Personalized mathematical models of blood flows

Yuri Vassilevski$^{1,2,3}$

1 Marchuk Institute of Numerical Mathematics RAS  
2 Moscow Institute of Physics and Technology  
3 Sechenov University

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Working group for modeling of blood flows and vascular pathologies

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► Automated segmentation of blood vessels (coronary, cerebral)
► Blood flow models (1D, 3D, 1D-3D)
► Personalized estimate of hemodynamic significance of stenoses (coronary, cerebral)
► Angiogenesis and tumor growth, antiangiogenic therapy combined with chemical and radiological treatments
► Ultrasound vessel examination
► Non-invasive electrophisiological study of heart
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Co-authors

- Timur Gamilov
- Sergey Simakov
- Roman Pryamonosov
- Aleksander Danilov
- Aleksander Lozovskii
- Maxim Olshanskii
1D hemodynamic equations (flows in elastic tubes)

Mass and momentum balance

\[ \frac{\partial S_k}{\partial t} + \frac{\partial (S_k u_k)}{\partial x} = 0, \]
\[ \frac{\partial u_k}{\partial t} + \frac{\partial (u_k^2/2 + p_k/\rho)}{\partial x} = -\frac{8\pi \mu u_k}{S_k}, \]

\( k \) is index of the tube, \( t \) is the time, \( x \) is the distance along the tube, \( \rho \) is the blood density (constant), \( S_k(t, x) \) is the cross-section area, \( u_k(t, x) \) is the linear velocity averaged over the cross-section, \( p_k(S_k) \) is the blood pressure.

1D hemodynamic equations (flows in elastic tubes)

At the vessels junctions continuity of the total pressure and mass conservation

\[ p_i \left( S_i (t, \tilde{x}_i) \right) + \frac{\rho u_i^2 (t, \tilde{x}_i)}{2} = p_j \left( S_j (t, \tilde{x}_j) \right) + \frac{\rho u_j^2 (t, \tilde{x}_j)}{2}, \]

\[ \sum_{k=k_1, k_2, \ldots, k_M} \varepsilon_k S_k (t, \tilde{x}_k) u_k (t, \tilde{x}_k) = 0, \]

\( \varepsilon = 1, \tilde{x}_k = L_k \) for incoming tubes, \( \varepsilon = -1 \), and \( \tilde{x}_k = 0 \) for outgoing tubes

1D hemodynamic equations (flows in elastic tubes)

Elasticity of the tube wall:

\[ p_k(S_k) - p_{*k} = \rho c_k^2 f(S_k) \]

Personalized model of femoral artery stenosis

Boundary conditions and parameter identification

Boundary conditions:
inlet (arteries):

\[ Q = \alpha Q_{\text{heart}} \]

outlet (veins):

\[ Q = \alpha Q_{\text{heart}} \]

Parameter identification: Ultrasound measurements (before surgery), angles of bifurcations, vessel sizes...
## Simulation result

<table>
<thead>
<tr>
<th>Art.</th>
<th>Peak blood velocity (cm/s)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Presurgical Patient</td>
<td>Model</td>
<td>Postsurgical Patient</td>
<td>Model</td>
</tr>
<tr>
<td>3</td>
<td>148</td>
<td>149</td>
<td>150</td>
<td>155</td>
</tr>
<tr>
<td>4</td>
<td>48</td>
<td>54</td>
<td>65</td>
<td>70</td>
</tr>
<tr>
<td>12</td>
<td>103</td>
<td>93</td>
<td>69</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>&gt;300</td>
<td>340</td>
<td>-</td>
<td>71</td>
</tr>
<tr>
<td>7</td>
<td>-</td>
<td>67</td>
<td>98</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td>52</td>
<td>56</td>
<td>72</td>
<td>72</td>
</tr>
</tbody>
</table>

3 - common femoral, 4 - superficial femoral, 12 - deep femoral, 5 - occlusion, 7 - superficial femoral (dist), 9 - popliteal art.

MRI failed to connect branch of 12 to 9.
Ischemic heart disease and presonalized models

Ischemic heart disease is caused by

- pathology of microvasculature (therapy)
- pathology of coronary arteries (revascularization)
Ischemic heart disease and personalized models

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- pathology of coronary arteries (revascularization)

Indication for revascularization
- before 2014: Vascular occlusion factor (relative lesion cross-sectional area) $VOF > 0.7$
- after 2014: Fractional flow reserve $FFR < 0.75$

Fractional flow reserve (FFR)

Clinical practice: endovascular intervention, expensive transducer

Kopylov Ph., Bykova A., Vassilevski Yu., Simakov S. Role of measurement of fractional flow reserve (FFR) in coronary artery atherosclerosis. Therapeutic archive, 2015 87 (9)
Virtual fractional flow reserve $\text{FFR}_{CT}$

- Hemodynamic simulation based on personalized data:
  - Computed Tomographic Coronary Angiography (DICOM)

- $\text{FFR}_{CT} = \frac{P_{\text{dist}}}{P_{\text{aortic}}}$
Virtual fractional flow reserve $FFR_{CT}$

- Hemodynamic simulation based on personalized data:
  - Computed Tomographic Coronary Angiography (DICOM)

- $FFR_{CT} = \frac{P_{\text{dist}}}{P_{\text{aortic}}}$

- Advantages of $FFR_{CT}$
  - non-invasivity
  - physiological significance of each of multiple lesions
  - virtual stenting
  - applicability to any segment of the coronary tree
Virtual fractional flow reserve from 3D simulations

3D Navier-Stokes equations

HeartFlow has gained U.S. Food and Drug Administration (FDA) approval for the use of FFR$_{CT}$ as a class II Coronary Physiologic Simulation Software Device

Virtual fractional flow reserve from 3D simulations
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Difficulties of FFR$_{CT}$ evaluation by 3D simulations:
▶ boundary conditions for 3D problem
▶ simulation time
▶ frozen vascular walls (physics?) or FSI (expensive, coefficients?)

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- boundary conditions for 3D problem
- simulation time
- frozen vascular walls (physics?) or FSI (expensive, coefficients?)


Alternative approach: 1D hemodynamics
Patient-specific segmentation of coronary arteries
# Automatic segmentation and skeletonization

<table>
<thead>
<tr>
<th>Input DICOM image</th>
<th>Segmentation of aorta and coronary arteries</th>
<th>Thinning and false twigs elimination</th>
<th>Skeleton-based graph reconstruction</th>
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![Input DICOM image](image1.png) ![Segmentation of aorta and coronary arteries](image2.png) ![Thinning and false twigs elimination](image3.png) ![Skeleton-based graph reconstruction](image4.png)

## Overview of pipeline for automatic network reconstruction

Automatic segmentation and skeletonization

Overview of pipeline for automatic network reconstruction


Aorta segmentation by isoperimetric distance trees

Automatic segmentation and skeletonization

Overview of pipeline for automatic network reconstruction

Frangi vesselness filter generates bigger values inside bright tubular structures
## Automatic segmentation and skeletonization

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### Overview of pipeline for automatic network reconstruction


Skeletonization produces vascular 1D computational network

Skeletonization efficiency

Skeletons of a coronary tree and of a micro-CT of vascular corrosion cast of rabbit kidney provided by J. Alastruey, Department of Bioengineering, King's College London, UK

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Rabbit kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution</td>
<td>$512 \times 512 \times 248$</td>
<td>$2000 \times 1989 \times 910$</td>
</tr>
<tr>
<td>Distance map</td>
<td>0.20 sec</td>
<td>58.12 sec</td>
</tr>
<tr>
<td>Thinning</td>
<td>0.79 sec</td>
<td>526.98 sec</td>
</tr>
<tr>
<td>False twigs cleaning</td>
<td>0.15 sec</td>
<td>16.61 sec</td>
</tr>
<tr>
<td>Graph construction</td>
<td>0.13 sec</td>
<td>12.27 sec</td>
</tr>
<tr>
<td>Skeleton segments</td>
<td>22</td>
<td>4302</td>
</tr>
</tbody>
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Coronary hemodynamics in silico


- On arterial entry unsteady flux (1Hz, 65ml) is scaled to HR and systolic/diastolic pressures, venous pressure (12 mmHg) is given.
Coronary hemodynamics in silico


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- Compression of arteries during systola by myocard:
  \[ p_{*k} = P_{ext}^{cor}(t), \quad R_{k}^{syst} = 3R_{k}^{diast} \]

\( P_{ext}^{cor} \) is normalised by the ventricular pressure
Coronary hemodynamics in silico


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- Resistance of microcirculation
  \[ p_k (S_k (t, \tilde{x}_k)) - p_{veins} = R_k S_k (t, \tilde{x}_k) u_k (t, \tilde{x}_k) \]

![Diagram of coronary hemodynamics network](image)
Coronary hemodynamics in silico


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- \( c_k \) and \( R_k \) are chosen to agree with literature
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- Stenosis with fraction \( \alpha \): \( S_0^{st} = (1 - \alpha)S_0 \)
Computation of virtual fractional flow reserve

reconstructed arterial part based on two anonymous patient-specific data sets

Computation of virtual fractional flow reserve
FFR$_{CT}$ within Multivox toolbox

Medical computer systems, Lomonosov Moscow State Univ.
Personalized model of blood flow in left ventricle

- reference domain $\Omega_0$
- transformation $\xi$ mapping $\Omega_0$ to $\Omega(t)$ is given
- $v$ and $u$ denote velocities and displacements in $\Omega_0$
- $\xi(x) := x + u(x)$, $F := \nabla \xi = I + \nabla u$, $J := \det(F)$
- Cauchy stress tensor $\sigma$
- pressure $p$
- density $\rho$ is constant
Model of incompressible fluid flow in a moving domain

Navier-Stokes equations in reference domain $\Omega_0$

Let $\xi$ mapping $\Omega_0$ to $\Omega(t)$, $\mathbf{F} = \nabla \xi = \mathbf{I} + \nabla \mathbf{u}$, $J = \det(\mathbf{F})$ be given.
Model of incompressible fluid flow in a moving domain

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Dynamic equations

$$\frac{\partial v}{\partial t} = (J\rho_f)^{-1} \text{div} (J\sigma_f F^{-T}) - \nabla v \left( F^{-1} \left( v - \frac{\partial u}{\partial t} \right) \right) \quad \text{in } \Omega_0$$
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Fluid incompressibility

$$\text{div} (J F^{-1} v) = 0 \quad \text{in } \Omega_0 \quad \text{or} \quad J \nabla v : F^{-T} = 0 \quad \text{in } \Omega_0$$
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Constitutive relation for the fluid stress tensor

$$
\sigma_f = -p_f I + \mu_f ((\nabla v)F^{-1} + F^{-T}(\nabla v)^T) \quad \text{in } \Omega_0
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Mapping $\xi$ does not define material trajectories $\rightarrow$ quasi-Lagrangian formulation
Finite element scheme

Let $V_h, Q_h$ be Taylor-Hood $P_2/P_1$ finite element spaces.
Find $\{v^k_h, p^k_h\} \in V_h \times Q_h$ satisfying b.c.
("do nothing" $\sigma F^{-T} n = 0$ or no-penetration no-slip $v^k = (\xi^k - \xi^{k-1})/\Delta t$)

\[
\int_{\Omega_0} J_k \frac{v^k_h - v^{k-1}_h}{\Delta t} \cdot \psi \, dx + \int_{\Omega_0} J_k \nabla v^k_h F^{-1}_k \left( v^{k-1}_h - \frac{\xi^k - \xi^{k-1}}{\Delta t} \right) \cdot \psi \, dx -
\]

\[
\int_{\Omega_0} J_k p^k_h F^{-T}_k : \nabla \psi \, dx + \int_{\Omega_0} J_k q F^{-T}_k : \nabla v^k_h \, dx +
\]

\[
\int_{\Omega_0} \nu J_k (\nabla v^k_h F^{-1}_k F^{-T}_k + F^{-T}_k (\nabla v^k_h)^T F^{-T}_k) : \nabla \psi \, dx = 0
\]

\[
\int_{\Omega_0} J_k \nabla v^k : F^{-T}_k q \, d\Omega = 0
\]

for all $\psi$ and $q$ from the appropriate FE spaces
Finite element scheme

The scheme
- semi-implicit
- produces one linear system per time step
- first order in time (may be generalized to the second order)
Finite element scheme

The scheme
- semi-implicit
- produces one linear system per time step
- first order in time (may be generalized to the second order)
- unconditionally stable (no CFL restriction) and 2nd order accurate, proved with assumptions:
  - $\inf_Q J \geq c_J > 0$, $\sup_Q (\|F\|_F + \|F^{-1}\|_F) \leq C_F$
  - LBB-stable pairs (e.g. $P_2/P_1$)
  - $\Delta t$ is not large

The law of motion for the ventricle walls is known thanks to ceCT scans → 100 mesh files with time gap 0.0127 s → u given as input → FSI reduced to NSE in a moving domain

- 2 - aortic valve (outflow)
- 5 - mitral valve (inflow)
3D: left ventricle of a human heart

- Quasi-uniform mesh: 14033 vertices, 69257 elements, 88150 edges.
- Boundary conditions: Dirichlet $\mathbf{v} = \frac{\partial \mathbf{u}}{\partial t}$ except:
  - Do-nothing on aortal valve during systole
  - Do-nothing on mitral valve during diastole
- Time step 0.0127 s is too large!
  $\implies$ refined to $\Delta t = 0.0127/20$ s
  $\implies$ Cubic-splined $\mathbf{u}$.
- Blood parameters: $\rho_f = 10^3$ kg/m$^3$, $\mu_f = 4 \cdot 10^{-3}$ Pa $\cdot$ s.
Open source software

- ITK-SNAP - www.itksnap.org
- Ani3D - sf.net/p/ani3d
Open source software

- ITK-SNAP - www.itksnap.org
- Ani3D - sf.net/p/ani3d
- INMOST - www.inmost.org
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- Ani3D - sf.net/p/ani3d
- INMOST - www.inmost.org
- CRIMSON - www.crimson.software
Announcement of workshops, 7-11 October 2019
Far East Federal University, island Russky, Vladivostok, Russia

Week of Applied Mathematics & Mathematical Modelling

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- 11th Workshop on Numerical Methods and Mathematical Modelling in Biology and Medicine
- 3d Workshop on Multiscale Methods and Large-scale Scientific Computing
- 6th Russian-Chinese Workshop on Numerical Mathematics and Scientific Computing