $\mathbf{S}_n$ and $\mathbf{S}_{n-1}$, respectively.

The CFD analysis of the GYRO blood pump is performed at 2000 rpm and 5.0 L/min flow rate. The velocity and pressure data are recorded at every 1.2 ms. A particle tracer is applied on the accumulated data and the RBC deformation is computed along the particle traces. Figure 1 shows the hemolysis along 66 particle

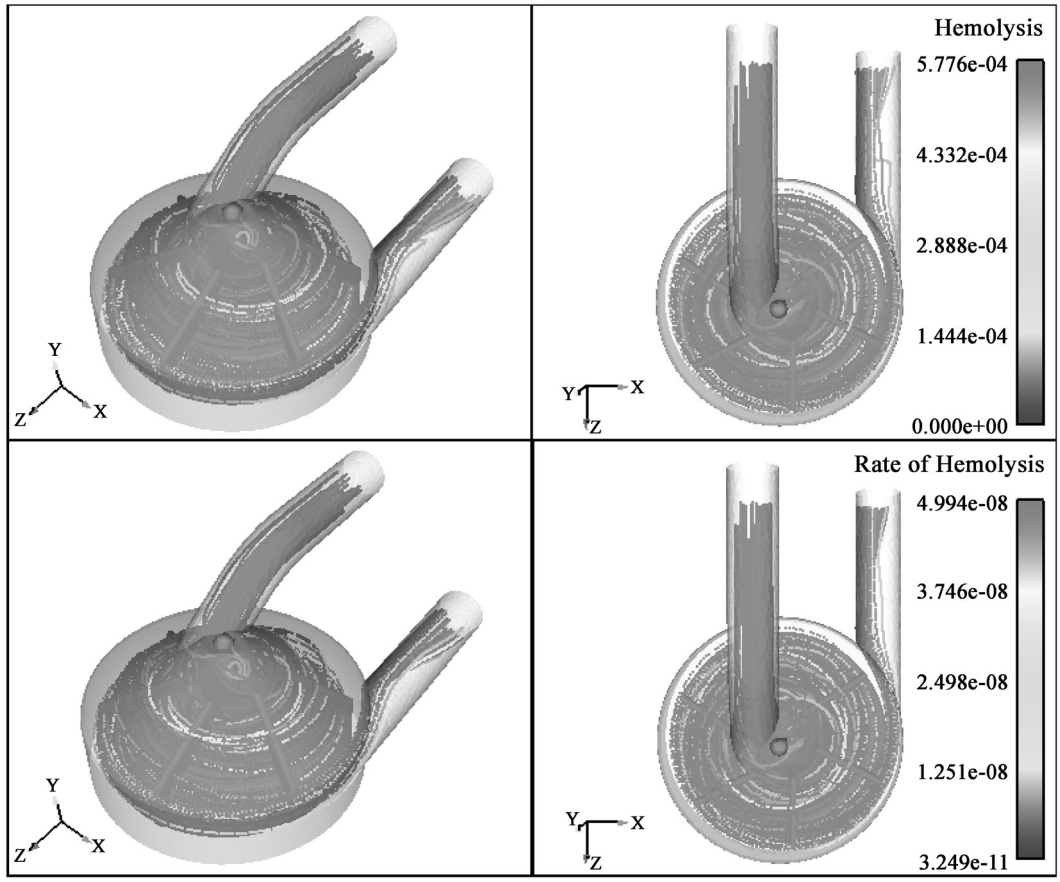


Fig. 1. GYRO blood pump: hemolysis $\frac{\Delta Hb}{Hb}$ [%] and rate of hemolysis along the particle traces.

traces in the blood pump. The hemolysis is reported in $\frac{\Delta Hb}{Hb}$. The ratio $\frac{\Delta Hb}{Hb}$ can be related to the Normalized Index of Hemolysis (NIH), the standard clinical index used to report hemolysis [9] in flow loop tests:

$$\mathrm{NIH(g/100\,L)} = 100 \times \frac{\Delta Hb}{Hb} \times (1 - Hct) \times \kappa, \tag{18}$$

where Hct is the blood hematocrit (45% for a healthy person) and $\kappa$ is the hemoglobin content of blood (150 g/L for a healthy person). An average hemolysis over the sample of particle traces was found to be $\frac{\Delta Hb}{Hb^7} = 7.41 \times 10^{-7}$, resulting in NIH value of 0.00722 g/100 L. The predicted hemolysis matches very well with the experimentally measured hemolysis of 0.007 g/100 L [10].

## 4. Summary

We have presented a three-dimensional implementation of the new tensor-based blood damage model; the hemolysis computations were decoupled from the flow solver and hence could be easily implemented following any CFD analysis. The hemolysis predictions made with the new model match closely the experimentally-measured value available for the same pump configuration.

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