Investigating platelet motion towards vessel walls in the presence of red blood cells
(Complex Fluids in Biological Systems)

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Blood is a Heterogeneous Medium

1. **Plasma**
   - water-based solution
   - contains electrolytes and proteins
   - incompressible Newtonian fluid

2. **Red blood cells**
   - 40% of blood by volume
   - highly deformable cells
   - used for oxygen transport

3. **Platelets**
   - 0.3% of blood by volume
   - rigid elliptical cells
   - repair damaged vessel wall
Platelets

- The main function of platelets is to repair damage to vessels...
- ... but platelet concentration in blood is low.
- Fortunately, platelets are not uniformly distributed in blood but are highly concentrated near vessel walls.
- How does this occur? What factors affect the distribution of platelets in blood?
This profile depends on hematocrit (% of red blood cells).

(\textit{x-axis} is distance from wall, \textit{y-axis} is concentration of platelets)
This profile also depends on shear rate.

(x-axis is distance from wall, y-axis is concentration of platelets)

250 sec$^{-1}$  560 sec$^{-1}$  800 sec$^{-1}$  1220 sec$^{-1}$
We want to simulate a large number of red blood cells and platelets in a blood vessel over a considerable amount of time. This is computationally expensive.

We use a parallel version of an immersed boundary-lattice Boltzmann method to solve for the coupled system of fluid-filled cells immersed in a fluid of similar density.
The lattice Boltzmann equations govern the behavior of particle distribution functions $f(\mathbf{x}, \mathbf{e}_i, t)$ that live at each lattice node $\mathbf{x}$ at time $t$. $\mathbf{e}_i$ are the discretized velocity vectors on a lattice defined by:

$$
\mathbf{e}_i = \begin{cases} 
(0, 0) & \text{for } i = 0 \\
(c \cos(\pi(i - 1)/4), c \sin(\pi(i - 1)/4)) & \text{for } i = 1, 3, 5, 7 \\
(c\sqrt{2} \cos(\pi(i - 1)/4), c\sqrt{2} \sin(\pi(i - 1)/4)) & \text{for } i = 2, 4, 6, 8,
\end{cases}
$$

where $c = \frac{h}{\delta t}$ is the particle speed.
The equations governing the particle distribution functions are:

$$f_i(x + \delta_t e_i, t + \delta_t) - f_i(x, e_i, t) = -\frac{1}{\tau} \left[ f_i(x, t) - f_i^{eq}(\rho(x, t), u(x, t)) \right]$$

where $f_i(x, t)$ is shorthand for $f(x, e_i, t)$, $\tau$ is the relaxation parameter and $f^{eq}$ is the equilibrium distribution.
The exact form of $f_i^{eq}$ depends on lattice geometry. For our nine-velocity model it is:

$$f_i^{eq}(\rho, \mathbf{u}) = \rho w_i \left( 1 + \frac{\mathbf{e}_i \cdot \mathbf{u}}{c_s^2} + \frac{(\mathbf{e}_i \cdot \mathbf{u})^2}{2c_s^4} - \frac{\mathbf{u} \cdot \mathbf{u}}{2c_s^2} \right)$$

where $c_s = \frac{c}{\sqrt{3}}$ is the speed of sound and the weights, $w_i$, are

$$w_i = \begin{cases} 
4/9 & \text{for } i = 0 \\
1/9 & \text{for } i = 1, 3, 5, 7 \\
1/36 & \text{for } i = 2, 4, 6, 8.
\end{cases}$$

The macroscopic quantities $\rho(\mathbf{x}, t)$ and $\mathbf{u}(\mathbf{x}, t)$ are the density and macroscopic fluid velocity.
Lattice Boltzmann Method

The macroscopic quantities can be obtained by evaluating the hydrodynamic moments of $f_i(x, t)$.

**Fluid Density**

$$\rho(x, t) = \sum_i f_i(x, t)$$

**Momentum Density**

$$\rho(x, t)u(x, t) = \sum_i f_i(x, t) e_i$$
Relation to Navier Stokes

In the limit that
\[
\frac{||\mathbf{u}||}{c} \to 0 \text{ and } \frac{h}{L} \to 0,
\]
where \( L \) is the hydrodynamic length scale, the lattice Boltzmann equations approximate the Navier Stokes equations. The macroscopic quantities:

\[
p(x, t) = c_s^2 \rho = \frac{1}{3} \rho \quad \text{and} \quad u(x, t)
\]

from the lattice Boltzmann method are equivalent to the velocity and pressure of the Navier Stokes equations. In addition the viscosity is

\[
\mu = \rho c_s^2 \delta_t \left( \tau - \frac{1}{2} \right).
\]
How can we couple the background fluid dynamics to a cellular membrane submersed in the fluid?

- Fluid lies on Eulerian grid \((\mathbf{x})\)
- Boundary lives on Lagrangian grid \((\mathbf{X}(q, t))\)
Immersed Boundary Method

Typically, the fluid is governed by the incompressible Navier Stokes equations:

\[ \nabla \cdot \mathbf{u} = 0 \]

\[ \rho \left[ \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right] = -\nabla p + \mu \nabla^2 \mathbf{u} + \mathbf{F}_f, \]

where the external force is imposed by the presence of the immersed boundary object (in our case a cellular membrane).
Immersed Boundary Method

- The force felt by fluid is related to the force felt by the boundary:

\[ F_f = \int F_{IB} \delta(x - X(q, t)) dx. \]
Immersed Boundary Method

- The force felt by fluid is related to the force felt by the boundary:

\[
F_f = \int F_{IB} \delta(x - X(q, t)) \, dx.
\]

- The boundary moves with the fluid velocity:

\[
\frac{\partial X}{\partial t}(q, t) = u(X, t) = \int u(x, t) \delta(x - X(q, t)) \, dx.
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Immersed Boundary Method

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- We discretize the delta function:

\[ \delta(x) = \hat{\delta}(x_1) \times \hat{\delta}(x_2), \]

where \[ \hat{\delta}(x_i) = \begin{cases} \frac{1}{4h} \left( 1 + \cos \left( \frac{\pi x_i}{2h} \right) \right) & \text{for } |x_i| \leq 2h \\ 0 & \text{for } |x_i| > 2h \end{cases}. \]
We can include an external force into the lattice Boltzmann equations with the following additions:

\[
\begin{align*}
    f_i(x + e_i \delta_t, t + \delta_t) - f_i(x, t) &= \frac{1}{\tau} (f_i(x, t) - f_i^{eq}(\rho, v)) + \\
    &\quad \delta_t \mathcal{W}_i \left[ \frac{(1 - \frac{1}{2\tau}) (F_f \cdot e_i)}{c_s^2} + \frac{A : (e_i e_i^T - c_s^2 I)}{2c_s^4} \right],
\end{align*}
\]

where \( \rho v = \rho u + \frac{\delta_t F_f}{2} \) and the matrix \( A \) is

\[
A = -\frac{\delta_t + \rho \beta}{\delta_t \tau} (u F_f^T + F_f u^T).
\]
What is $F_f$?

Recall that the force on the membrane is distributed to the fluid.

$$F_f = \int F_{IB} \delta(x - X(q, t)) dx.$$ 

How do we model the behavior of cellular membranes that resist stretching and have a non-circular equilibrium shape?

$$F_{IB} = \frac{\partial T}{\partial l} = \frac{\partial}{\partial l} (T t + q n).$$
**What is $F_f$?**

$$F_{IB} = \frac{\partial T}{\partial l} = \frac{\partial}{\partial l}(Tt + qn).$$

We use a one-dimensional version of the Skalak membrane law:

$$T_{iso}^{sk} = G(\lambda^2 - 1)(1 - C\lambda^2(\lambda^2 + 1)),$$

where $\lambda = \frac{ds}{dS}$ is the principal stretch ratio.
What is $F_f$?

$$F_{IB} = \frac{\partial T}{\partial l} = \frac{\partial}{\partial l} (Tt + qn).$$

We use a one-dimensional version of the Skalak membrane law:

$$T_{iso}^{sk} = G(\lambda^2 - 1)(1 - C\lambda^2(\lambda^2 + 1)),$$

where $\lambda = \frac{ds}{dS}$ is the principal stretch ratio. Then we set the bending energy to be minimized at some equilibrium shape

$$q = \frac{d}{dl} [E_B(\kappa(l) - \kappa_0(l))],$$

where $\kappa(l)$ is the instantaneous curvature and $\kappa_0(l)$ is the curvature of minimum energy.
Whole Blood Simulation

Wall shear rate is 800 sec$^{-1}$ and hematocrit is 40%.

.... now some movies!
Preliminary Results: Comparison to Eckstein’s Data

**LB-IB Simulation**

- Number of Platelets vs Distance From Wall (µm)

**Eckstein’s experiment**

- Concentration @ 10^3 (#/µm²) vs Distance From Wall (µm)

- Lines represent different percentages: 13%, 39%, 65%
Lateral movement of platelets is highly sensitive to the presence of red blood cells.

without RBCs

with RBCs
Future Directions

- Speed up code (OpenMP/MPI?)
- Vary parameters
  - Hematocrit
  - Deformability of RBCs
  - Shear rate
  - Platelet shape and size
  - Vessel diameter
- Understand why lateral platelet motion occurs
- Find a way to incorporate the effect of red blood cells on platelets into coagulation models