Computational micro-hemodynamics

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Aim of the Study

Some points for the motivation:

- Interest to investigate a complex problem which has a big importance to the health state of an individual
- Deformability properties of RBCs (and other cells) is currently not clinically used
- Develop miniaturised diagnosis devices (e.g. lab-on-chip, lab-on-CD), and devices for cell separation
- Blood test is a common checkup (cheap and not very invasive)

Approach:

Investigate RBC deformability through in-vitro experiments (under a confocal microscope) and **computational simulations** (using Lagrangian particle method - MPS).

Example of Experimental Results

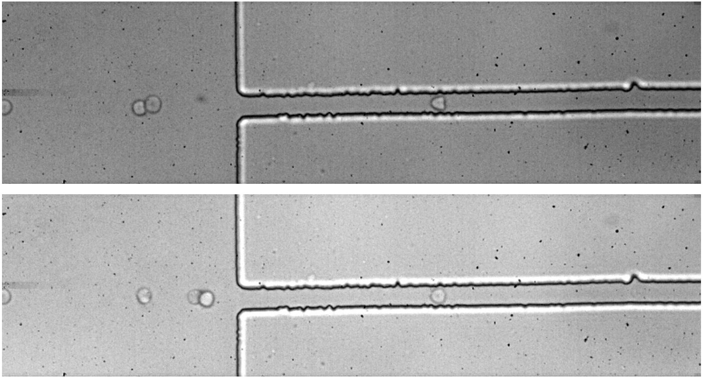


Figure : Single RBC flow in a capilary under different flow rates. (NB. flow is right to left)

Example of Experimental Results

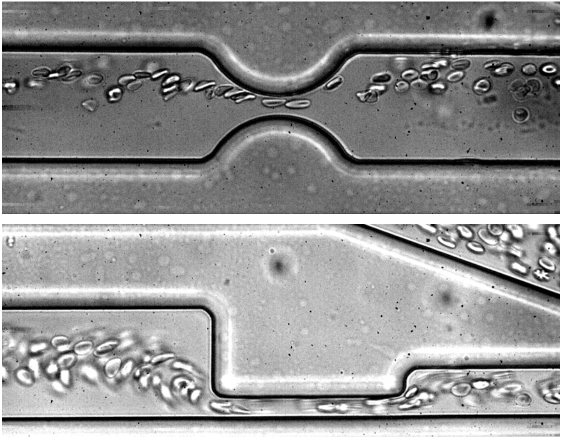
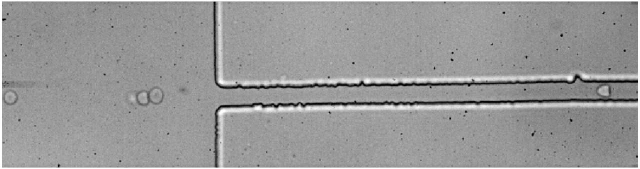
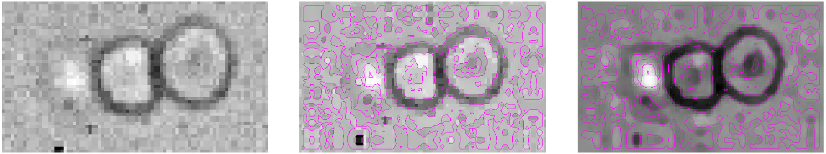


Figure : Flow through constrictions. (NB. flow is right to left)

Image processing





original Perona-Malik Novel approach

Figure : Developed automatic image processing methods for filtering, contrast enhancement and segmentation.

The Moving Particle Semi-implicit method (MPS):

- mesh-free Lagrangian particle method
- solves Navier-Stokes equations for an incompressible fluid

$$\frac{1}{\rho}\frac{D\rho}{Dt} + \nabla \cdot \mathbf{u} = 0 \qquad ; \qquad \frac{D\mathbf{u}}{Dt} = -\frac{\nabla P}{\rho} + \nu \nabla^2 \mathbf{u} + \mathbf{f}$$

it works by:

- nodal interpolation: compact support radial function
- derivatives in the Navier-Stokes equations are substituted by discrete operators (strong formulation)
- is a predictor - corrector method (projection method)

Compact support and weight function

The particle interactions are restricted to within a finite radius r_e.

The weighting (shape) function is:	$w(r) = \begin{cases} \frac{r_e}{r} - 1 & 0 < r < r_e \\ 0 & r_e < r \end{cases}$
A scalar variable ϕ at any point i is given by:	$\phi_i = \frac{1}{\sum_{j=1}^{N} w(r_{ij})} \sum_{j=1}^{N} w(r_{ij}) \phi_j$

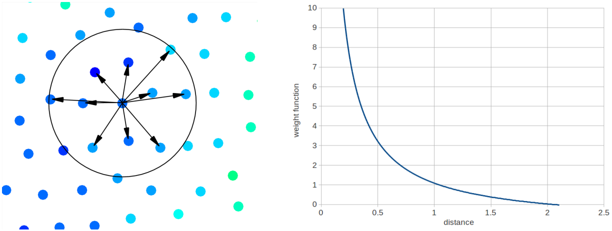


Figure : Example of particle compact support and weight function.

Incompressibility

- each particle represents a lumped volume of fluid
- idea is therefore to keep a constant distribution of particles

Introduce the *particle number density* at position i as:

$$n_i = \sum_{j \neq i}^{N} w(r_{ij})$$

where $N =$ number of particles; $r_{ij} =$ distance between particles i and j.

For incompressible flows this number should be *constant* $= n^0$.

We note that $\rho_i \propto n_i$.

Time stepping

MPS is a predictor-corrector method: $\mathbf{u}_i^{n+1} = \mathbf{u}_i^* + \mathbf{u}_i^{**}$, where * and ** denote the predictor and corrector stages, and $\mathbf{x}_i^{n+1} = \mathbf{x}_i^n + \Delta t \cdot \mathbf{u}_i^{n+1}$.

The **momentum** equation $\left(\frac{D\mathbf{u}}{Dt} = -\frac{\nabla P}{\rho} + \nu\nabla^2\mathbf{u} + \mathbf{f}\right)$

$$\frac{D\mathbf{u}}{Dt} = \frac{\mathbf{u}^{n+1} - \mathbf{u}^n}{\Delta t} = \frac{\mathbf{u}^{**} + (\mathbf{u}^* - \mathbf{u}^n)}{\Delta t} = -\frac{\nabla p}{\rho} + (\mathbf{f} + \nu\nabla^2\mathbf{u})$$

$$\text{predictor}: \quad \mathbf{u}^* = \mathbf{u}^n + \Delta t(\mathbf{f} + \nu\nabla^2\mathbf{u}) \quad ; \quad \text{corrector}: \quad \mathbf{u}^{**} = -\frac{\Delta t}{\rho}\nabla p$$

The **continuity** equation $\left(\frac{1}{\rho}\frac{D\rho}{Dt} + \nabla \cdot \mathbf{u} = 0\right)$

$$\frac{1}{\rho}\frac{D\rho}{Dt} = \frac{\rho^{n+1} - \rho^n}{\rho\Delta t} = \frac{\rho^{**} + (\rho^* - \rho^n)}{\rho\Delta t} = -\nabla \cdot (\mathbf{u}^{**} + \mathbf{u}^*)$$

$$\text{predictor}: \quad \frac{1}{\rho}\frac{\rho^* - \rho^n}{\Delta t} = -\nabla \cdot \mathbf{u}^* \quad ; \quad \text{corrector}: \quad \frac{1}{\rho}\frac{\rho^{**}}{\Delta t} = -\nabla \cdot \mathbf{u}^{**}$$

Time stepping

(from previous slide)

$$\text{predictor}: \quad \mathbf{u}^* = \mathbf{u}^n + \Delta t(\mathbf{f} + \nu\nabla^2\mathbf{u}) \quad ; \quad \text{corrector}: \quad \mathbf{u}^{**} = -\frac{\Delta t}{\rho}\nabla p$$

$$\text{predictor}: \quad \frac{1}{\rho}\frac{\rho^* - \rho^n}{\Delta t} = -\nabla\cdot\mathbf{u}^* \quad ; \quad \text{corrector}: \quad \frac{1}{\rho}\frac{\rho^{**}}{\Delta t} = -\nabla\cdot\mathbf{u}^{**}$$

For incompressibility $\frac{D\rho}{Dt} = 0$, hence $n^0 = n^* + n^{**}$.

Since $\rho \propto n$; $\quad \frac{1}{\rho}\frac{\rho^{**}}{\Delta t} = \frac{1}{n^0}\frac{n^{**}}{\Delta t} = -\nabla\cdot\mathbf{u}^{**}$.

Substitution in $\mathbf{u}^{**} = -\frac{\Delta t}{\rho}\nabla p$ we obtain $\quad \nabla^2 p = \frac{-\rho}{\Delta t^2}\frac{n^* - n^0}{n^0}$

Summary of method

Step	Equation
predictor stage	$\mathbf{u}^* = \mathbf{u}^n + \Delta t(\mathbf{f}) + \Delta t(\nu\nabla^2\mathbf{u}^*)$ $\mathbf{x}_i^* = \mathbf{x}_i^n + \Delta t \cdot \mathbf{u}_i^*$
compute pressure	$\nabla^2 p = \frac{-\rho}{\Delta t^2}\frac{(n^* - n^0)}{n^0}$
corrector stage	$\mathbf{u}^{n+1} = \mathbf{u}^* + \mathbf{u}^{**} = \mathbf{u}^* - \frac{\Delta t}{\rho}\nabla p^{n+1}$ $\mathbf{x}_i^{n+1} = \mathbf{x}_i^n + \Delta t \cdot \mathbf{u}_i^{n+1}$

Differential operators

The **gradient** in MPS is given by:

$$\nabla \phi_i = \frac{d}{n^0} \sum_{j \neq i}^{N} w(r_{ij}) \frac{(\phi_j - \phi_i)(\mathbf{x}_j - \mathbf{x}_i)}{|\mathbf{x}_j - \mathbf{x}_i|^2}$$

while the **Laplacian** is modelled as:

$$\nabla^2 \phi_i = \frac{2d}{\lambda n^0} \sum_{j \neq i}^{N} w(r_{ij})(\phi_j - \phi_i)$$

where: $\lambda = \frac{\sum_{j \neq i}^{N} w(r_{ij}) r_{ij}^2}{\sum_{j \neq i}^{N} w(r_{ij})}$;
$d = 3$ in 3D and $d = 2$ in 2D.

Summary of method

Step	Equation
predictor stage	$\mathbf{u}_i^* = \mathbf{u}_i^n + \Delta t \left(\nu \frac{2d}{\lambda n^0} \left(\sum_{j \neq i}^N w(r_{ij})(\mathbf{u}_j^* - \mathbf{u}_i^*) \right) + \mathbf{f} \right)$ $\mathbf{r}_i^* = \mathbf{r}_i^n + \Delta t \cdot \mathbf{u}_i^*$
particle number	$n_i^* = \sum_{j \neq i}^N w(r_{ij})$
pressure	$\sum_{j \neq i}^N \left(w(r_{ij}) P_j^{n+1} \right) - P_i^{n+1} \left(\sum_{j \neq i}^N w(r_{ij}) \right) = -\frac{\rho \lambda (n_i^* - n^0)}{\Delta t^2 2d}$
pressure gradient	$\nabla P_i^{n+1} = \frac{d}{n_i^*} \sum_{j \neq i}^N w(r_{ij})(P_j^{n+1} - (P_i^{n+1})) \frac{(\mathbf{r}_j - \mathbf{r}_i)}{\lvert r_{ij} \rvert^2}$
corrector stage	$\mathbf{u}_i^{n+1} = \mathbf{u}_i^* - \Delta t \frac{1}{\rho} \nabla P_i^{n+1}$ $\mathbf{r}_i^{n+1} = \mathbf{r}_i^n + \Delta t \cdot \mathbf{u}_i^{n+1}$

Modelling RBCs

In simulating blood in small vessels, the constitutive components (i.e. the cells) *must be modelled*.

The approach is to use a *spring network model* for the membranes:

- tension/compression spring
- bending spring
- penalisation force (e.g. area and volume constraints)

Springs act as *body force terms* in the predictor stage.

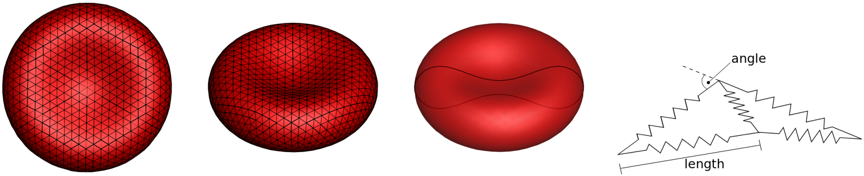


Figure : Red blood cell membrane spring network model.

Results: Different structural parameters

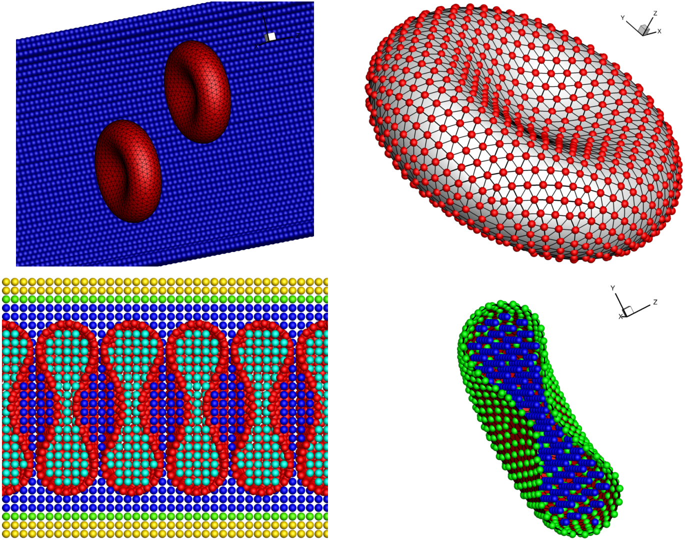
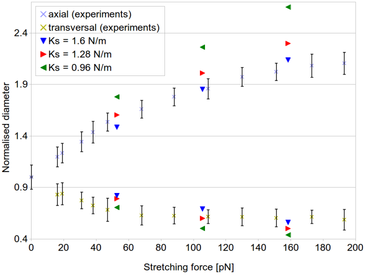
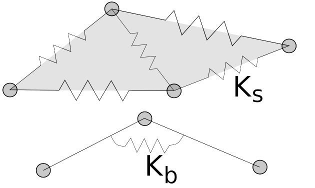
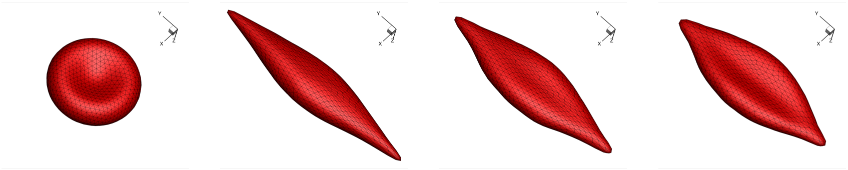


Figure : Discretisation of the domain and red blood cells.

Testing different spring stiffness coefficients







at rest	9.6 μNm	12.8 μNm	16.0 μNm

Figure : Testing static stretching with 100 pN force, Kb$= 3.2 \times 10^{-11}$ N.

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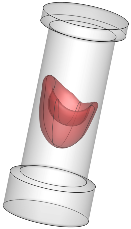
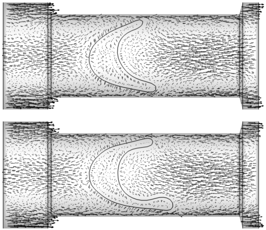
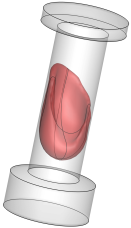
Results of flow simulations



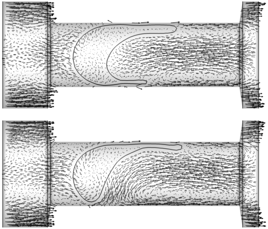
$\Delta p = 12.1$ Pa,
diameter=7.8μm



relative velocity in two orthogonal planes



$\Delta p = 20$ Pa,
diameter=6μm



relative velocity in two orthogonal planes

Figure : RBC flowing in a constricted vessel, showing cross sections of the relative velocity ($u' = u - \overline{u}$).

Results of flow simulations

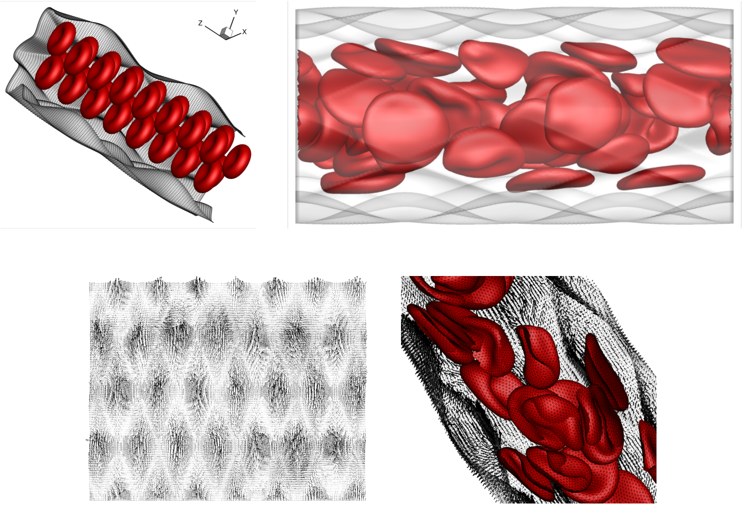


Figure : RBC flowing in small vessel - modelling endothelial cells.

Results: RBCs in straight pipe

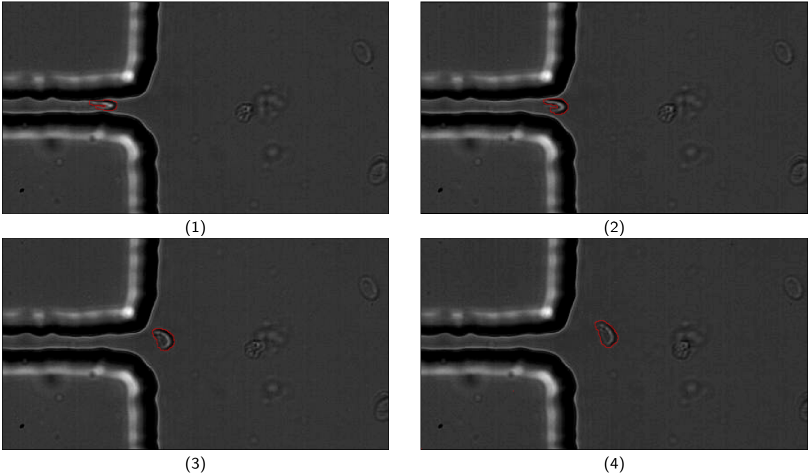
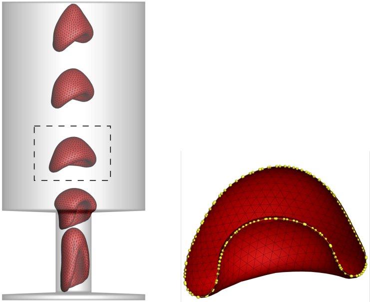
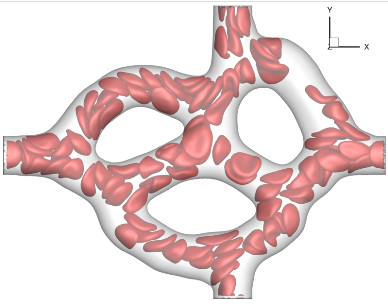


Figure : Experiment of RBC flowing in small constriction.

Results of flow simulations



Simulations in a discontinuous constriction



RBC flowing in model capillary . network of the retina

Conclusions and Future Work

Conclusion:

- can perform RBC tracking of experimental data;
- can simulate blood flow in capillaries;
- can compare with some benchmark studies.

Future Work:

- more benchmark studies;
- model cell adhesion;
- model cell hemolysis;
- observe cell migration in relation to the flow field;
- use simulation to develop devices for studying patient specific properties;

Acknowledgements

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- Rui Lima & co-workers (Polytechnic Institute of Bragança, ESTiG/IPB)

Gradient operator

Given a scalar quantity ϕ, the gradient vector for particles at positions $\mathbf{x}_i$ and $\mathbf{x}_j$ is: $\nabla \phi_{ij} = \frac{(\phi_j - \phi_i)}{|\mathbf{x}_j - \mathbf{x}_i|} \cdot \frac{(\mathbf{x}_j - \mathbf{x}_i)}{|\mathbf{x}_j - \mathbf{x}_i|}$

The gradient in MPS, where there are several neighbouring particles j and an interpolation is performed using the weight function, is written as:

$$\nabla \phi_i = \frac{d}{n^0} \sum_{j \neq i}^{N} w(r_{ij}) \frac{(\phi_j - \phi_i)(\mathbf{x}_j - \mathbf{x}_i)}{|\mathbf{x}_j - \mathbf{x}_i|^2}$$

where d is the number of space dimensions, hence $d = 3$ in 3D and $d = 2$ in 2D.

Laplacian operator

The Laplacian is modelled as diffusion problem: $\frac{d\phi}{dt} = \alpha\nabla^2\phi$ with $\alpha > 0$.

For an initial condition of a point source of unit magnitude, the solution is given by $\phi(x,t) = \left(\frac{1}{\sqrt{4\pi\alpha t}}\right)^d \exp\left(-\frac{r^2}{4\alpha t}\right)$, hence a normal distribution with mean $= 0$ and variance $= 2d\alpha t$.

The variance distribution of ϕ increases by $2d\alpha\Delta t$ during time step Δt. Therefore the quantity transferred from particle i to the neighbouring particles should have the same variance increase: $\Delta\phi_{i\to j} = \frac{2d\alpha\Delta t}{\lambda n^0}\phi_i w(r_{ij})$

A normalisation appears due to the discretisation $\lambda = \frac{\sum_{j\neq i}^N w(r_{ij})r_{ij}^2}{\sum_{j\neq i}^N w(r_{ij})}$.

Putting it all together: $\nabla^2\phi_i = \frac{2d}{\lambda n^0}\sum_{j\neq i}^N w(r_{ij})(\phi_j - \phi_i)$