Mathematical modeling of general hemodynamic and its application for studying liquid and matter flows in human body.

M. Abakumov , A. Borzov, A.Bunicheva, A. Dreval, A. Khrulenko, A.Mozokhina, S. Mukhin, N. Sosnin

Lomonosov Moscow State University, faculty of Computational Mathematics and Cybernetics

Hemodynamic modeling:

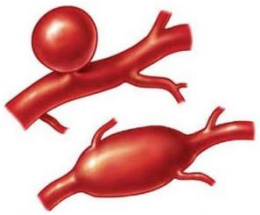
- **Local models**
- **Global hemodynamic**
- **Multi-scale modeling**

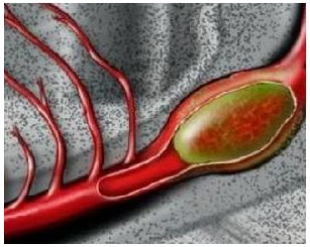
Local models

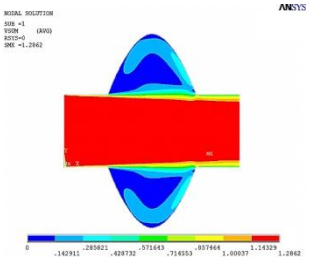
2D-3D simulation in complex domain with respect to elastic properties, rheology of blood, etc., on the base of Navier-Stokes equations.

$$\begin{cases} div(\vec{v}) = 0 \\ \frac{\partial \vec{v}}{\partial t} + (\nabla, \vec{v})\vec{v} + p = -\nu \; rot \; rot\vec{v} \end{cases} + \quad \sigma_{ij} = \frac{dF_{ij}}{dS_i} \quad \mu = \varepsilon'/\varepsilon \quad + \quad E = \sigma_n/\varepsilon \quad + \quad \bullet\bullet\bullet$$

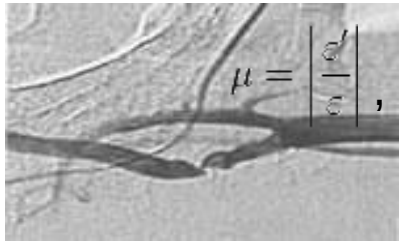
Aneurysm

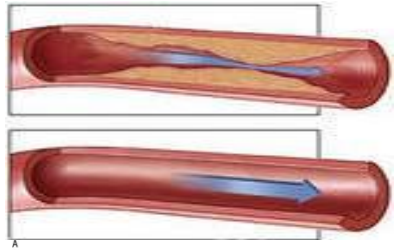


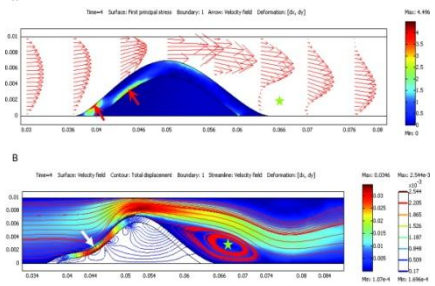




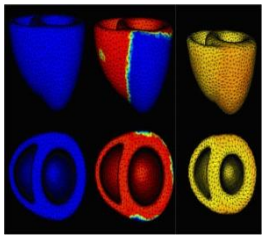
Stenosis

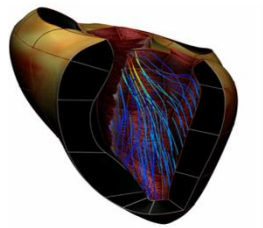


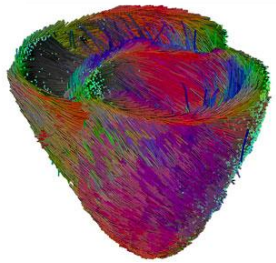




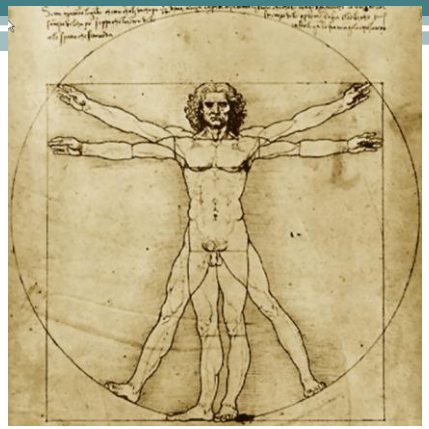
Heart







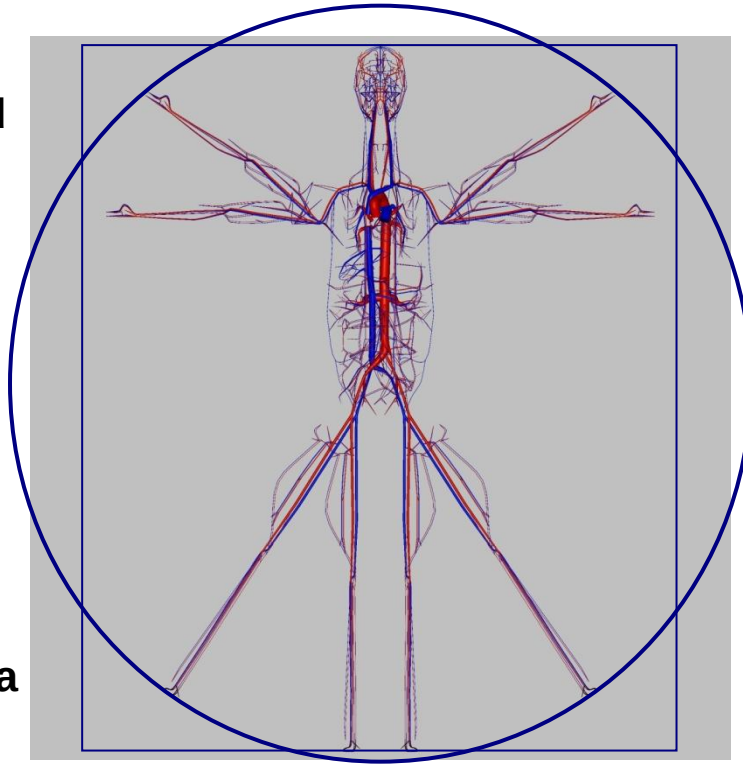
Global model CVSS



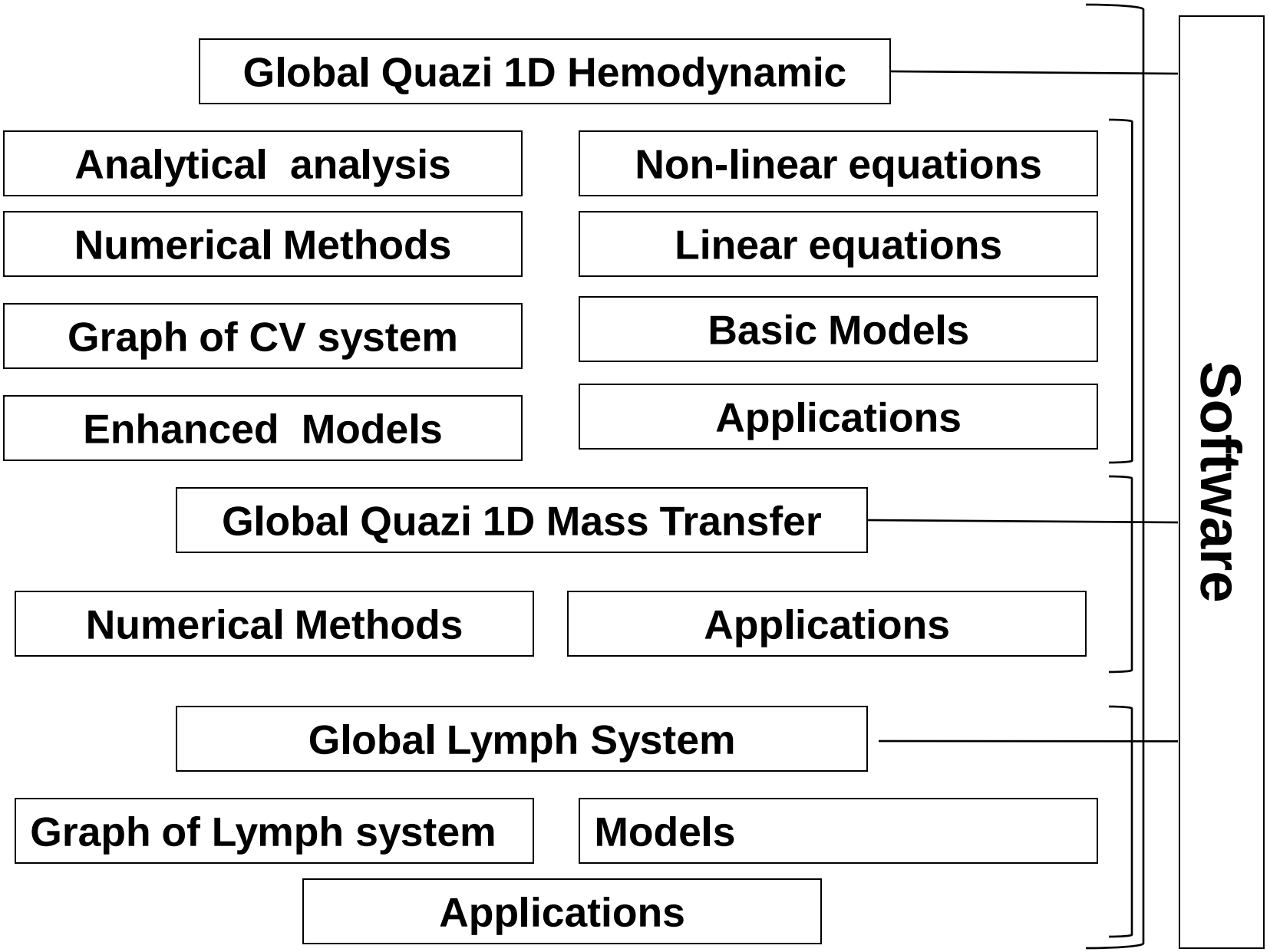
The model is aimed to carry out estimation of hydrodynamic blood flow (velocity, pressure, cross-section) along the graph, which is physiologically adequate to human cardiovascular system, and to represent the main characteristics of blood circulation system .

Applications

- Modeling of functioning of the circulatory system and its regulation.
- Simulation and investigation of CVS diseases and their treatments.
- Modeling the influence of various organs on the functioning of CVS.
- Modeling of circulatory system influence of the functioning of various organs.
- Simulation of transfer by the circulatory system of various substances (gases, enzymes, drugs and so on) and their influens on different organs.
- Modeling the influence of CVS topology changes (as a result of surgery, injuries, etc.)
- Etc.



CVSS - Cardio-Vascular Simulating System-project and software

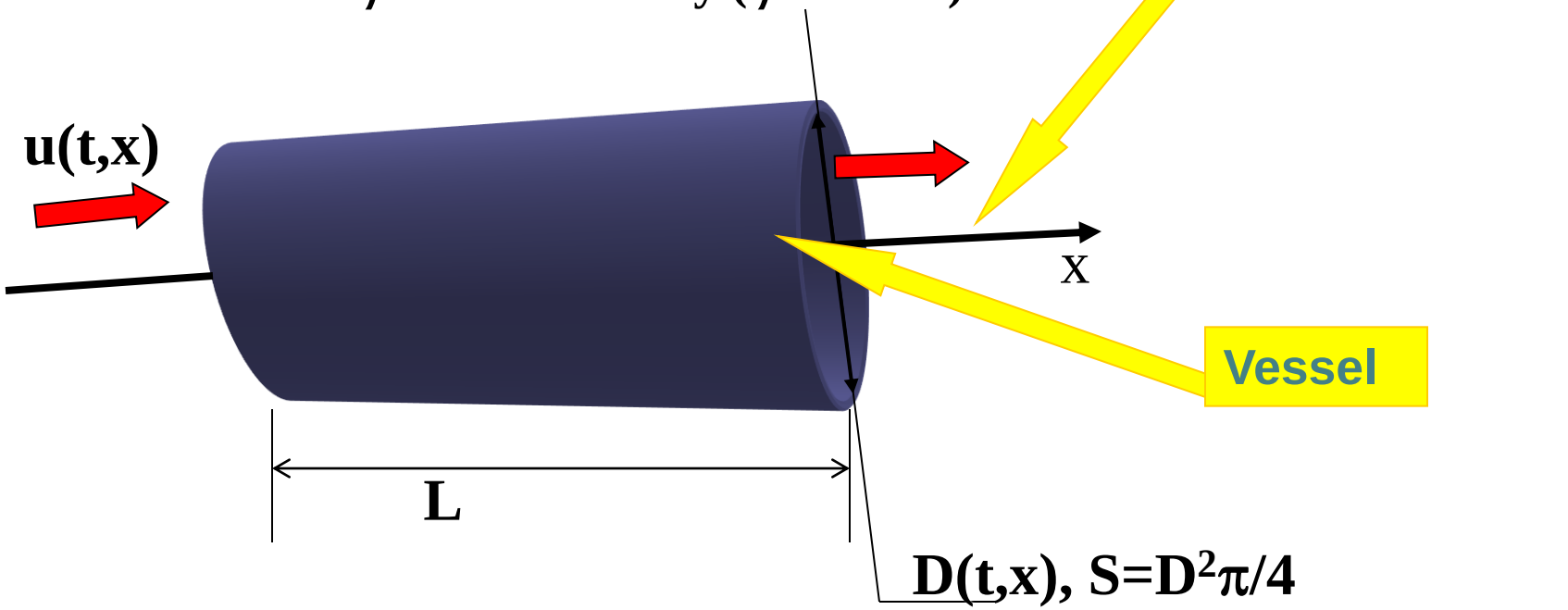

Global Quazi 1D Hemodynamic
Analytical analysis
Non-linear equations
Numerical Methods
Linear equations
Graph of CV system
Basic Models
Enhanced Models
Applications
Global Quazi 1D Mass Transfer
Numerical Methods
Applications
Global Lymph System
Graph of Lymph system
Models
Applications
Software

The goal of CVSS project is to create mathematical models, numerical methods and corresponding software for numerical simulations of cardiovascular flow in quazi 1D aproximation. For this purpose cardiovascular system is associated with the graph of vessels (links) and tissues (nodes). Each vessel is taken as a one-dimensional flexible pipe, which is oriented in 3-D space and connected either with other vessels or with tissues. Diameters of vessels are not constant and depend upon a great number of physiological and physical parameters, such as pressure, coefficient of flexibility, gravitation, etc. Vessel can be taken as a certain vessel or as a group of similar vessels. Tissues are characterized with their volume, their ability to produce or sorb a certain amount of blood, Darcy coefficient an so on. Series of models of heart with different complexity are considered. Pressure, velocity of blood, diameter of vessel, which are estimated at any point of cardiovascular graph, are taken as basic functions to be computed as a result of numerical simulation.

“Theory”

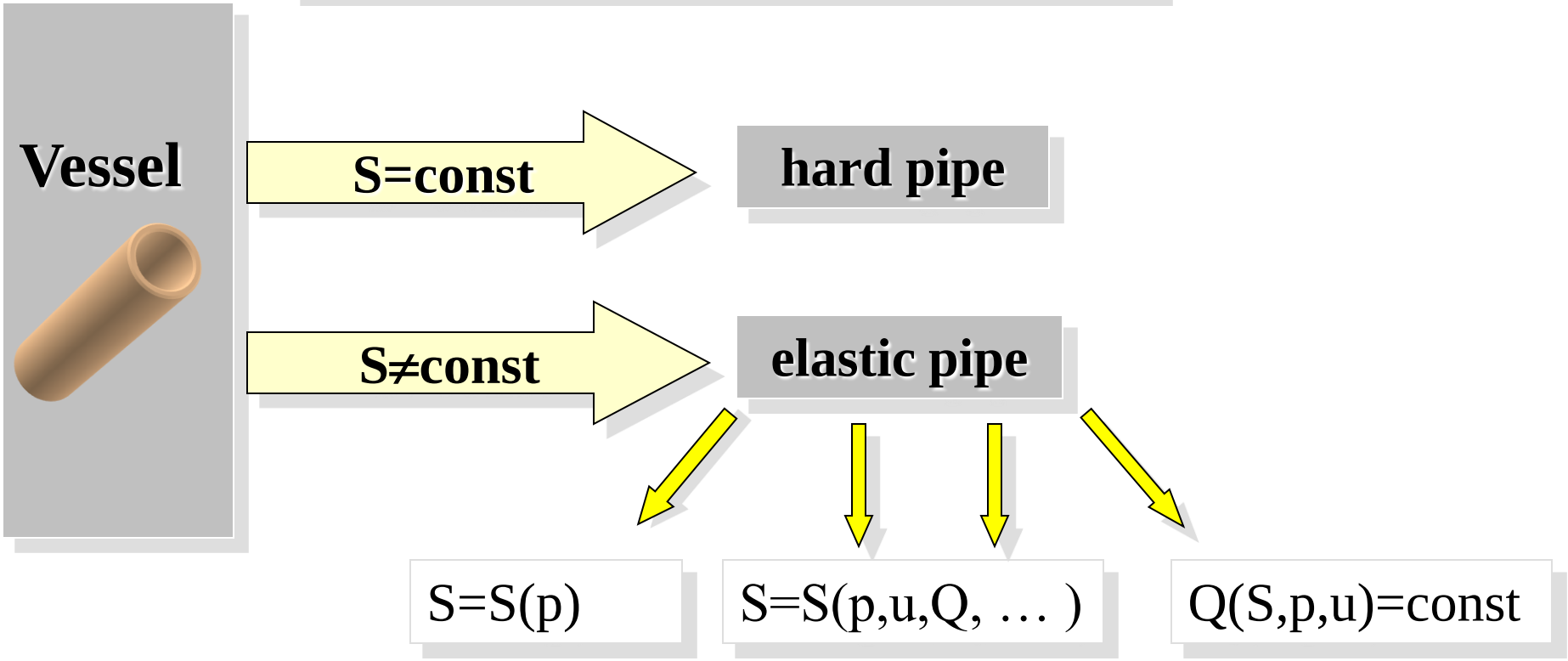
Notations

S(t,x) **–cross-section area**
u*(t, x)* -velocity of blood flow
p(t,x) **-pessure**
Q(t,x) **- blood flow *(Q=Su)***
t **- time**
x **- local space coordinate**
ρ **- blood density (*ρ = const*).**



Sequence of hierarchical models

Models of cardiovascular vessels



Diameter of vessel can be constant or not constant and can depends upon a great number of physiological and physical parameters, such as pressure, coefficient of flexibility, gravitation, etc. This dependence we will call the "equation of state" . Walls of vessel is supposed to be thin.

Assumptions

We assume blood to be uncompressible viscous liquid and mark out several types of blood flows which appear in vascular modeling.

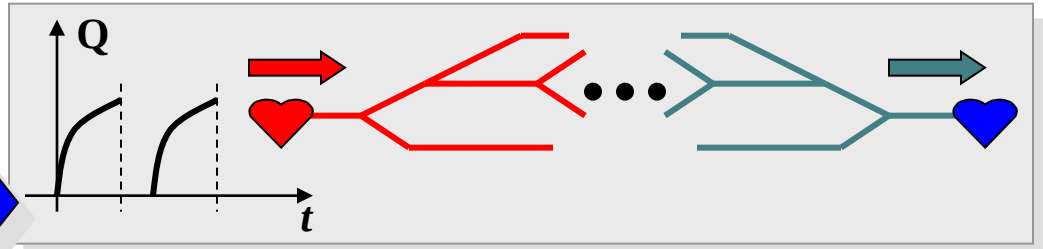
1. In practice, velocity *u(t,x)* of blood flow is much less then the speed $\theta(t,x)$ of propagation of small disturbances, $|u / \theta| << 1$.

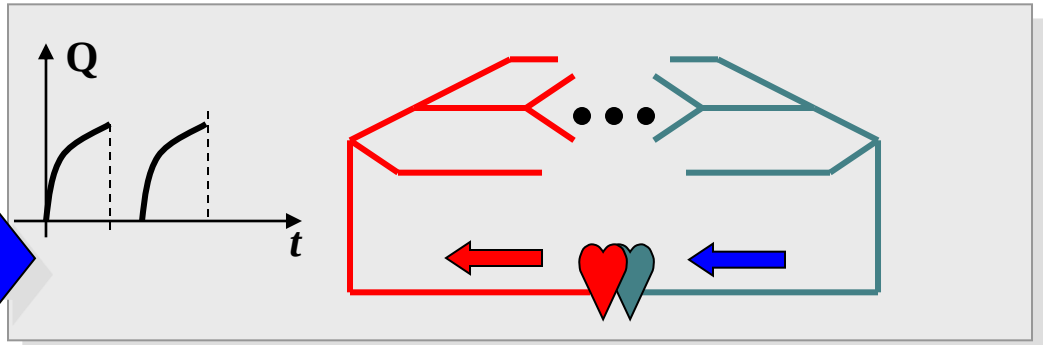
2. Considered types of blood flow:

- Stationary flow
- Quasi-stationary flow. Heart output flow *Q* or pressure *p* are given as time dependent functions (for example, periodical functions).
- Quasi-stationary flow in self-contained (conservative) system of vessels with given or self-regulating heart output flow or pressure functions.

General principals of blood flow mathematical description in a vessel

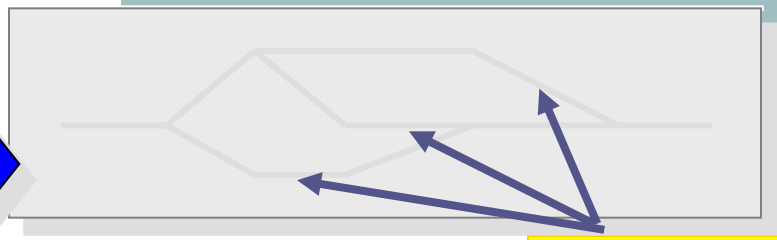
1. The use of conservation laws
2. Quasi one-dimensional approach
3. The account of viscous effects
4. The account of external forces influence (acceleration, gravitation, vibration, etc.)





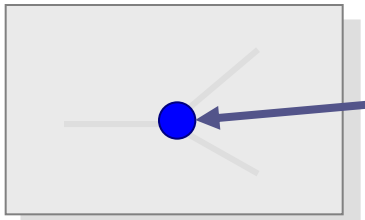
Elements of integrated model

1. A system of vessels (cardiovascular system or it's part) - vascular graph.

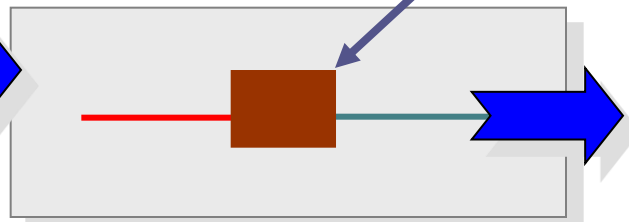


Vessels -arcs (links) of graph

2. Nodes of vascular graph
   - areas of vessels bifurcation
   - tissues
   - organs
   - etc.



nodes



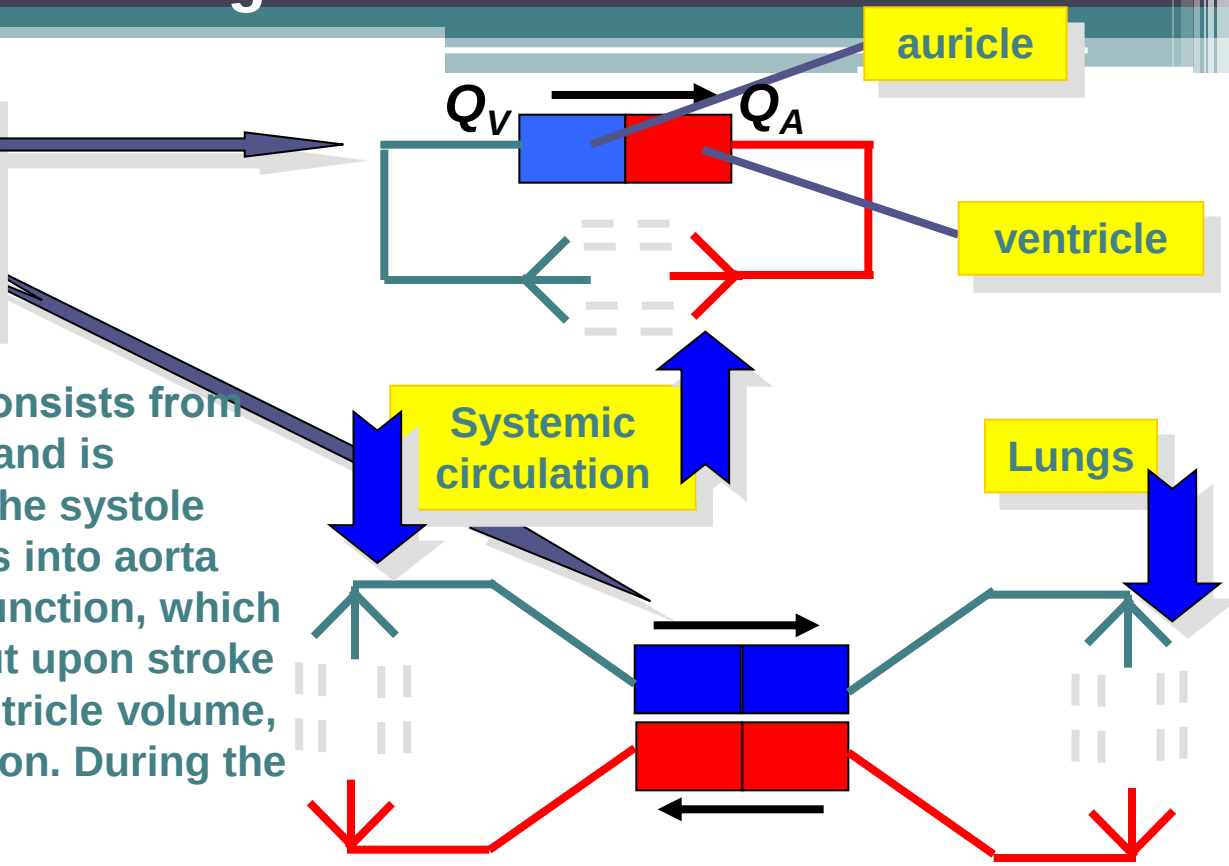
Tissues, muscles

kidney, liver, intestines, spleen, lungs, ...

- Nodes, which represent areas of vessels bifurcation, are described by the flow conservation law and the continuity of pressure or Bernulli integral. As a 0D model of tissues or muscles Darcy low can be taken.
- Each organ must be described by specific model, in the simplest case – 0D model.
- Note, that models in node of graph can be so complex as the stated problem requires.

Elements of integrated model

3. Heart is described by **two** or **four** chambers heart model.



"Two chambers" heart model consists from two cells: auricle and ventricle and is considered as a pump. During the systole blood from ventricle propagates into aorta according to the given *Q* or *P* function, which depends not only upon time, but upon stroke volume, current auricle and ventricle volume, aortic arch baroceptors and so on. During the diastole auricle is filling up.

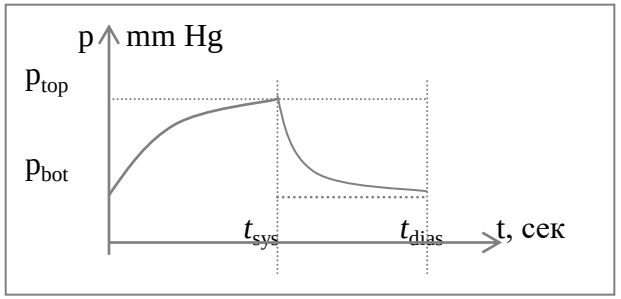
"Four chambers' model is arranged from "two chambers" models with different characteristics.

A simplest example of "two chambers" heart model

$$Q(t)=\begin{cases} q_{top}-\dfrac{1}{t_{sys}^2}(q_{top}-q_{bot})(t-t_{sys})^2, & 0\le t\le t_{sys} \\ q_{bot}, & t_{sys}<t\le t_{dias} \end{cases}$$

$$V_k = V_{KD} - \int_0^t Q_A(\tau)d\tau, 0 < t \le t_{sys}$$

$$V_k = V_{KS} + \int_{t_{sys}}^t Q_V(\tau)d\tau, t_{sys} < t \le t_{dias}$$



Mathematical model on a graph

According to principles formulated above, we can construct mathematical model on a graph of vessels.

1. To each arch (vessel) of a graph corresponds a "hemodynamic" system of equations

$$\frac{\partial S}{\partial t}+\frac{\partial uS}{\partial x}=0$$

$$\frac{\partial u}{\partial t}+\frac{\partial}{\partial x}\left(\frac{u^2}{2}\right)+\frac{1}{\rho}\frac{\partial p}{\partial x}=F_T+F_{TP}$$

$$s=s(p)\quad .$$

$$\frac{ds}{dp}\geq 0.$$

2. To each node of a graph, which is "a bifurcation node", two bifurcation equations are corresponded

$$\sum_i z_i s_i u_i = 0,$$

$$\frac{u_i^2}{2}+\frac{p_i}{\rho}=\frac{u_j^2}{2}+\frac{p_j}{\rho},\quad i\neq j$$

***i,j* –numbers of converging arches in this node, z_i – considering the direction of local arch coordinates.**

3 . To each node, which represent tissue, mass conservation law and Darcy low are corresponded.

$$z_i s_i u_i + z_j s_j u_j = 0,$$

$$z_i s_i u_i = k_d(p_i - p_j)\quad ,$$

***K_d*- Darcy coefficient**

NOTATIONS

S(t,x) –cross-section area
u(t, x) -velocity of blood flow
p(t,x) -pressure
t - time
x - local space coordinate
ρ - blood density ($\rho = const$).
F_T – viscous force
F_T – external force

Properties of hemodynamic equations

Hemodynamic system of equations has a hyperbolic type when equation of state meets the requirement ***dS/dp>0***. In this case there are two **characteristics**, two **invariants** and the speed of propagation of small disturbances exists – **"sonic speed"** (like gas dynamics). These circumstances make possible to analyze solution of the system by means of analytic methods and help to construct numerical methods in a proper way .

$$\frac{\partial s}{\partial t}+\frac{\partial us}{\partial x}=0 \quad ,$$

$$\frac{\partial u}{\partial t}+\frac{\partial}{\partial x}\left(\frac{u^2}{2}+\frac{p}{\rho}\right)=F_T+F_{TP},$$

$$s=s(p)$$

$$\frac{ds}{dp}>0$$

characteristics

$$\frac{dx}{dt}=u\pm c,$$

sonic speed

$$c=\sqrt{\frac{s}{\rho\theta}},$$

$$\frac{|u|}{c}=M<<1$$

invariants

$$\pm 2\frac{d(\sqrt{s})}{\sqrt{\rho\theta}}+du=(F_T+F_{TP})dt$$

Due to the fact that velocity of blood flow actually is much less then the sonic speed, it turned out that in many cases we can use linear approach for HMD problems

Numerical methods and algorithms

1. Special format of graph description was constructed. It allows user to pay no attention to the way how solver treats the topology of vascular graph.

2. Conservative finite-difference scheme with second order of approximation on each arch of graph was taken as a base. At the same time scheme is homogeneous, so it does not depends upon concrete arch.

3. Two different variants of finite-difference schemes provided for better reliability of numerical calculations.

4. The total non-linear system of equations is solved with help of iteration methods (Newton method, successive iterations on coefficients of equations).

5. The obtained linear system of equations is solved mainly by direct methods.

$$\delta p_j^k + As_j^3\,\delta p_{j+1}^k + Bs_j^1\,\delta u_{j-1}^k + Bs_j^2\,\delta u_j^k + Bs_j^3\,\delta u_{j+1}^k = -Fs_j$$

$$s_j^1 = -\left(\frac{u_{j-1}^k}{2} + \frac{a_{j-1/2}^k}{h}\right)\frac{\sigma_1\tau}{h}\theta_{j-1}^k,$$

$$s_j^2 = \left(1 + (a_{j+1/2}^k + a_{j-1/2}^k)\frac{\sigma_1\tau}{h^2}\right)\theta$$

$$s_j^3 = \left(\frac{u_{j+1}^k}{2} - \frac{a_{j+1/2}^k}{h}\right)\frac{\sigma_1\tau}{h}\theta_{j+1}^k,$$

$$Bs_j^1 = -\frac{\sigma_1\tau}{2h}s_{j-1}^k,$$

$$Bs_j^2 = 0,$$

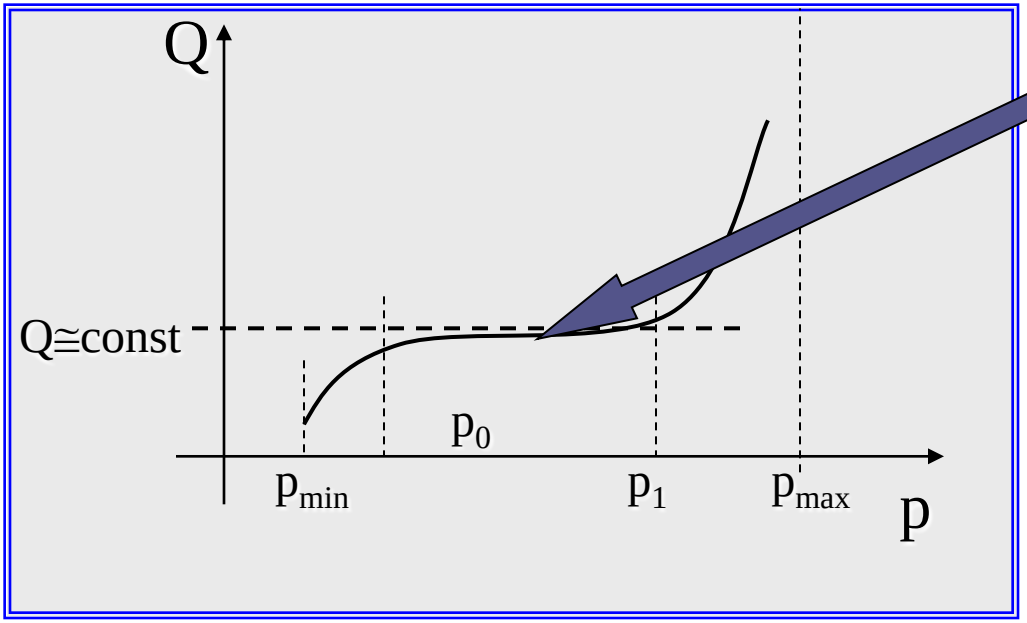
$$Bs_j^3 = \frac{\sigma_1\tau}{2h}s_{j+1}^k,$$

$$-\breve{s} + (s_{j+1}^k u_{j+1}^k - s_{j-1}^k u_{j-1}^k)\frac{\sigma_1\tau}{2h} + (\breve{s}_{j+1}\breve{u}_{j+1} - \breve{s}_{j-1}\breve{u}_{j-1})\frac{(1-\sigma_1)\tau}{2h} -$$

$$-(a_{j+1}^k s_{j+1}^k - (a_{j+1/2}^k + a_{j-1/2}^k)s_j^k + a_{j-1/2}^k s_{j-1}^k)\frac{\sigma_1\tau}{h^2} -$$

$$-(\breve{a}_{j+1/2}\breve{s}_{j+1} - (\breve{a}_{j+1/2} + \breve{a}_{j-1/2})\breve{s}_j + \breve{a}_{j-1/2}\breve{s}_{j-1})\frac{(1-\sigma_1)\tau}{h^2}\quad .$$

Example of specific «equation of state» - Ostoumov-Beyliss effect



Effect of autoregulation in cerebral arteries

This effect can be simulated by equation of state in following form

$$S(t,x)=\begin{cases} S=S(p), & p_{\min}\le p\le p_0 \\ S=\dfrac{Q_0}{u}, & p_0\le p\le p_1 \\ S=S(p), & p_1\le p\le p_{\max} \end{cases}$$

As numerical experiments show, the effect of "steady blood flow" in main cerebral arteries is performed mostly by topology of cerebral vessels.

We must take into account, that different types of state equations can strongly influence on the type of mathematical problem

Equation of state

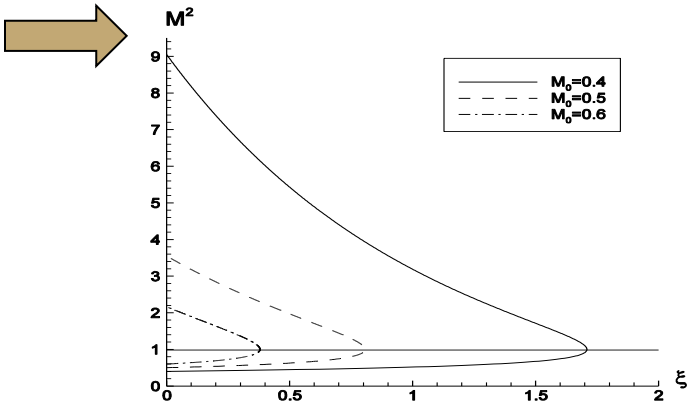
In case of stationary flow **the influence** of equation of state on the properties of solution of hemodynamic equations is studded analytically. It is shown that in this case the solution at the interval satisfies the equation

$$-Q_0^2\left[\ln S(p)-\ln S(p(0))\right]+\frac{1}{\rho}\int_{p(0)}^{p(x)}S^2(p)dp=-8\pi\nu Q_0 x \qquad 0<x<l,\ Q_0=Su=const$$

It is possible to draw out some conclusions, for a example:

- **For linear** equation of state $S(p)=S_0+A(p-p_0), A=const.$ the solution satisfies the equation $\frac{d\xi}{dM}=\frac{1-M^2}{M^3},\ \xi=\frac{12\pi\nu}{Q_0}x,$ where M- Mach number , ξ -self-similar variable/

As it follows from the the behavior of integral curves, the flow in this case cannot change its type from susonic to supersonic.



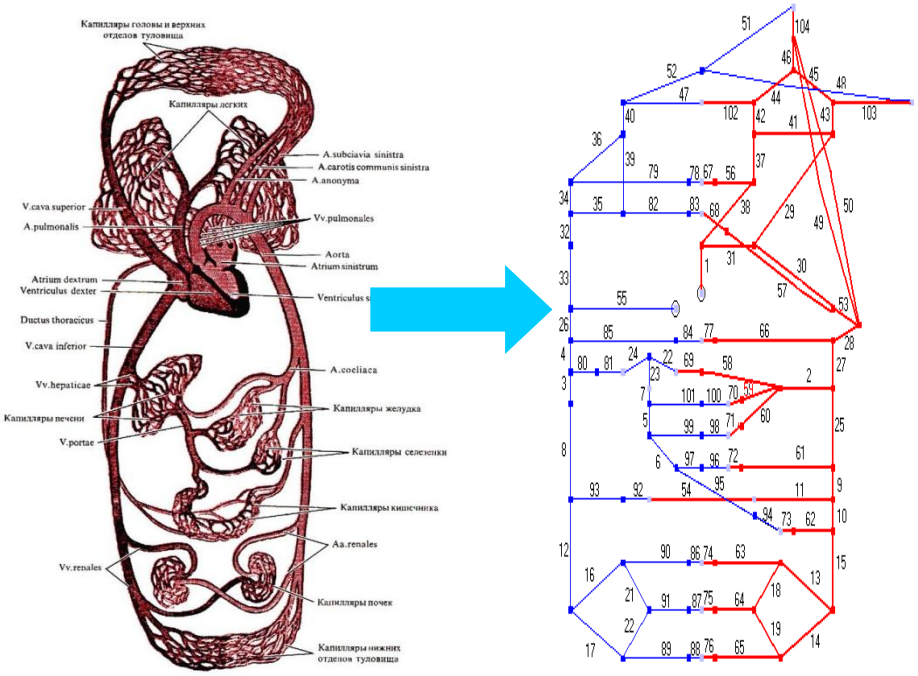
- **Any subsonic** solution exists only on the finite segment of vessels length.

$$\xi_{kp}=\ln M_0+\frac{1}{2}\left(\frac{1}{M_0}-1\right),\quad M_0<1$$

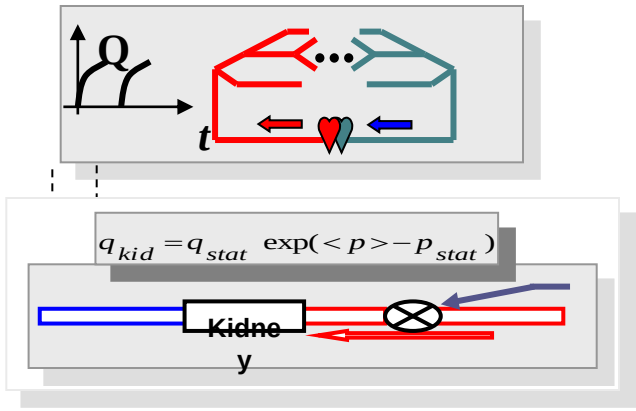
Analysis of stationary solutions shows, that in dependence upon the properties of vessel and flow parameters effect of «locking vessel» is possible .

Adequacy of mathematical model to properties of cardiovascular system functioning

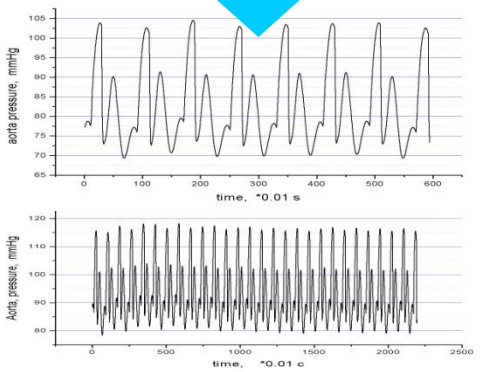
Formal mathematical description of blood circulation system to a graph



Application of various models of cardiovascular system elements



Renal outflow q_{kid}



CVSS software tool gives possibility to carry out high accuracy estimation of hydrodynamic blood flow features along the graph, which physiologically adequate to human cardiovascular system, allows to represent the main characteristics of of blood circulation system

Linear analysis

Linear analysis

Linear approximation of hemodynamic equations (LHMD)

Evolution of small disturbances of velocity and pressure from stationary solutions of hemodynamics is described on each arch of vascular graph by the system of linearized hemodynamic equations:

$$\begin{cases} p_{i\,t} + \bar{u}_i p_{i\,x_i} + \rho \bar{c}_i^2 u_{i\,x_i} = 0, \\ u_{i\,t} + \dfrac{1}{\rho} p_{i\,x_i} + \bar{u}_i u_{i\,x_i} = 0, \end{cases}$$

$$\bar{c}_i = \sqrt{\frac{\bar{s}_i}{\rho \bar{\theta}_i}},$$

$$\bar{s}_i = S_i(\bar{p}_i), \qquad \bar{\theta}_i = \left.\frac{dS_i(P_i)}{dP_i}\right|_{P_i = \bar{p}_i}.$$

This system of equations supplied with linearized equation in internal nodes of graph:

$$\sum_i z_i (\bar{s}_i u_i(x_{i,\,\text{гр.}}, t) + \bar{\theta}_i \bar{u}_i p_i(x_{i,\,\text{гр.}}, t)) = 0,$$

$$\bar{\alpha}_i p_i(x_{i,\,\text{гр.}}, t) + \bar{\beta}_i u_i(x_{i,\,\text{гр.}}, t) = \bar{\alpha}_j p_j(x_{j,\,\text{гр.}}, t) + \bar{\beta}_j u_j(x_{j,\,\text{гр.}}, t),$$

and with linearized boundary conditions in boundary nodes of graph.

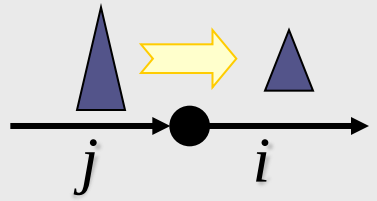
Each of progressing waves is described by the following formula:

$$f_i^{-z_i}(x_i-\bar{\lambda}_i^{-z_i}t)=\begin{cases}-\dfrac{z_i}{\rho\bar{c}_i}\varphi_i(x_i-\bar{\lambda}_i^{-z_i}t)+\psi_i(x_i-\bar{\lambda}_i^{-z_i}t), & \text{если } x_{i,\,гр.}-l_i\le z_i(x_i-\bar{\lambda}_i^{-z_i}t)\le x_{i,\,гр.};\\ \displaystyle\sum_{j\in\Omega(k)}\kappa^u_{j\to i}\left(\frac{z_j}{\rho\bar{c}_j}\varphi_j\left(x_{j,\,гр.}-\frac{\bar{\lambda}_j^{z_j}}{\bar{\lambda}_i^{-z_i}}\left(x_{i,\,гр.}-(x_i-\bar{\lambda}_i^{-z_i}t)\right)\right)+\right.\\ \left.+\psi_j\left(x_{j,\,гр.}-\dfrac{\bar{\lambda}_j^{z_j}}{\bar{\lambda}_i^{-z_i}}\left(x_{i,\,гр.}-(x_i-\bar{\lambda}_i^{-z_i}t)\right)\right)\right)+G_i\left(\dfrac{1}{\bar{\lambda}_i^{-z_i}}\left(x_{i,\,гр.}-(x_i-\bar{\lambda}_i^{-z_i}t)\right)\right),\\ \text{если}\quad x_{i,\,гр.}<z_i(x_i-\bar{\lambda}_i^{-z_i}t)\le x_{i,\,гр.}-z_i\bar{\lambda}_i^{-z_i}T,\ \ \forall i\in\Omega(k),\ \ k=1,\dots,m.\end{cases}$$

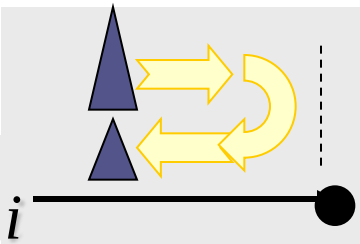
Coefficients $\kappa^u_{i\to i}$ and $\kappa^u_{j\to i}$ we name "transport coefficients".
They control the evolution of velocity and pressure waves when they pass through bifurcation nodes of vascular graph and determine amplitudes of formed waves.

$$\kappa^u_{j\to i}=-\frac{2z_iz_j\bar{s}_j(\rho\bar{\alpha}_j\bar{c}_j-\bar{\beta}_j\bar{m}_j)}{(\rho\bar{\alpha}_i\bar{c}_i-z_i\bar{\beta}_i)(\rho\bar{\alpha}_j\bar{c}_j-z_j\bar{\beta}_j)\sum_{l=1}^{n}\dfrac{\bar{s}_l(1-z_l\bar{m}_l)}{\rho\bar{\alpha}_l\bar{c}_l-z_l\bar{\beta}_l}}$$

Coefficient determines amplitude of velocity wave while passing from arch *j* to arch *i*



$$\kappa^u_{i\to i}=\frac{\rho\bar{\alpha}_i\bar{c}_i+z_i\bar{\beta}_i}{\rho\bar{\alpha}_i\bar{c}_i-z_i\bar{\beta}_i}-\frac{2\bar{s}_i(\rho\bar{\alpha}_i\bar{c}_i-\bar{\beta}_i\bar{m}_i)}{(\rho\bar{\alpha}_i\bar{c}_i-z_i\bar{\beta}_i)^2\sum_{l=1}^{n}\dfrac{\bar{s}_l(1-z_l\bar{m}_l)}{\rho\bar{\alpha}_l\bar{c}_l-z_l\bar{\beta}_l}},$$



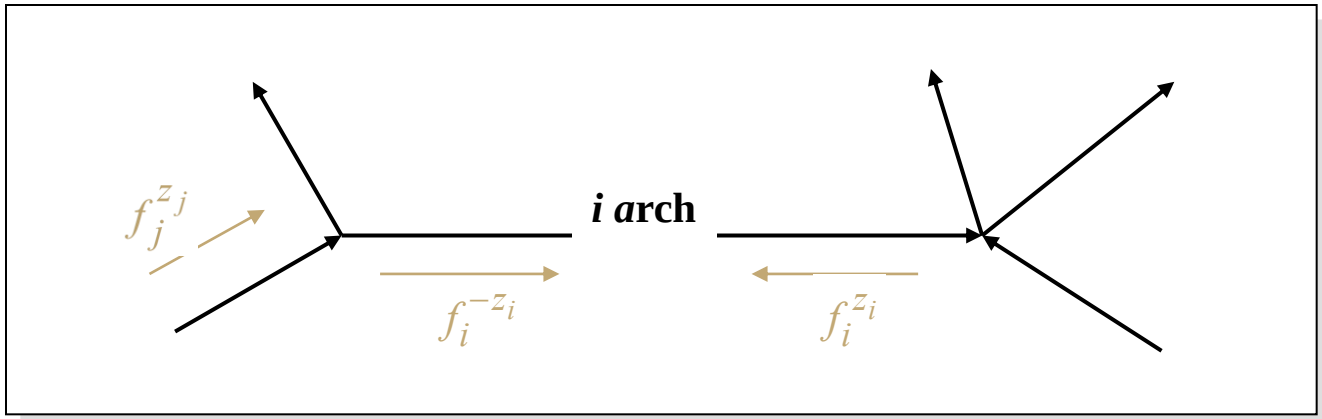
Coefficient determines amplitude of velocity wave in arch *i* while reflecting from node

General solution of LHD equations on the i-*th* arch of graph is a superposition of progressing waves of general form, which propagate in opposite directions :

$$p_i(x_i,t) = z_i \frac{\rho \bar{c}_i}{2}\left(f_i^{z_i}(x_i - \bar{\lambda}_i^{z_i} t) - f_i^{-z_i}(x_i - \bar{\lambda}_i^{-z_i} t)\right), \qquad u_i(x_i,t) = \frac{1}{2}\left(f_i^{z_i}(x_i - \bar{\lambda}_i^{z_i} t) + f_i^{-z_i}(x_i - \bar{\lambda}_i^{-z_i} t)\right),$$

$$\bar{\lambda}_i^{z_i} = \bar{u}_i + z_i \bar{c}_i, \quad \bar{\lambda}_i^{-z_i} = \bar{u}_i - z_i \bar{c}_i, \quad i = 1,\ldots,n.$$

Waves of velocity and pressure, propagating through nodes of vascular graph, change their amplitudes and phases of duration

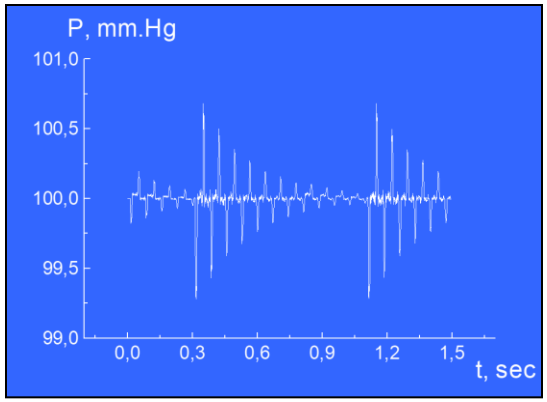


$$f_i^{-z_i}(x_i - \bar{\lambda}_i^{-z_i} t) = \sum_{j \in \Omega(k)} \kappa_{j \to i}^{u} f_j^{z_j}\left(x_{j,\,гр.} - \frac{\bar{\lambda}_j^{z_j}}{\bar{\lambda}_i^{-z_i}}\left(x_{i,\,гр.} - (x_i - \bar{\lambda}_i^{-z_i} t)\right)\right)$$

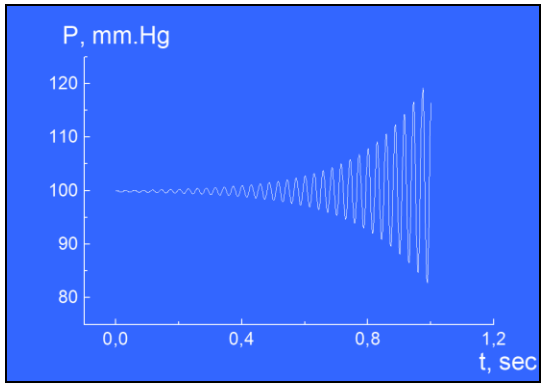
Linear analysis

Types of pulse pressure and velocity wave propagation along artery part of vascular system

Regime with limited amplitude of wave



Regime with increasing amplitude of wave



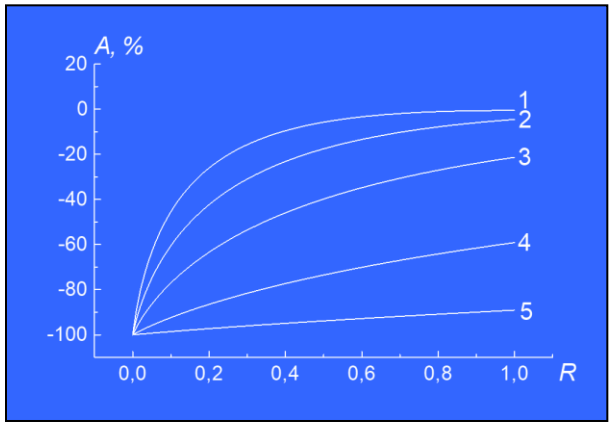
Evolution of amplitude of pulse waves is defined by values of passing and reflecting coefficients in all nodes of bifurcation. In particular we can obtain matrix, which consists of passing and reflecting coefficients in all nodes of the graph. If absolute value of the product of all matrix determinants in each node is more than 1, then amplitude of pulse waves grows up with the time.

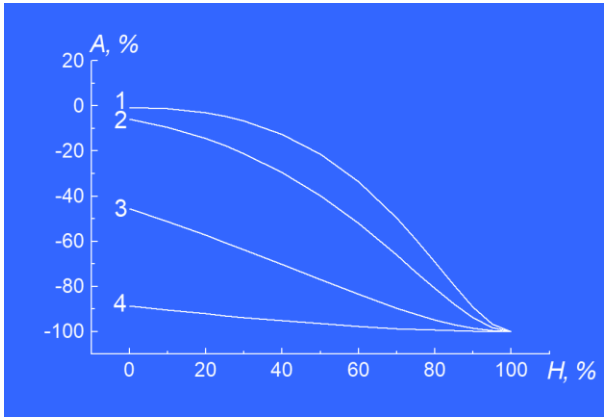
$$\left| \prod_{l=1}^{m} \det T^{l} \right| > 1$$

$$T^{l} = \begin{pmatrix} k^{l}_{1\to 1} & \dots & k^{l}_{n\to 1} \\ \vdots & \ddots & \vdots \\ k^{l}_{1\to n} & \dots & k^{l}_{n\to n} \end{pmatrix}$$

Takaysu disease

The results, obtained by means of analytic methods, allowed to establish relationship between degree of symptoms of Takaysu disease (deficient pulse, determined, in mathematical terms, by values of transport coefficients) and the degree of arterial involvement.





1 - H=0%, 2 - H=25%, 3 - H=50%
4 - H=75%, 5 - H=90%

1 - R=1, 2 - R=0.5, 3 - R=0.1
4 - R=0.01

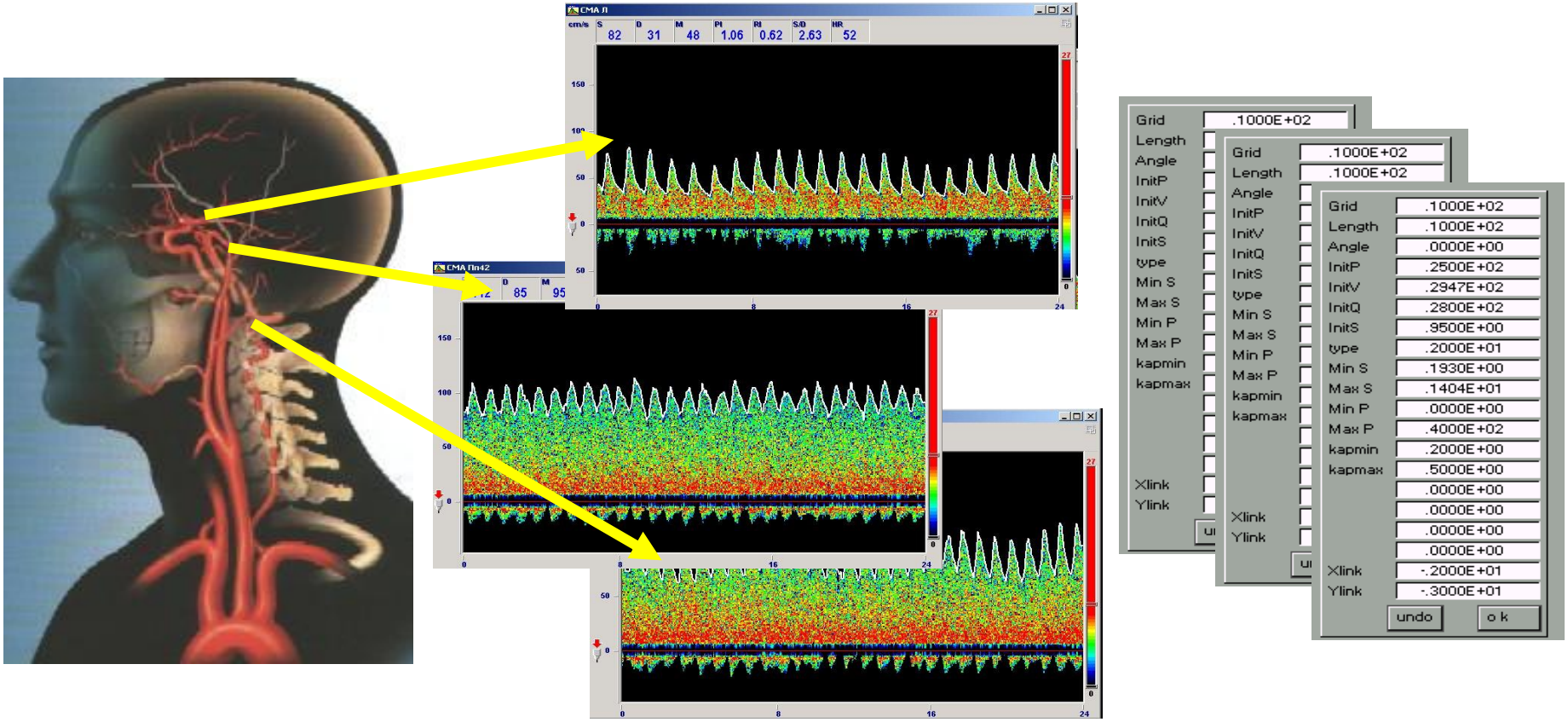
$$A = \frac{A_i - A_{i,\,н.}}{A_{i,\,н.}} 100\%, \qquad R = \frac{\bar{\theta}}{\bar{\theta}_{н.}}, \qquad H = \frac{\bar{s}_{н.} - \bar{s}}{\bar{s}_{н.}} 100\%,$$

$A_{i,\,н.}$ - **Amplitude of pulse wave in i-*th* vessel in uninjured vascular system**

A_i - **Amplitude of pulse wave i i-*th* vessel in injured vascular system**

Software

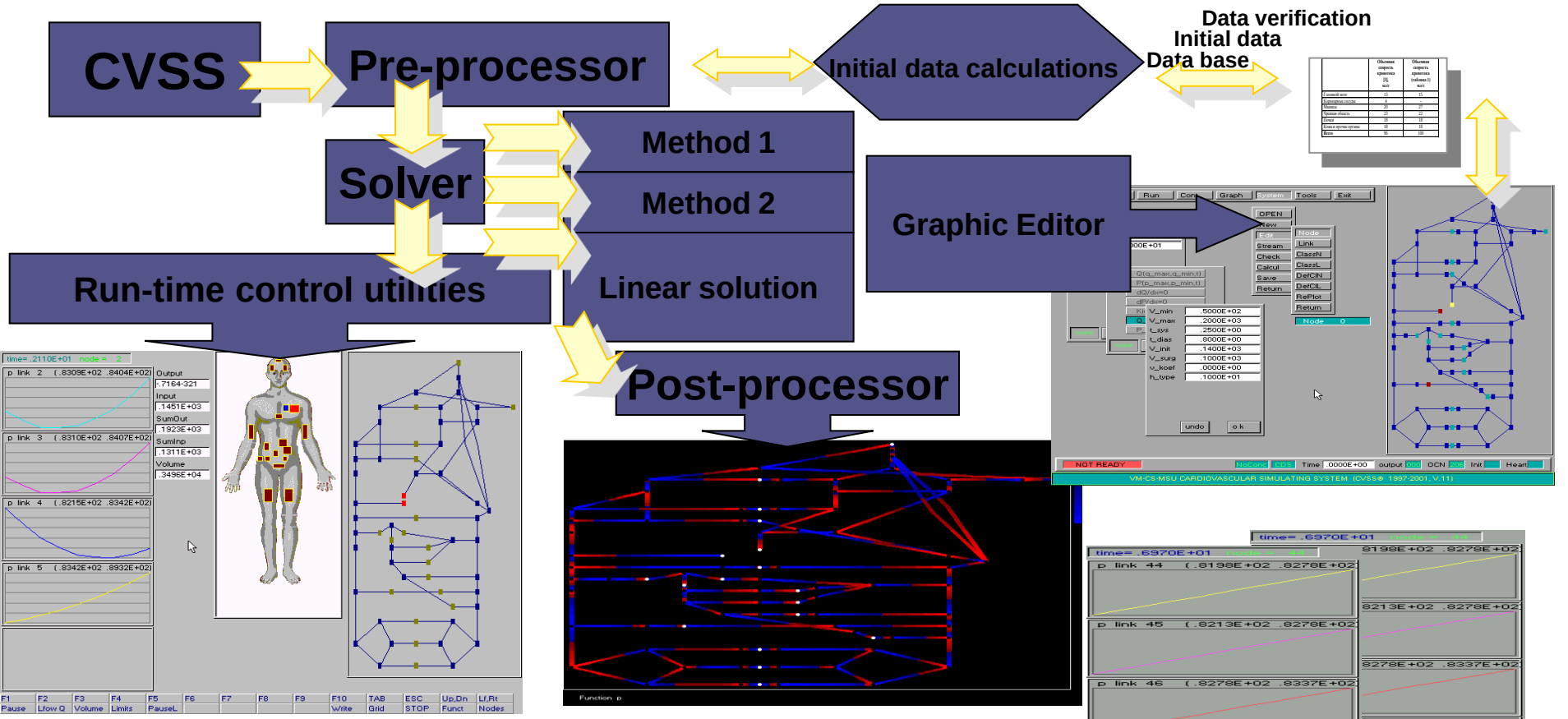
Ability to consider personalized parameters of human cardiovascular system



Development of data base of main arteries and venous properties allows to study general hemodynamics regularities.

The adaptation of models parameters to personal clinical data of the patient, taking into account identified pathological and topological features, allows to use CVSS software in practical means.

CVSS (Cardio-Vascular Simulating System ver.6.0-11.2) software (research version) was created to perform hemodynamics computer simulation



CVSS contains pro-processor, which allows to construct graphs of any complexity of the whole cardiovascular system or of any its part, as well as to input any system parameters. Also CVSS contains a set of mathematical models of such organs as heart, kidney, tissues, etc., models of various regulation systems.

Results of numerical simulation are presented numerically and visually, in the the form of data and graphic, representing calculated data on the selected vessels or on the whole graph. Special options to store and analyze all numerical data are available.

Features of the 3D version software

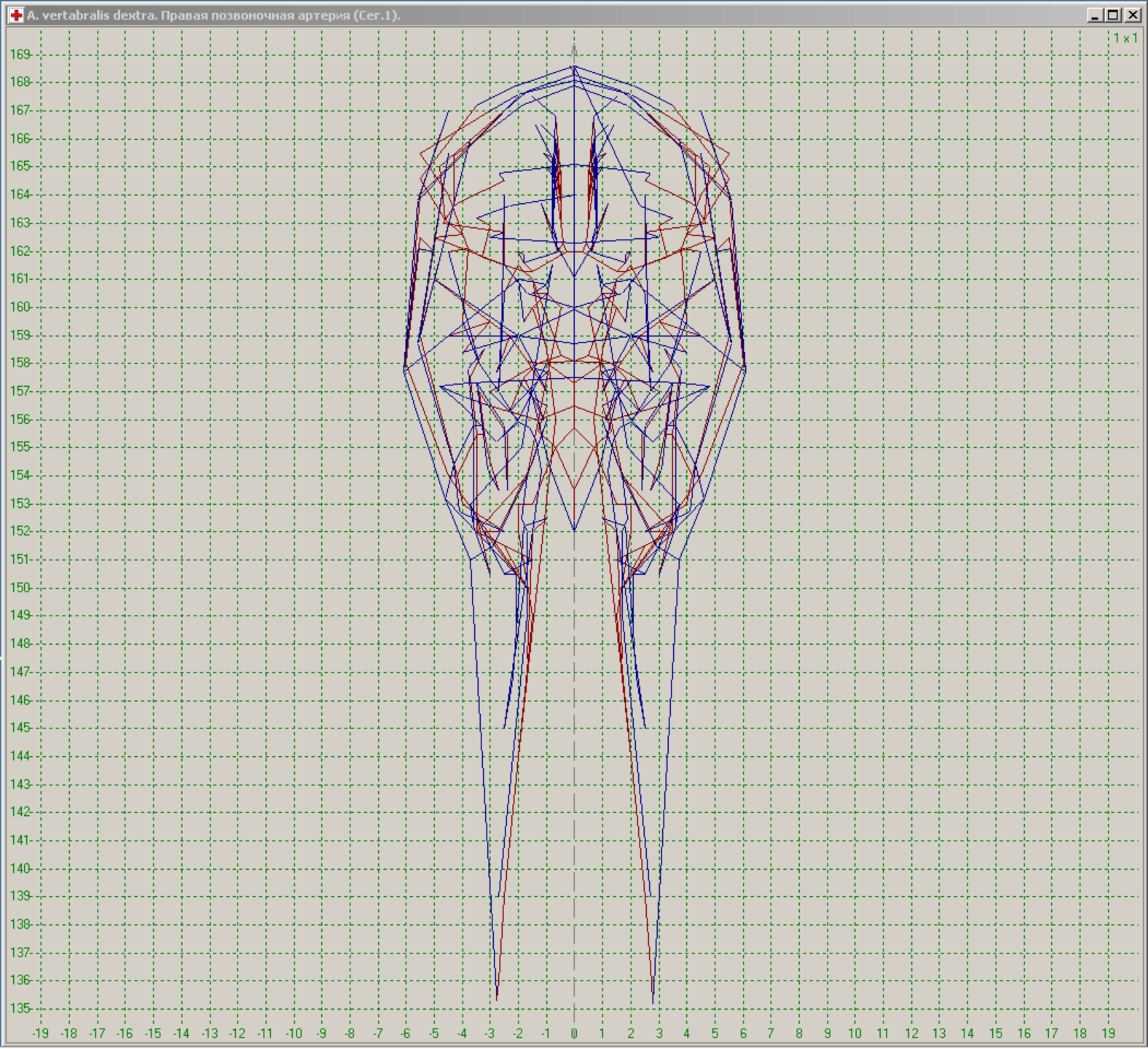
1) The representation of an arbitrary three-dimensional graph of cardiovascular system with the possibility of building it up, as well as narrowing.

2) Move the graph in general, as well as its parts in space to account for the influence of gravity when changing body position.

3) The use of realistic 3D models for visualization of blood vessels and the calculation results in the familiar visual form.

4) The development of advanced tools for editing, storage and control significantly increased input data volume.

5) Multi-threaded implementation of software for parallel computation process and visualization of the results.



601-602.mdl

Сосуды (Links)

Beg	End	Type	AV
1	3	0	1
2	4	0	1
3	51	0	1
4	103	0	1
5	43	0	1
6	41	0	1
7	8	0	1
7	32	0	1
7	36	0	1
8	9	0	1

1

Узлы (Nodes)

№	X	Y	Z
1	-2.8	135.3	14.52
2	2.8	135.3	13.75
3	-2.7	136	11.93
4	2.7	136.5	11.93
5	-2	144	14.2
6	-1.7	147.5	14.6
7	-1.7	150	14
8	-4.5	154	12
9	-6	158	11
10	-5.5	162.5	8

1

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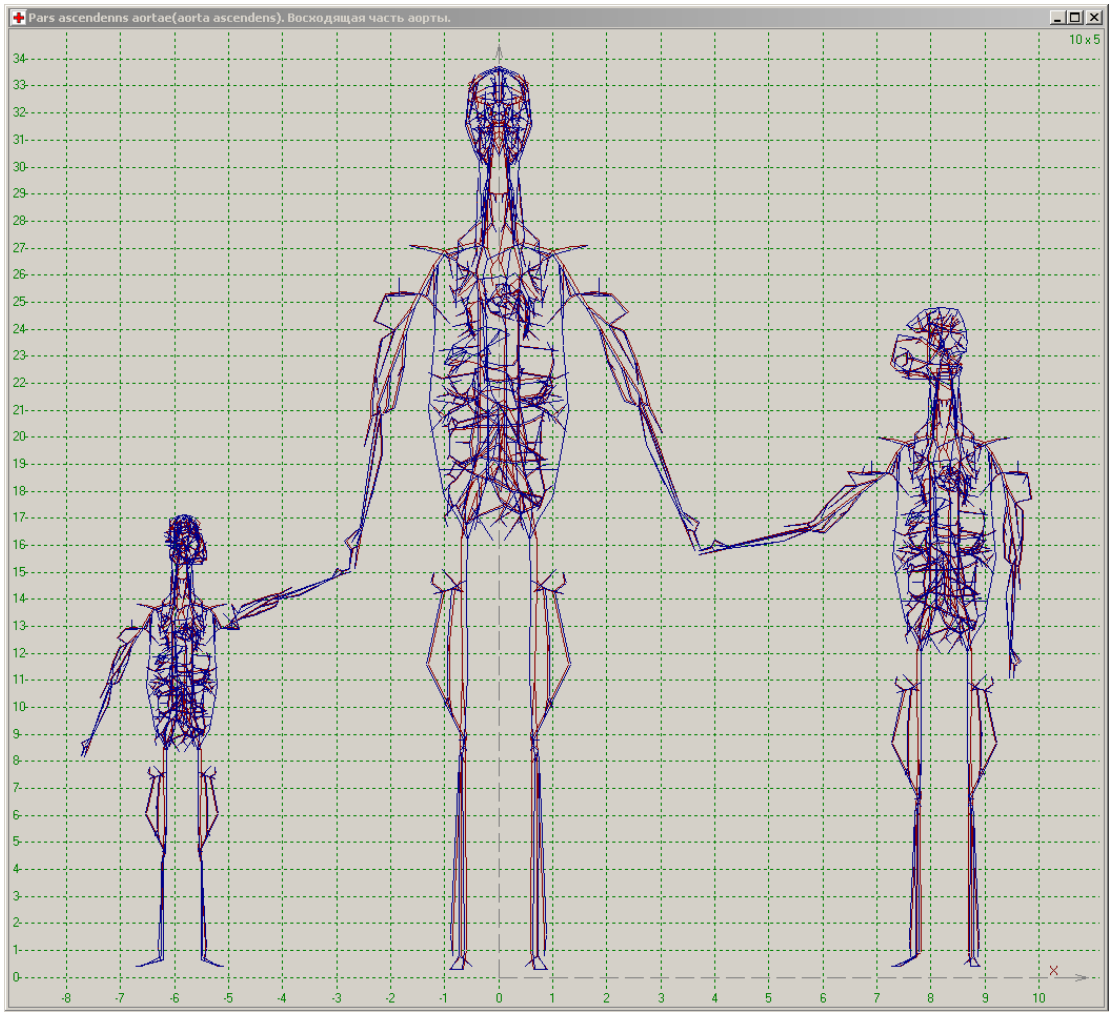
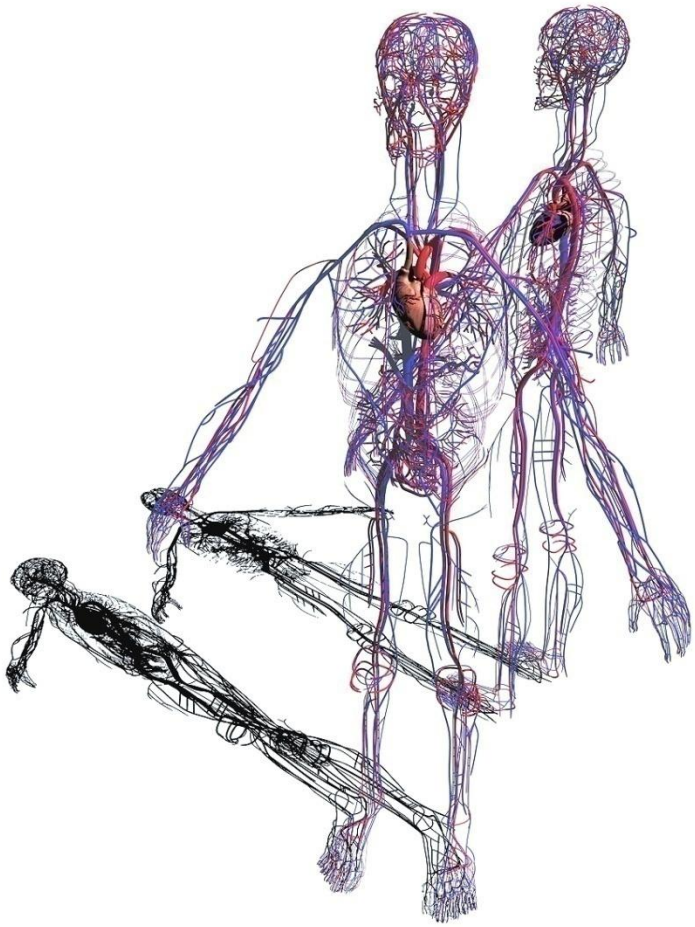
Вычисления ЛГД

Вычисления CVSS

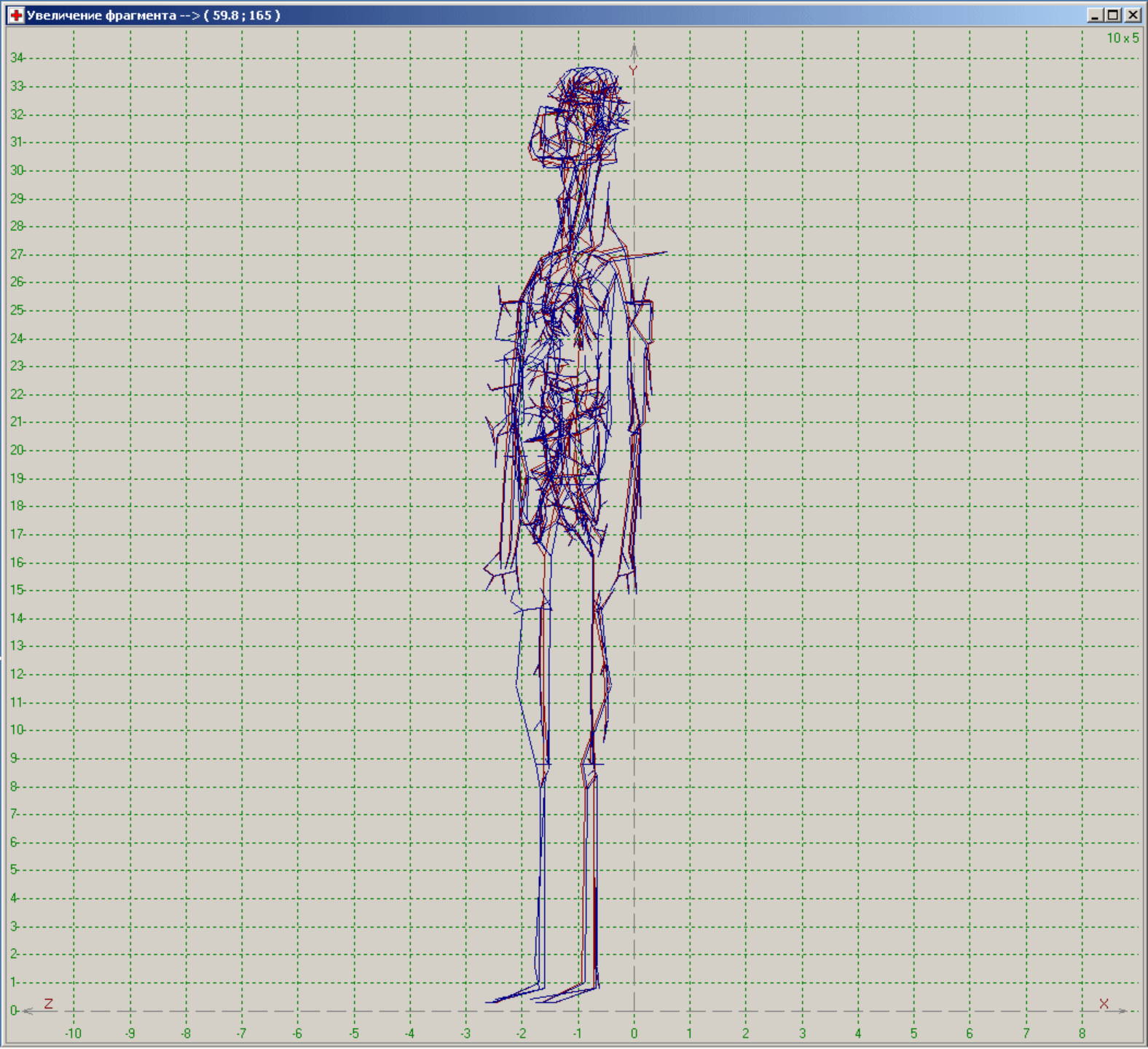
The development of new 3D models



Three-dimensional CVSS graph



ANATOMIUM 3D
A high resolution cardiovascular system 3D model



WithQDir500_1.mdl

Сосуды (Links)

Beg	End	Type	AV
1	2	50	1
2	3	50	1
3	4	50	1
3	99	100	1
4	5	50	1
4	339	100	1
5	6	50	1
5	107	100	1
6	7	50	1
7	8	50	1

1

Узлы (Nodes)

№	X	Y	Z
1	-1	128	17.8
2	-1.5	131	18.5
3	-1	132	17.12
4	-0.2	133	15.75
5	0.5	132	14.38
6	1.5	129	13
7	1	113	13.9
8	1	111	13.91
9	1	109	13.92
10	1	101	14.5

1

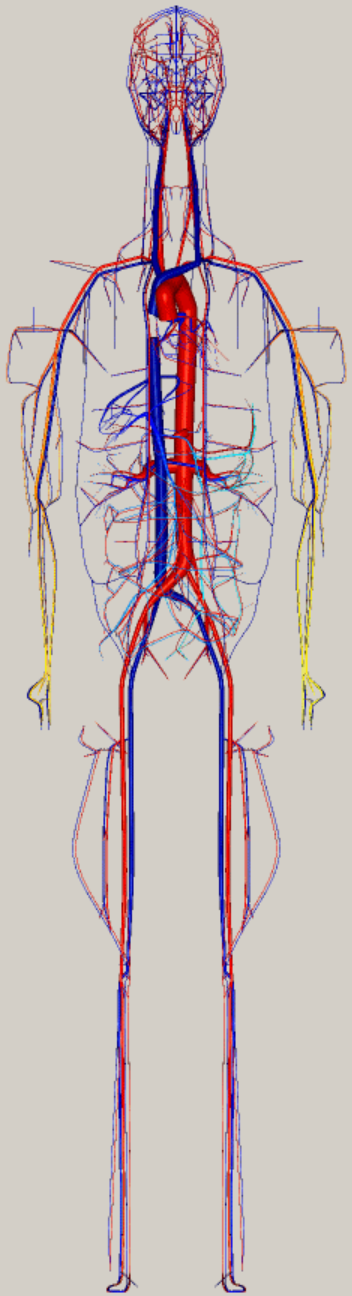
Сохранена 24.01.2012 13:43:09

Модель с корректно расставленными направлениями потоков QDir и радиусами сосудов для визуализации VisRad

Вычисления ЛГД

Вычисления CVSS

A. circumflexa humeri anterior. Передняя артерия, огибающая плечевую кость (Сег.3).



WD709.mdl

Вычисления

Графики

Убрать все окна

Отображение 3D

Отступы от Min и Max (%)

Min 0

Max 0

PAMin	0.889665
PAMax	0.997833
PVMin	0.0499
PVMax	0.198031

Зафиксировать Min и Max

Расчет

Продолжить вычисления

Начать заново

Остановить расчет

Параметры расчета

Время: 339.12

Отладка

Записать output.###

Считать output.###

Время < 1E+10

Дополнительно

Вычисления CVSS

Systemic circulation

Model of heart

Non-conservative model

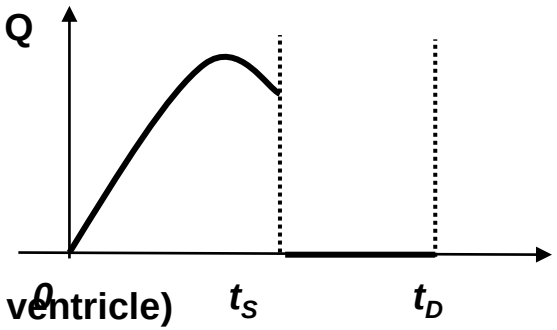
Graph of cardiac output approximates the experimental curve of flow or pressure

t_S – duration of systole

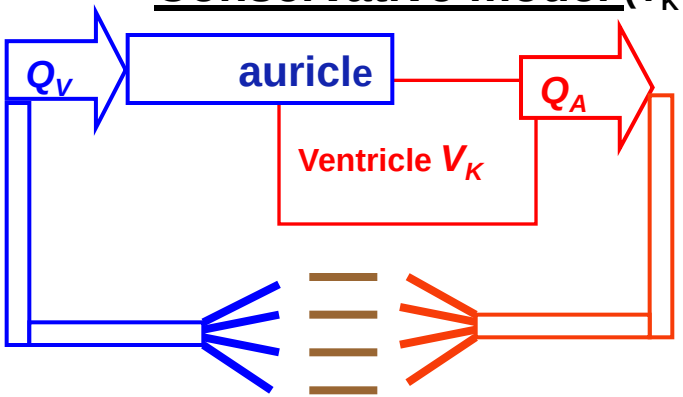
t_D – duration of diastole

V_{surg} – ударный выброс

V_{KD}, V_{KS} –volume of ventricle at the end diastole and systole



Conservative model (V_K – the current volume of blood in ventricle)



$$Q_A(t_S,t_D)=\begin{cases} V_{surg}(4t-\frac{3t^2}{t_S})\frac{1}{t_S^2}, & 0\le t\le t_S \\ 0, & t_S\le t\le t_S+t_D \end{cases}$$

specified parametric function of the cardiac output

$$V_k=\begin{cases} V_{KD}-\int_0^t Q_A(\tau)d\tau, & 0<t\le t_S \\ V_{KS}+\int_0^t Q_V(\tau)d\tau, & t_S\le t<t_D+t_S \end{cases}$$

calculated current volume of the ventricle

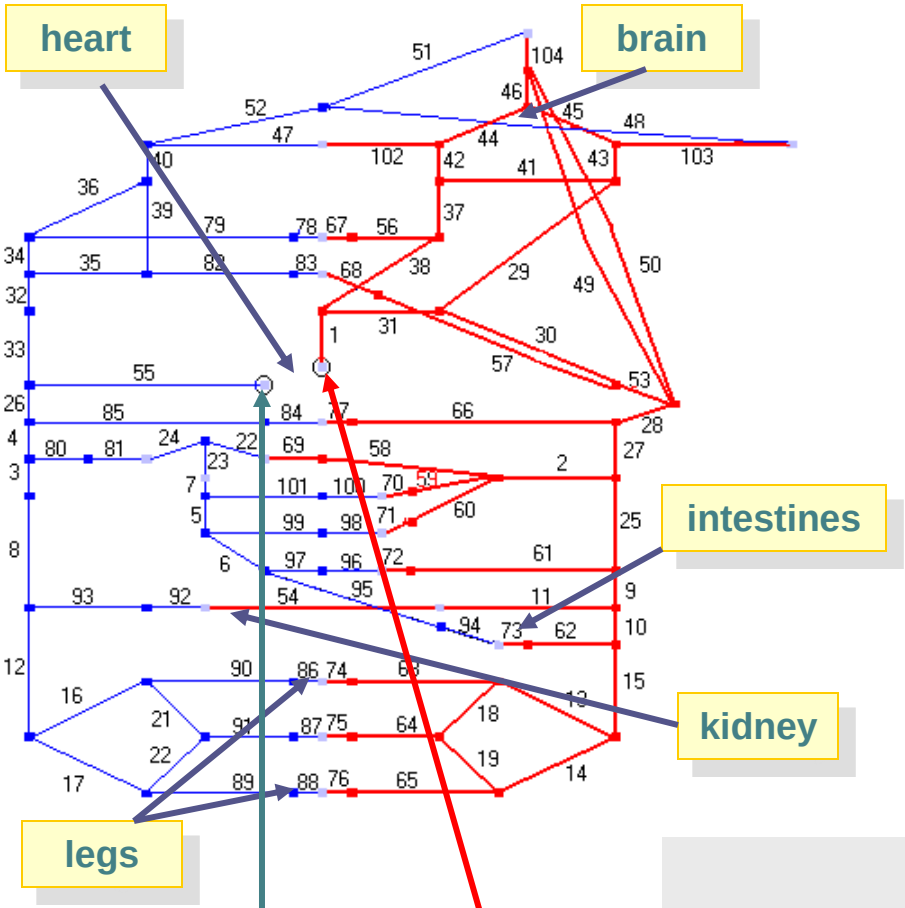
Blood flow Q_V flowing into the auricle determined by cardiac output and blood flow throughout the system. This model allows to keep blood volume, to investigate the mechanisms of regulation.

Regulation on the duration of systole and diastole : V_{surg}=*const*

Regulation of the cardiac output value according to the value of end diastolic volume V_{KD} : $V_{surg}= K_f V_{KD}$

Systemic circulation modeling

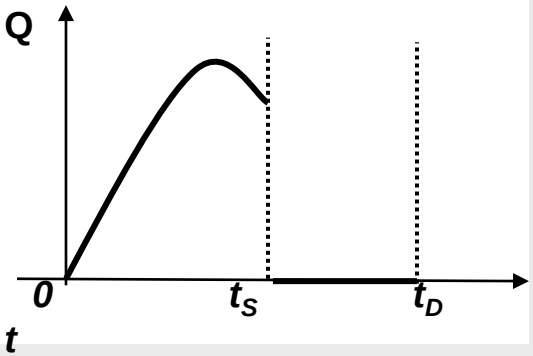
graph of systemic circulation



- Graph topology and content physiologically valid.
- Parameters of vessels(arteries,venous, resistive vessels, capacitive venous, etc.) and heart are in good agreement with physiological data
- All organs are presented by their resistance (in Darcy law)
- In this model heart is represented by self-regulated two sells pump

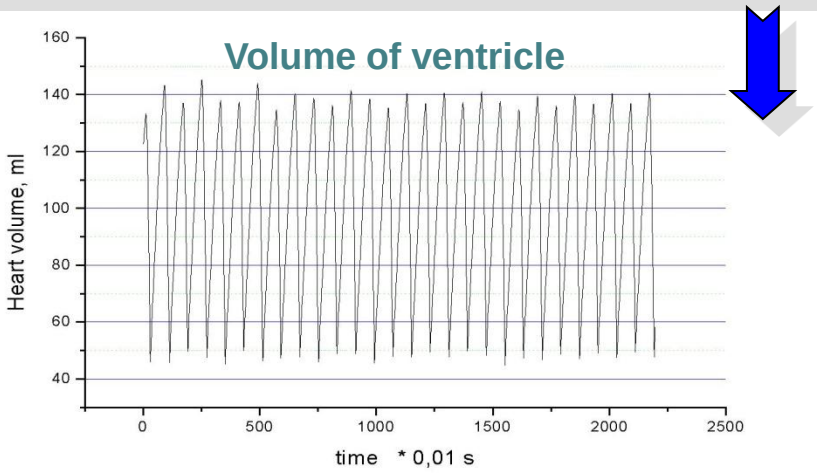
Stroke volume of heart is taken ≅ 85 ml, t_s=0.3 s, t_d=0.5 s.

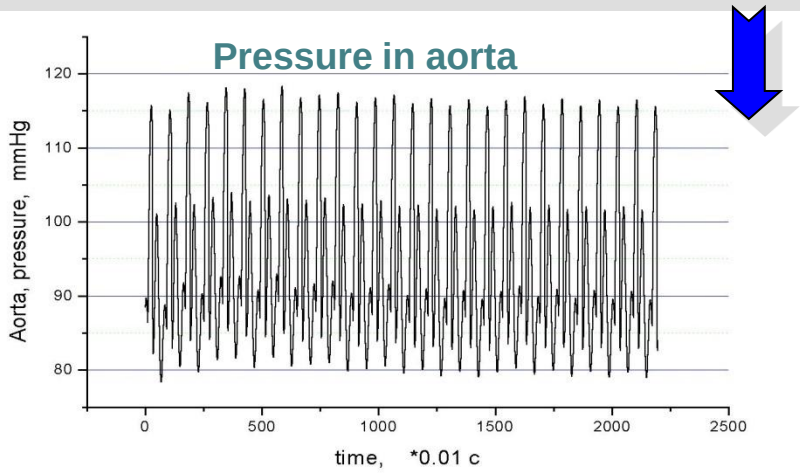
$$V_k = \begin{cases} V_{KD} - \int_0^t Q_A(\tau)d\tau, & 0 < t \le t_S \\ V_{KS} + \int_0^t Q_V(\tau)d\tau, & t_S \le t < t_D + t_S \end{cases}$$



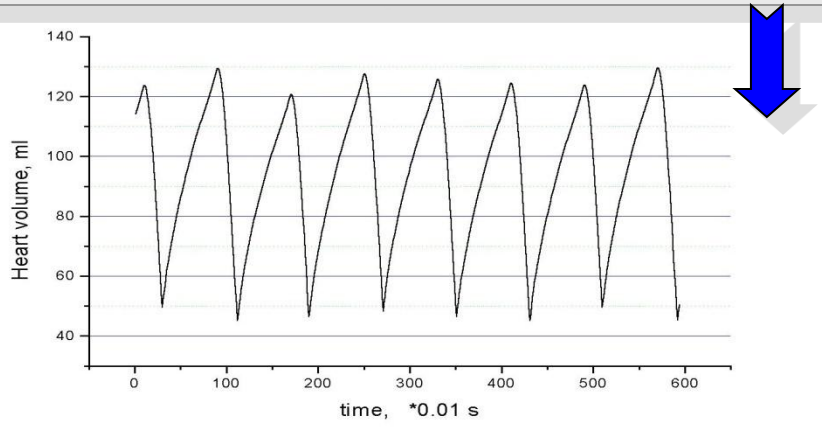
Systemic circulation modeling :quasi-stationary regime

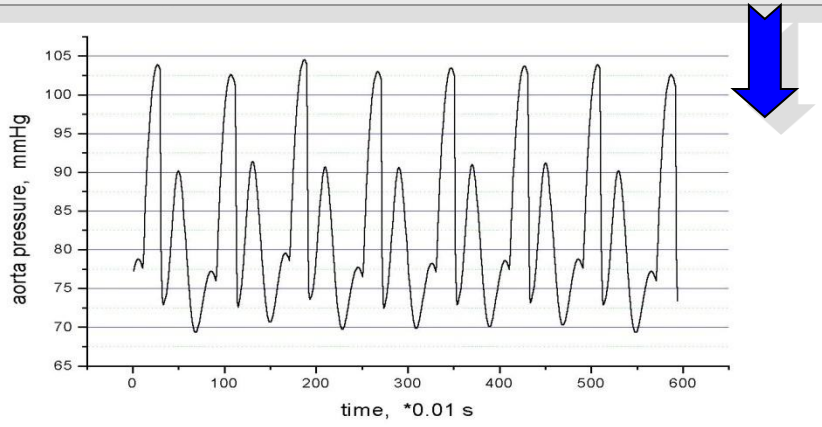
Stroke volume of heart is taken ≅ 85 ml, t_s=0.3 s, t_d=0.5 s. The flow in cardiovascular system is quasi-stationary in the sense that maximum and minimum pressure values does not change for a long time (at least 24 physical hours), and is quasi-periodical. The characteristics of blood flow is adequate to physiological one.





If stroke volume decreases up to 70 ml, the flow is still quasi-stationary and quasi-periodical, but maximum pressure in aorta falls from 118 mmHg up to 104 mmHg. This illustrates how heart parameters influence on hemodynamics in a whole.

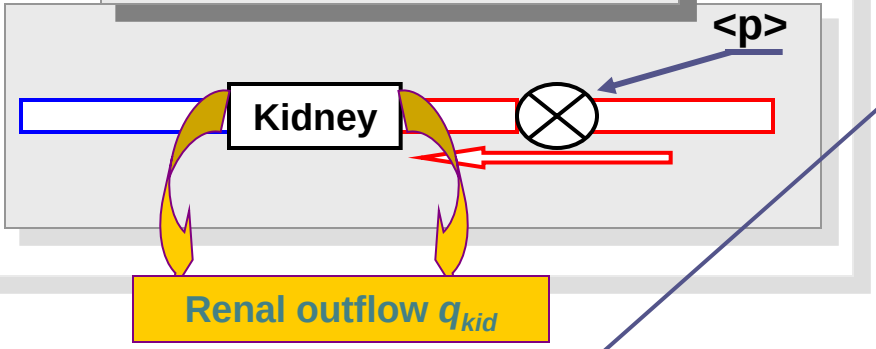


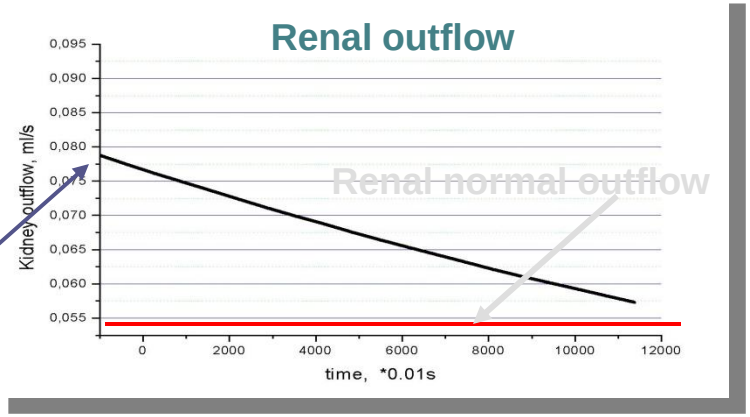


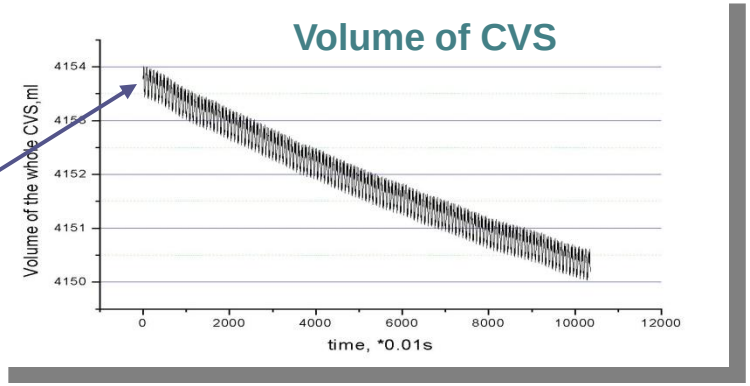
Systemic circulation modeling: renal regulating factor

The simplest kidney model look like that : if average renal pressure <*p*> lager then some p_{stat}, then renal outflow exponentially grows

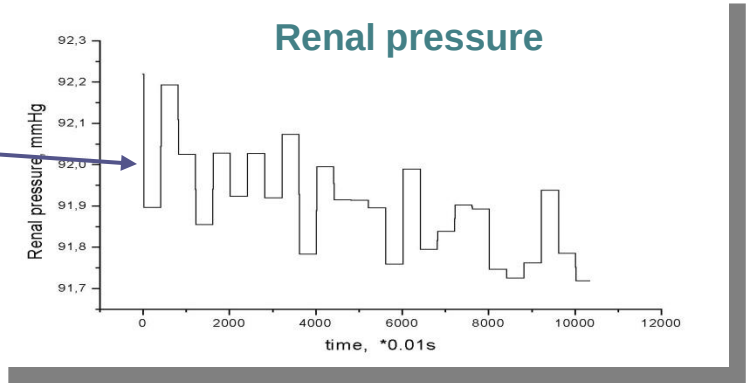
$$q_{kid} = q_{stat}\ \exp(< p > - p_{stat})$$



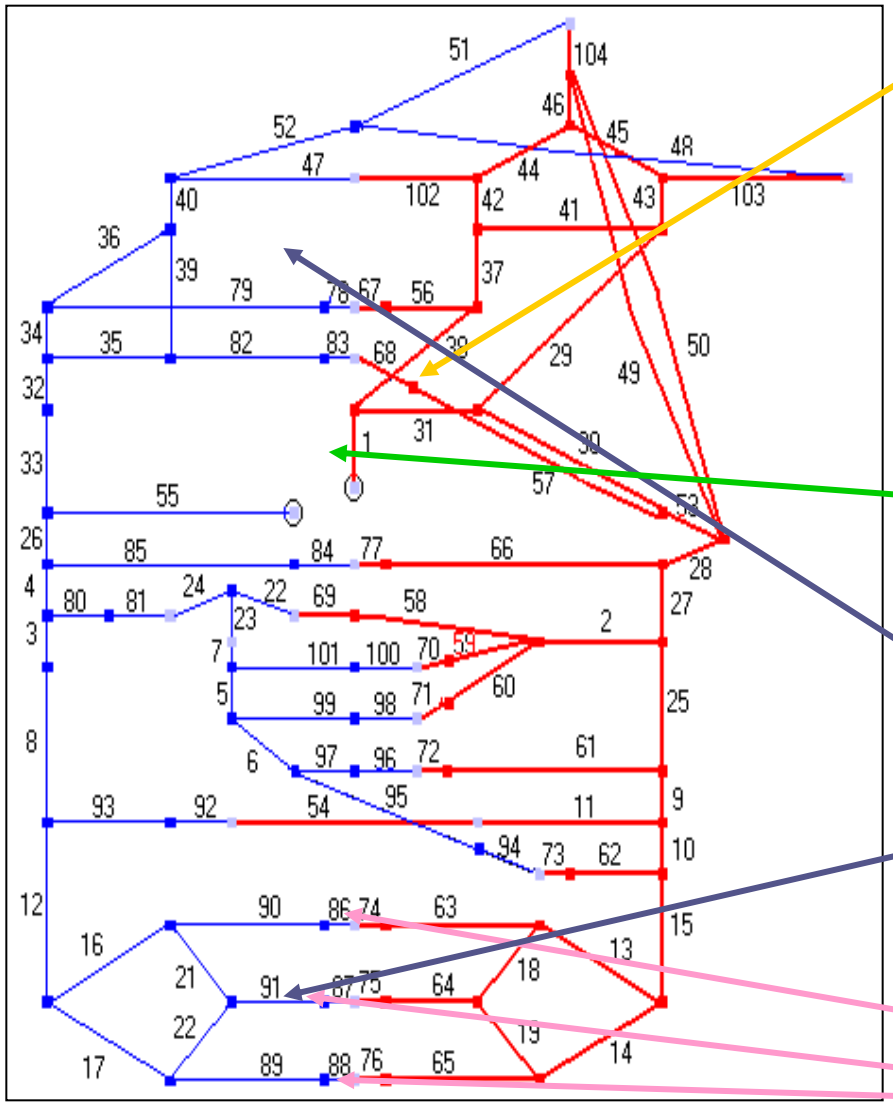




Numerical simulations show, that this model is good to explain and to study renal regulating factor. Really, if, for any reason, renal pressure increases, then renal flow immediately exponentially grows, volume of CVS decreases and renal pressure decreases strongly. Then, renal pressure goes down simultaneously with renal flow and CVS volume, and, exponentially, hemodynamics flow turns to its normal state.



Modeling the baroreceptor neurogenic regulation



Baroreceptors

A pressure change in the system and the aorta

The change of heart's functioning mode

The change in tissue filling

The change of tone of vessels

Modeling the baroreceptor neurogenic regulation

Schematic diagram of neurogenic regulation

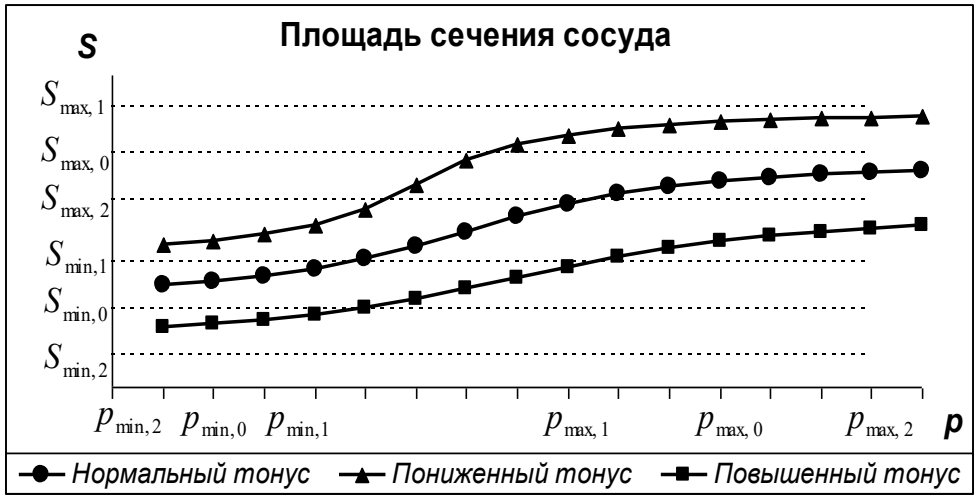
Increase of blood pressure → **Increase of impulses from baroreceptors** → **Reaction of CNS** → **•The decrease of vascular tone. •The increase in fullness of the tissues by the blood. •The decrease in the frequency of contractions of the heart.**

The decrease of blood pressure: the reverse process

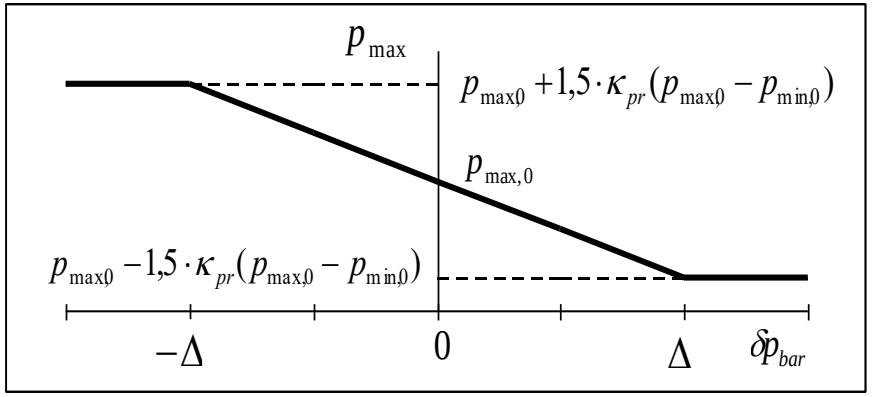
The mechanism of neuroregulation is configured to keep a specific value of pressure p_{bar} **in a vessel containing baroreceptors that respond to the deviation** $\delta p_{bar}(t)$,

$\delta p_{bar}(t) = p_{сред}(t) - p_{bar}$, **где** $p_{сред}(t) = \frac{1}{T}\int_{t-T}^{t} p(\tau)d\tau$ **– the average pressure in the vessel.**

Model of changes of vascular tone



The pressure increase leads to an increase in cross-sectional area and reduced stiffness of vessels wall

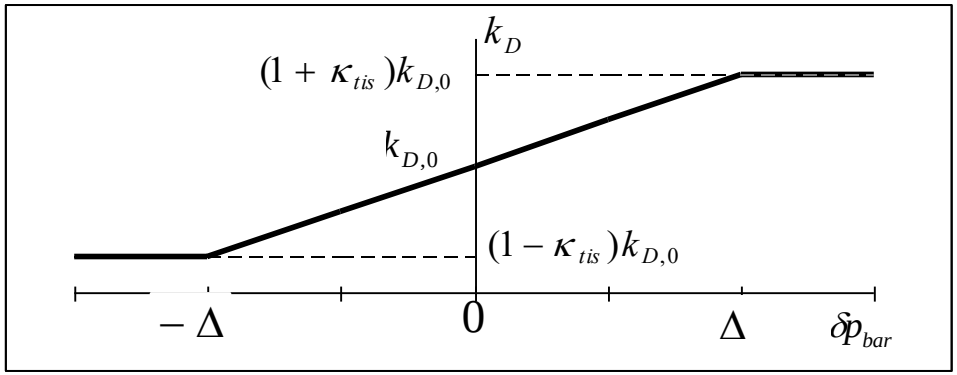


Modeling the baroreceptor neurogenic regulation

The model of change of fullness of the capillaries (tissues)

Increase (decrease) in pressure leads to an increase (decrease) in the number of capillaries in the tissues filled with blood. In the framework of 0D models that can be interpreted as the increase (decrease) of filtration coefficient in Darcy's law: $uS = K_D(p_1 - p_2)$

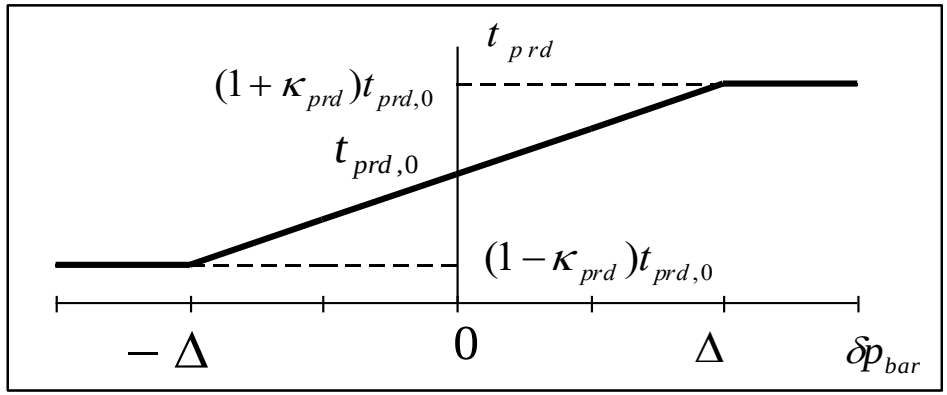
$$k_D = \begin{cases} (1-\kappa_{tis})k_{D,0}, & \delta p_{bar} < -\Delta \\ (1+\kappa_{tis}\dfrac{\delta p_{bar}}{\Delta})k_{D,0}, & -\Delta \le \delta p_{bar} \le \Delta \\ (1+\kappa_{tis})k_{D,0}, & \delta p_{bar} > \Delta \end{cases}$$



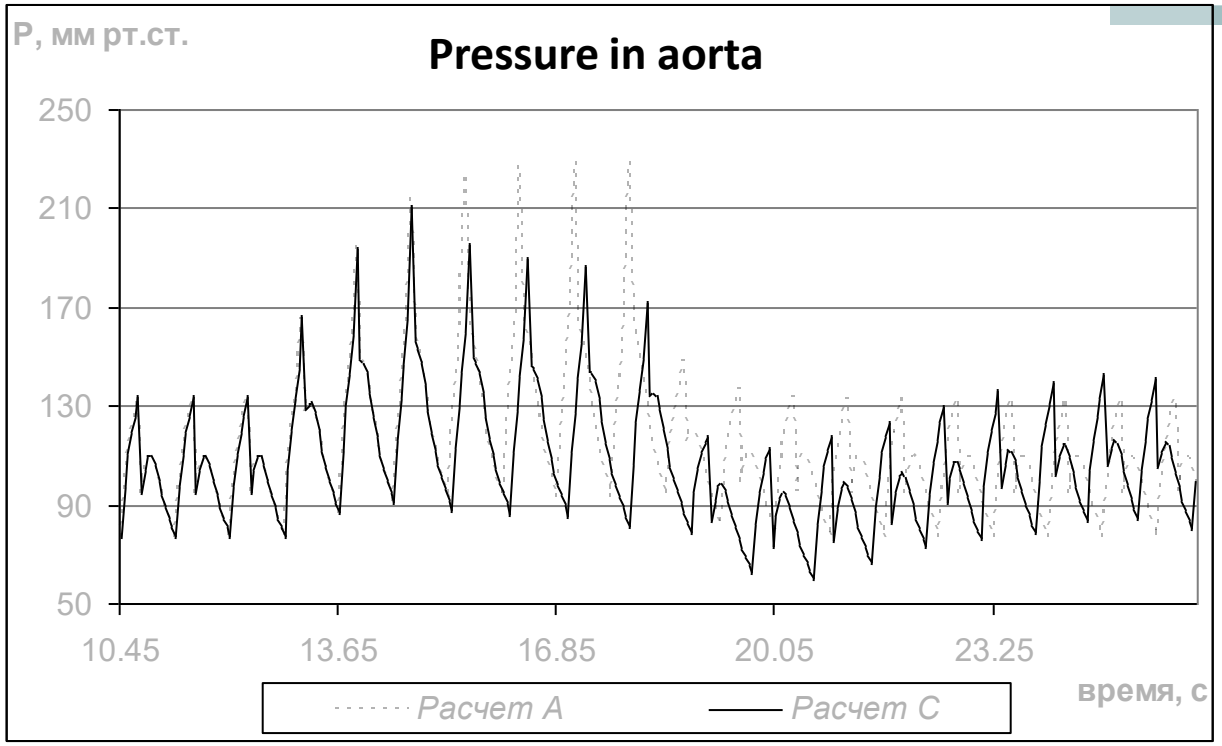
Model of contraction frequency changes in heart

Increase (decrease) in pressure leads to an increase (decrease) of duration of the cardiac cycle t_{prd} **.**

$$t_{prd} = \begin{cases} (1-\kappa_{prd})t_{prd,0}, & \delta p_{bar} < -\Delta \\ (1+\kappa_{prd}\dfrac{\delta p_{bar}}{\Delta})t_{prd,0}, & -\Delta \le \delta p_{bar} \le \Delta \\ (1+\kappa_{prd})t_{prd,0}, & \delta p_{bar} > \Delta \end{cases}$$

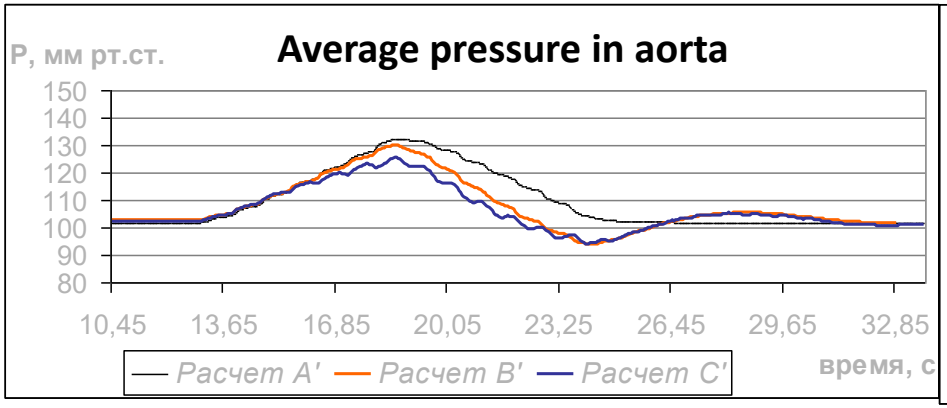


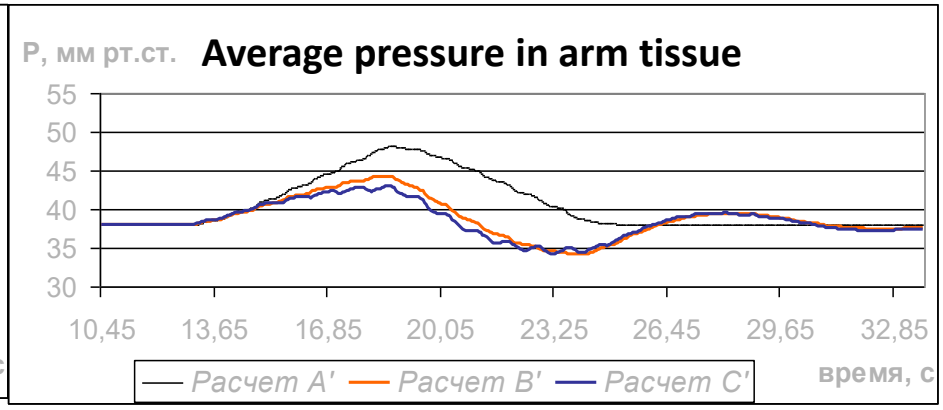
Modeling the baroreceptor neurogenic regulation



After a shot increase of blood pressure neurogenic regulation leads to return pressure to normal. Average pressure in the aorta and in the arteries of the hand reduced .

The calculation A – the flow without regulation, B – flow with partial control, C – flow with full regulation





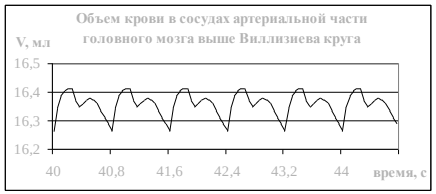
Cerebrospinal fluid flow

Kelly's model

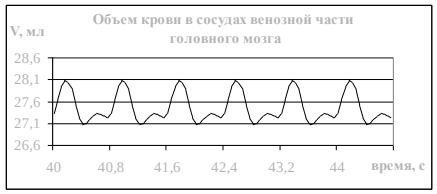
What causes the motion of spinal fluid ?
It is supposed, that the pulsating cerebral blood flow in area, restricted by solid cranial bones, causes pulsating lymph flow.

Volume of cerebral blood upon time

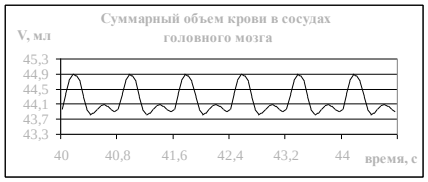
arterial



venous



Total volume



Experiment: appr. 1.0 ml per cardiac cycle

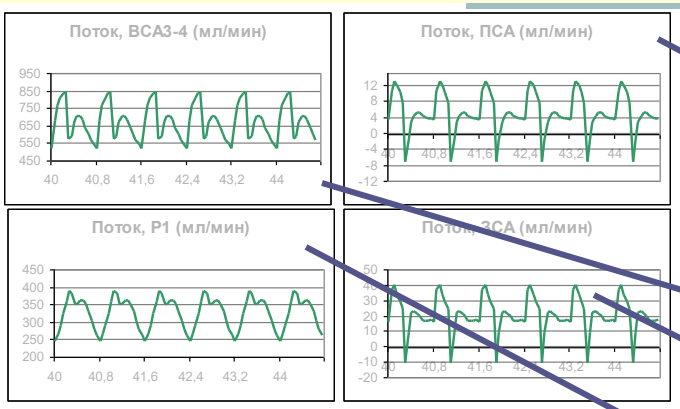
Numerical modeling: appr. 1.48 ml per cardiac cycle

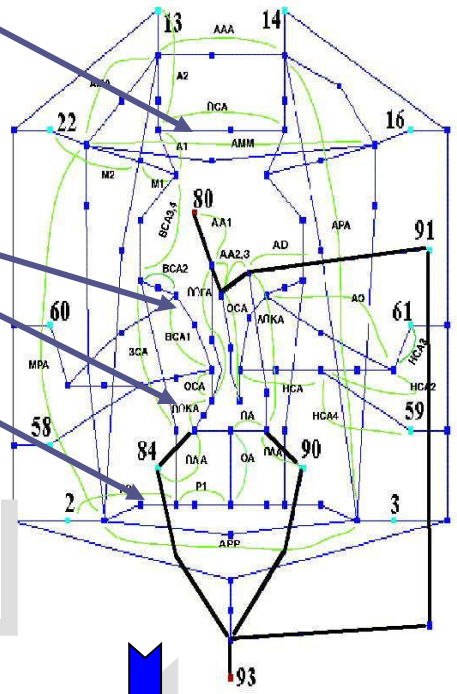
Cerebrospinal fluid flow

1

Graph of cerebral vessels + elements of the systemic circulation :

- two-chamber heart - aortic arch - arteries, veins, tissues of the hands - point resistance and generalized blood vessels with relevant volumes and resistive properties



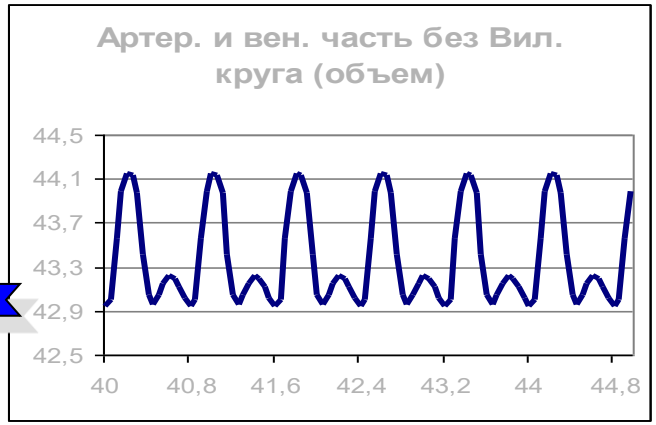


The model is closed

The interaction of pressure in the aorta and in the brain

2

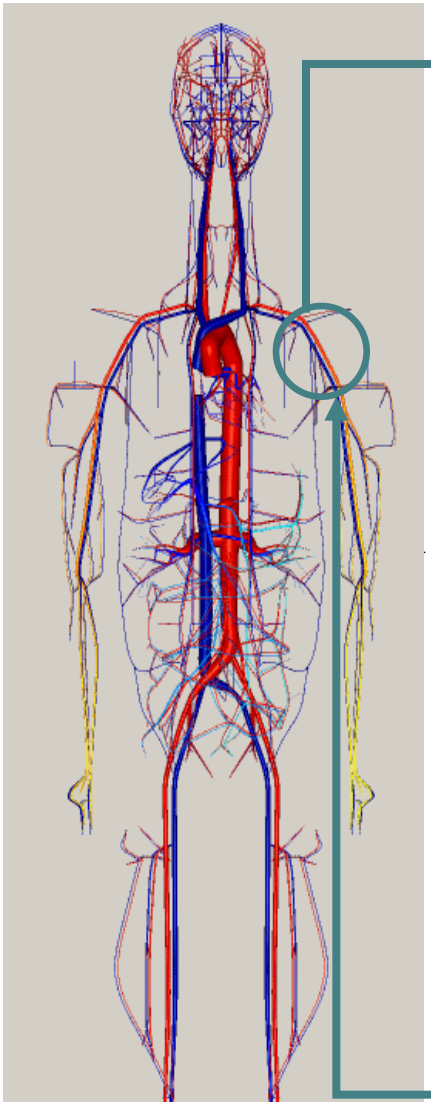
Analysis of changes of blood volume in the venous and arterial parts of the brain for assessment of CSF dynamics in brain according to model of Kelly.

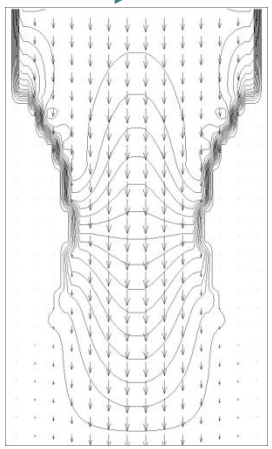


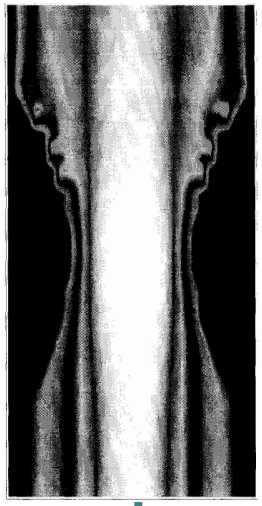
The changes in blood volume in the vessels above circle of Willis in calculations is 1.8 ml for one period of the heartbeat, which is consistent with experimental data according to which between the head and the spinal cord during the period of contraction of the heart circulates approximately 1 ml of cerebrospinal fluid.

Multiscale Modeling

Solution of 2D or 3D Navier-Stokes equations in selected vessels in order to investigate the flow in area of vessels wall singularities.







$$\begin{cases} div(\vec{v}) = 0 \\ \frac{\partial \vec{v}}{\partial t} + (\nabla, \vec{v})\vec{v} + p = -\nu \; rot \; rot\vec{v} \end{cases}$$

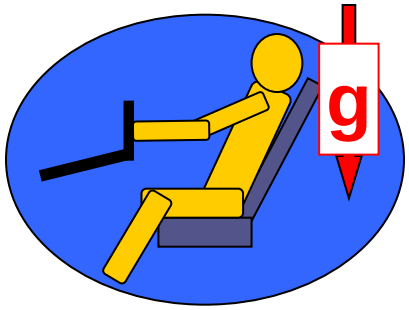
Such approach allows to analyze the mutual influence of global and local hemodynamics.

This is actual when blood flow studed in cases of stenosis, thrombus, etc.

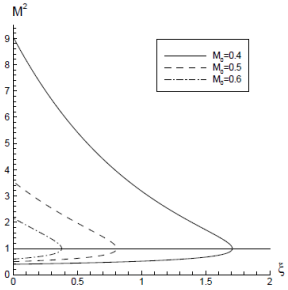
While global hemodynamics is computed in quazi one-dimensional case and is tuned on possibilities of PC, local 3D flow calculations may need parallel HPC abilities.

Gravitation

Gravitational influence



Theoretical studies of viscous fluid (blood) flow in the net of elastic vessels allow to understand, what are the problems which must be solved in order to carry out modeling of gravitational influence.

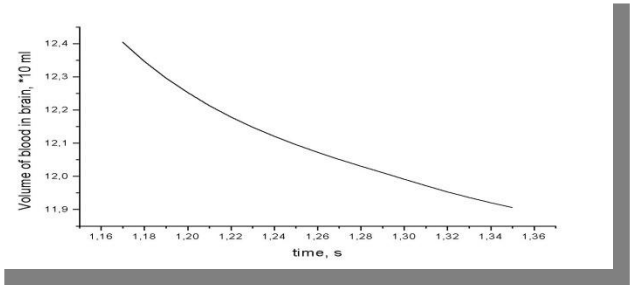


The performed methodic allows to investigate the influence of gravitational forces on human hemodynamics. Numerical simulation on a full graph (systemic circulation + cerebral circulation) helps to investigate changes in hemodynamics under growing gravity

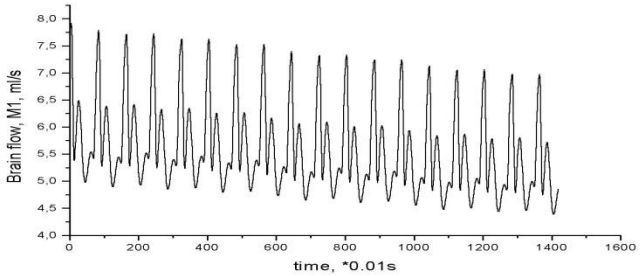
$$q(\tau_s, \tau_d, t) = \begin{cases} Q_{CB} \cdot (4t - 3t^2/\tau_s)/\tau_s^2, & 0 \leqslant t \leqslant \tau_s \\ q_{min}, & \tau_s < t \leqslant \tau_d. \end{cases}$$

$$P(g_{max}, g) = \begin{cases} P_C - g \cdot (P_C - P_{C_{min}})/g_{max}, & 0 \leqslant g < g_{max}, \\ P_{C_{min}}, & g \geqslant g_{max}. \end{cases}$$

Volume of blood in brains strongly falls under influence of gravitation force



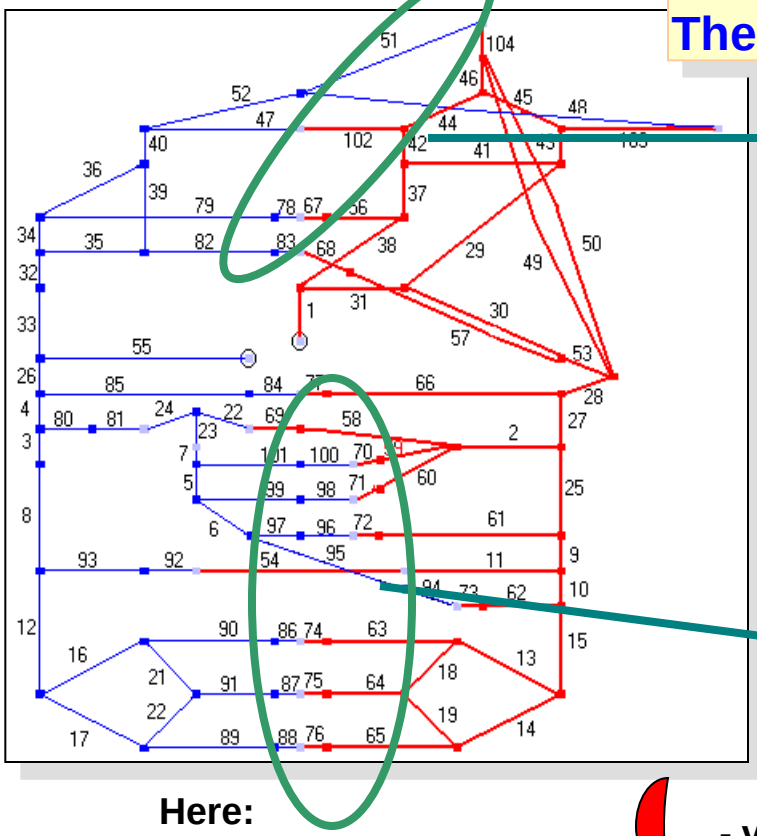
Blood supply of brain sections also decreases



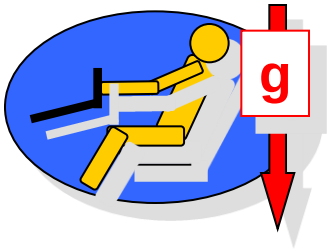
Quasi-stationary model of hemodynamics taking into account gravitational acceleration

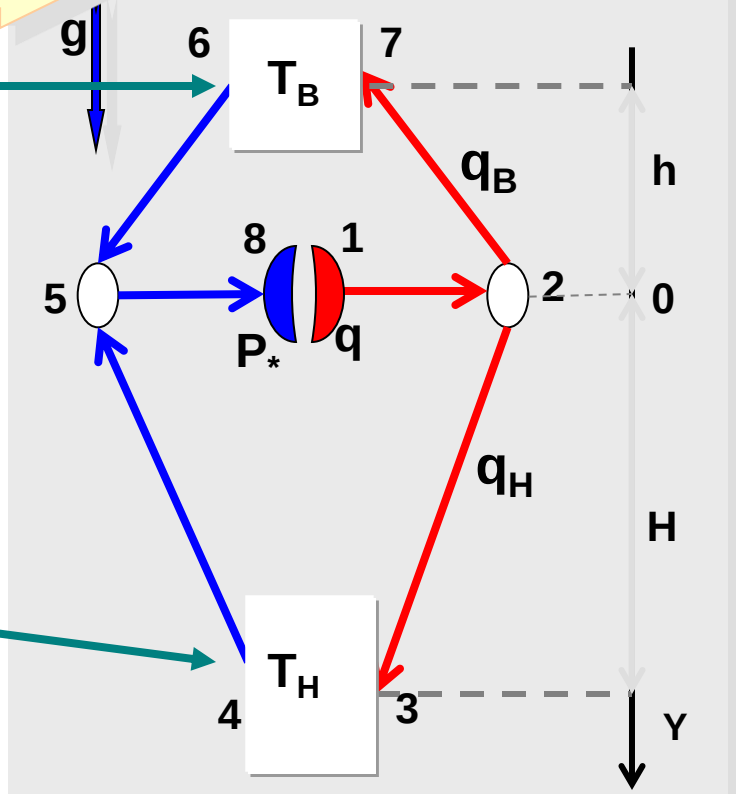
❑ **First step:assumption: S=S(x) – vessels are hard pipes, so HDM equations look like:**

$$\frac{\partial us}{\partial x} = 0, \quad \frac{\partial}{\partial x}\left(\frac{u^2}{2} + \frac{p}{\rho}\right) = F_{TP} + g\cos\varphi$$



The simplest graph





Here:
q – output heart flow,
P_* - pressure in auricle,

- ventricle
- auricle

- arterial part,
- venous part,

T_B, T_H – effective (integrated) tissues

Results of analytical investigation

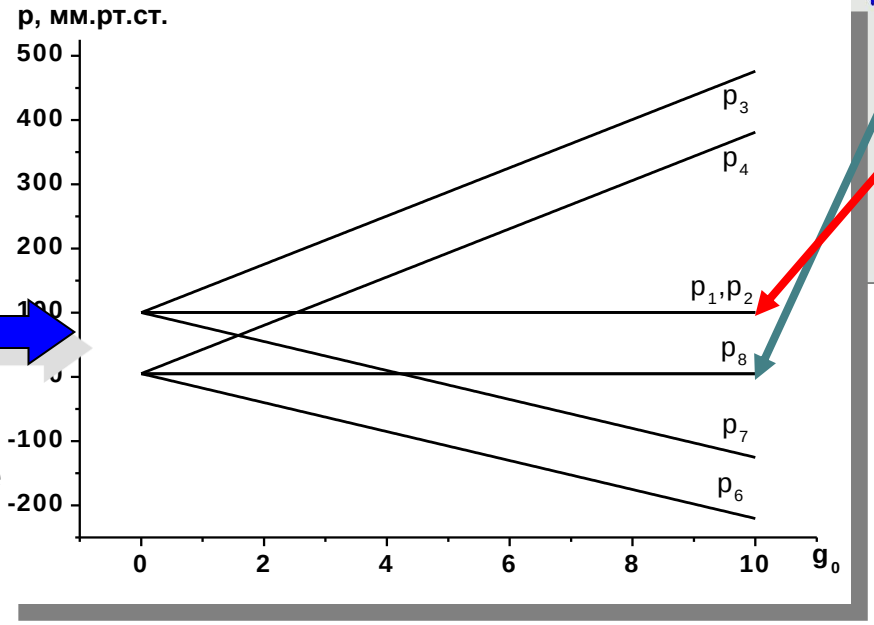
1

❑ **Hard** vessels:

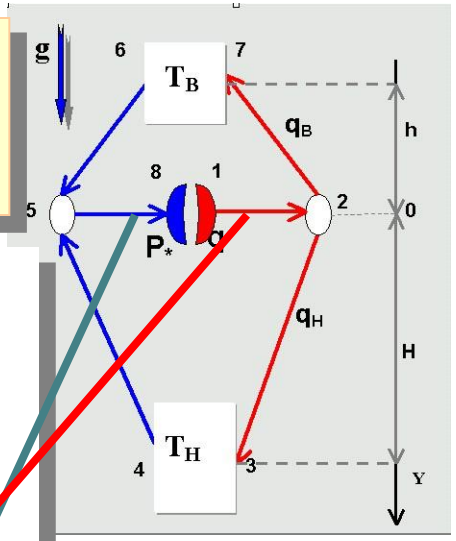
- in this case we can obtain explicit formula for flows:
(here χL – corresponding total resistance)

$$q_{B,H} = \frac{\langle \chi L \rangle_{B,H} \cdot q}{\langle \chi L \rangle_H + \langle \chi L \rangle_B} = const_{B,H}$$

- The pressure plot in vessels depending on g/g_H, $g_H \cong 10$ m/s^2 - acceleration of gravity looks like that.



Note, that pressure in vessels (5,8) and (1,2) practically does not vary while gravity grows.



2

❑ Influence of **flexibility** (vessels slightly elastic):

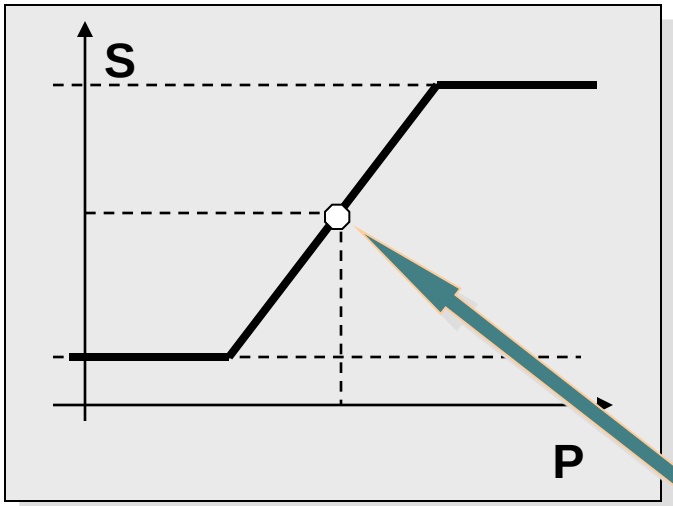
- flow change slightly in the comparison with the case of “hard” pipe.

- appearance of **supersonic** flows near nodes is possible.

3

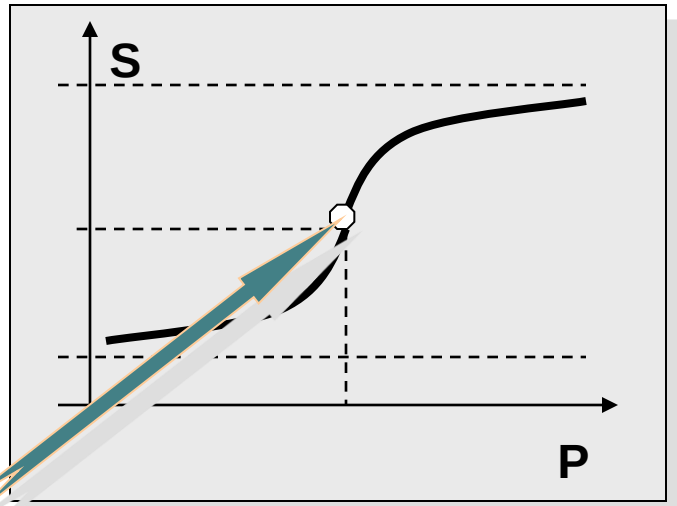
❑ *Influence of vessels* ***equation of state***

- *appearance of supersonic flows strongly* depends on the type of state equation



- location of "stationary" point also influence on type of flow

Stationary points



High possibility of supersonic flow

Low possibility of supersonic flow

4

❑ Influence of aurical pressure P_*.

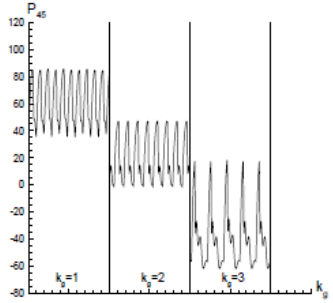
- when P_* vary then the picture of blood flow changes radically
- when P_* increases then pressure in aorta increases strongly.

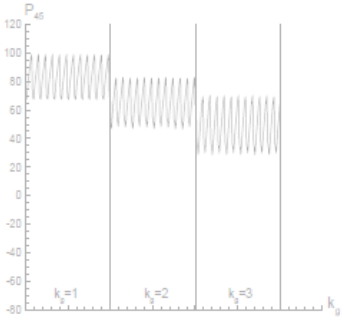
5

❑ Numerical modeling on the whole CVS graph proves obtained analytical results

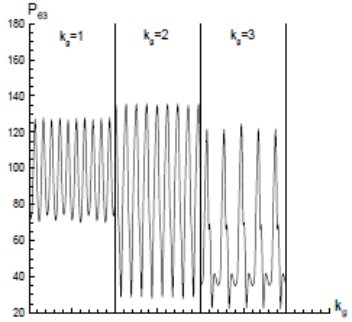
Gravitational influence

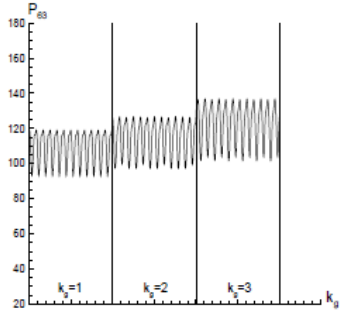
middle cerebral artery



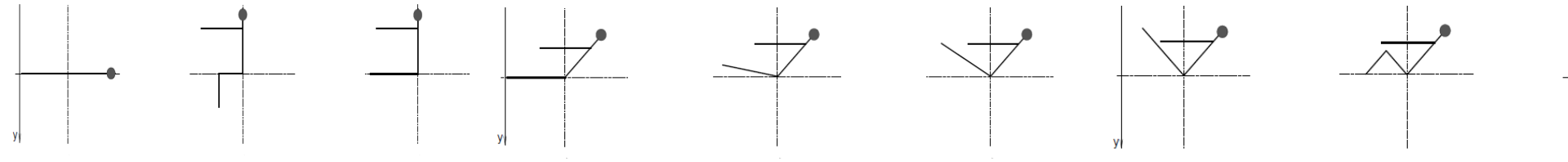


femoral artery





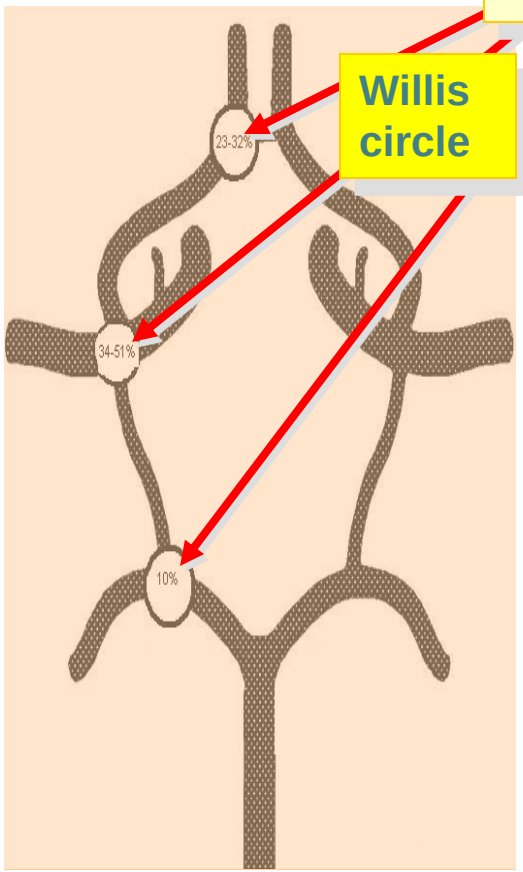
	$\overline{q}_{45}$, $k_g = 0$	$\overline{q}_{45}$, $k_g = 1$	$\overline{q}_{45}$, $k_g = 2$	$\overline{q}_{45}$, $k_g = 3$
N_1	0,9859	0,9854	0,9721	0,9449
N_2	0,7255	0,7263	0,4088	0,1127
N_3	0,8473	0,8497	0,6862	0,2670
N_4	1,0280	1,0330	1,0081	1,0231
N_5	1,0832	1,0870	1,1067	1,1338
N_6	1,0925	1,0955	1,1241	1,1508
N_7	1,0923	1,0959	1,1427	1,1664
N_8	1,0914	1,0934	1,1152	1,1670
N_9	1,0203	1,0222	1,0635	1,0219



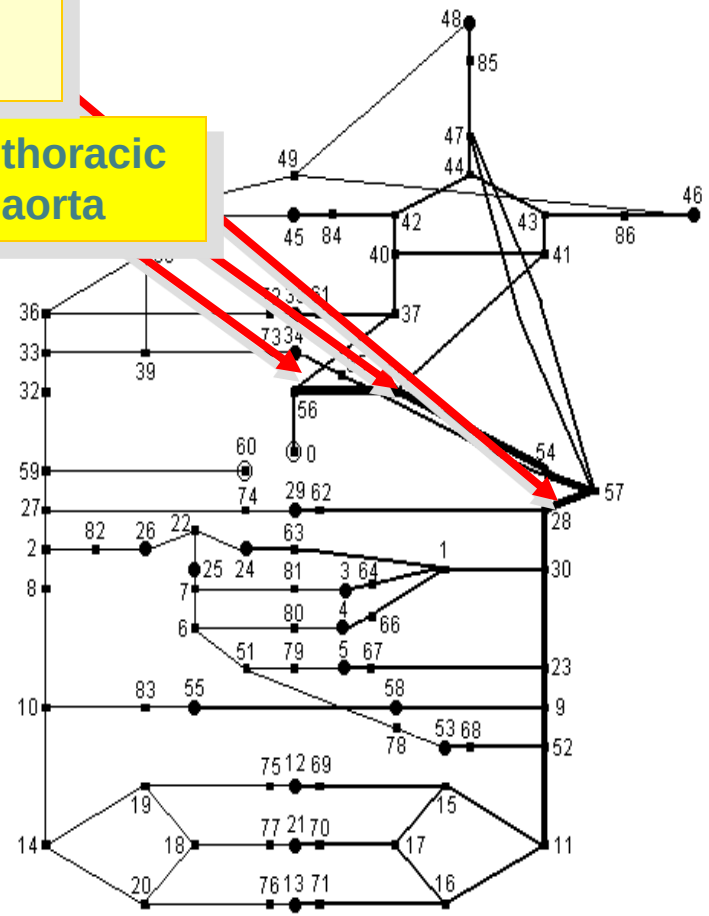
Cerebral Hemodynamic

A hemodynamic factor of arterial vessel aneurism development

Typical location of artery aneurism



Nodes number	Values of the matrix determinants
31	1.002
54	1.002
57	1.002
28	1.005
30	1.005
23	1.001
9	1.01
52	1.001

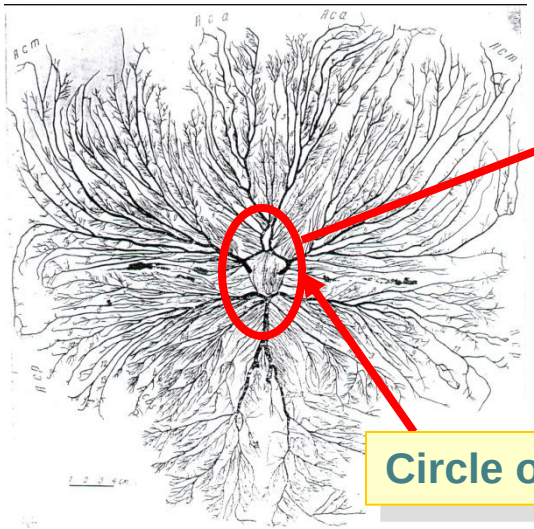


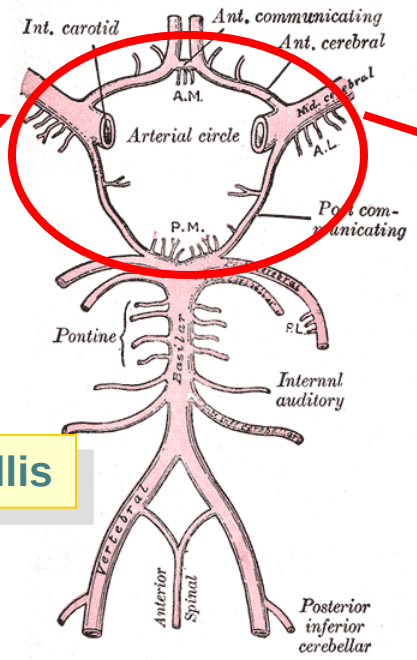
With the help of developed technique it is possible to construct a matrix of passing and reflection coeffitients in the nodes of vascular graph. An evident correlation between typical locations of artery aneursm of cerebral arteries (Willis circle), of thoracic aorta and certain numerical values of corresponding determinants of the matrix was noted.

Cerebral hemodynamics modeling

The first step in hemodynamics modeling is the construction of certain vascular graph. Let us consider the graph of main brain arteries up to the third order of bifurcation.

View of brain arteries



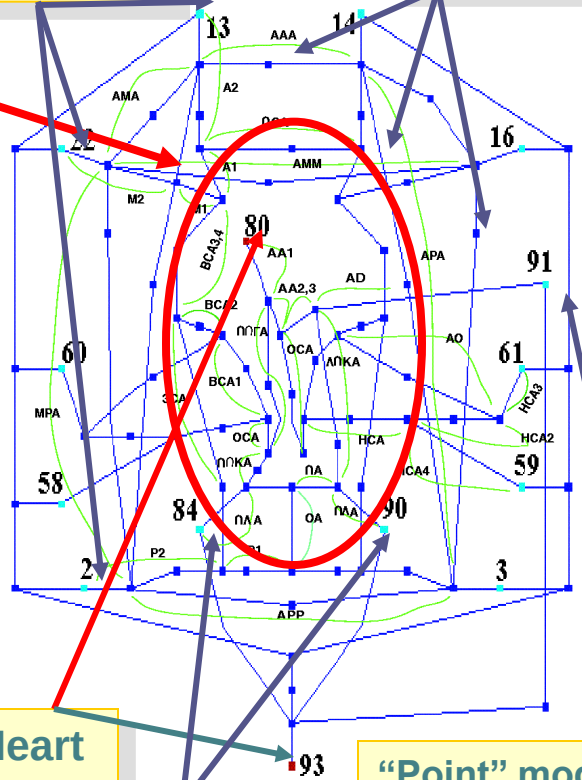


Circle of Willis

Model graph of brain arteries

Brain tissues

Collaterals



Heart

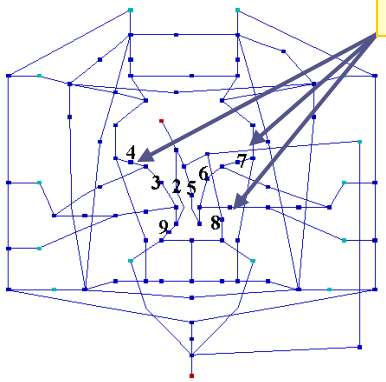
Arms

"Point" model of the rest part of CVS

According to the task of cerebral hemodynamics modeling the complexity of vascular graph can be different. Presented graph includes heart, arch of aorta, scheme of arms,vertebral arteries, carotids, Willis circle, arteries P1,P2,P3, A1,A2,A3,M1,M2,M3, collaterals and some others. Venous return presented schematically. The influence of the rest CVS described by "point model".

Cerebral hemodynamics modeling

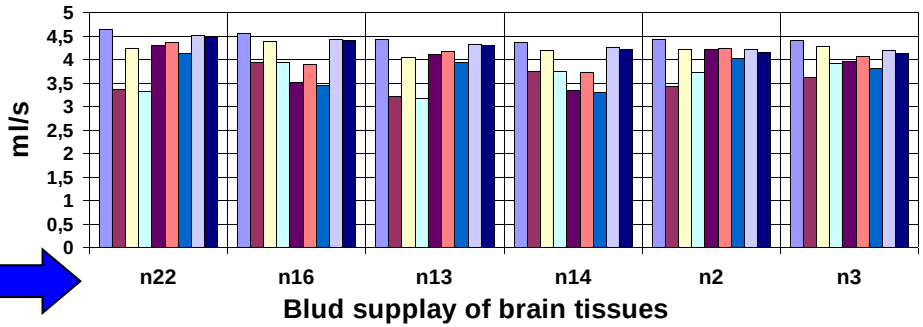
Patient P. had stenos 70%on right internal carotid artery and stenos 90% on left carotid artery. Parameters of his brain arteries (length, diameters, elastic properties, etc.) and heart activity were taken from clinical study. During the operation treating some cross-clamping (occlusions) of arteries in certain points (points 2-9 on the picture) were needed. The question : What will than happen with blood supply of different parts of brain?



Points of occlusion

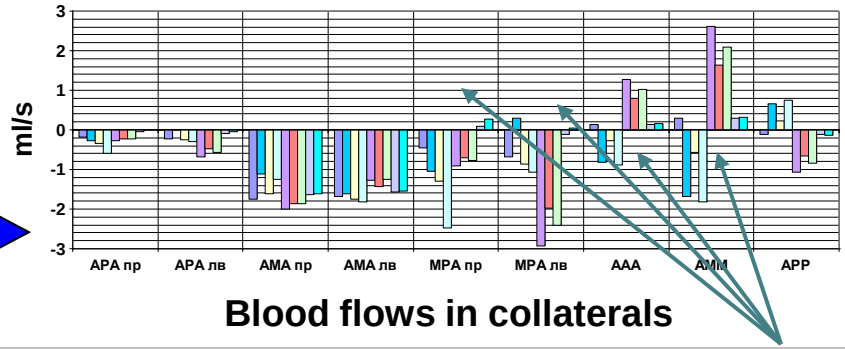
Results of mathematical simulation

It appears that in all cases blood supply of brain does not change dramatically - deficit is not more then 20%



Why is that ?

First column is the flow without occlusions.



The deficiency is made up by collateral circulation (not by the circle of Willis in this case)

Blood flows strongly change after cross-clamping in comparison with normal state

Mass transfer

Mass transfer

Thought the hemodynamic parameters are known, possibility to calculate transfer of substance blood appears. Let us assume, that $C_{l,k}(x,t)$ - mass concentration of *l* -th substance in *k*- th vessel, then mass transfer along the vessels net is described by system of equations

$$\frac{\partial C_{l,k}}{\partial t} + u_k \frac{\partial C_{l,k}}{\partial x} = D \frac{\partial^2 C_{l,k}}{\partial x^2} + f_{l,k}(x,t) + \varphi_k(C_{1,k},...,C_{l_C,k})$$

$$l = 1,2,...,l_C,\ \ k = 1,2,...,k_{link},\ \ 0 < x < L_k,\ \ t > 0$$

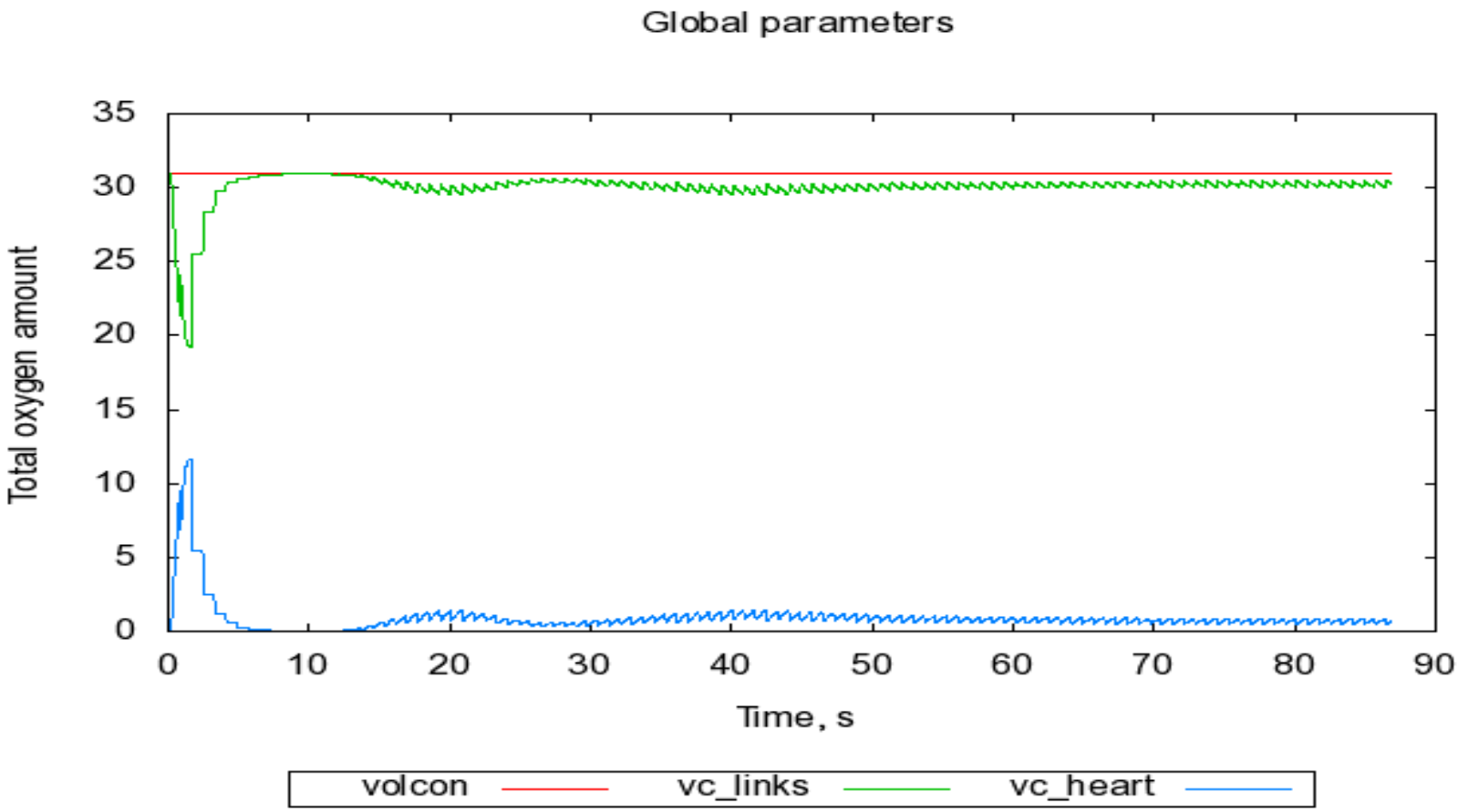
with boundary conditions at each inner node (linking conditions)

$$\sum_{i \in \mathit{III}(m)} z_i S_i \left(C_{l,i} u_i - D \frac{\partial C_{l,i}}{\partial x} \right) + f_m = 0 \qquad C_{l,k,i} = C_{l,k,j}, \quad i \neq j, \quad i, j \in \mathit{III}(m)$$

$$m = 0,1,...,m_{nodes}^{\,l = 1,2,...,l_C}$$

where $f_{l,k}$ and φ_k describe the external mass flows and chemical reactions correspondingly.

Propagation of the substance through the vessels



Propagation of the substance through the vessels

Иллюстрация 5

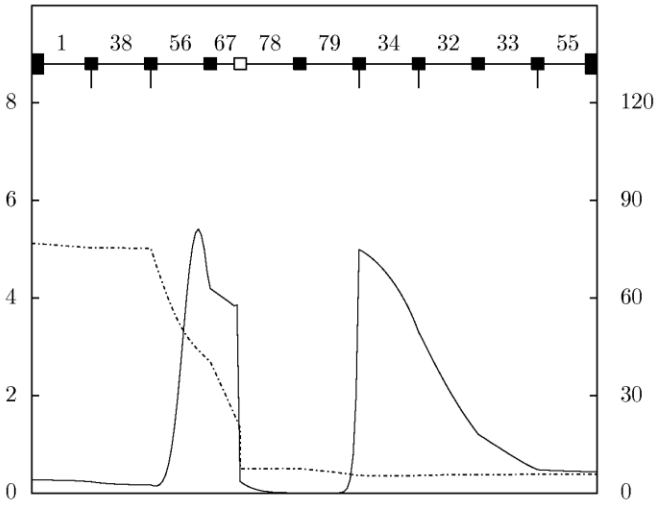


Иллюстрация 6

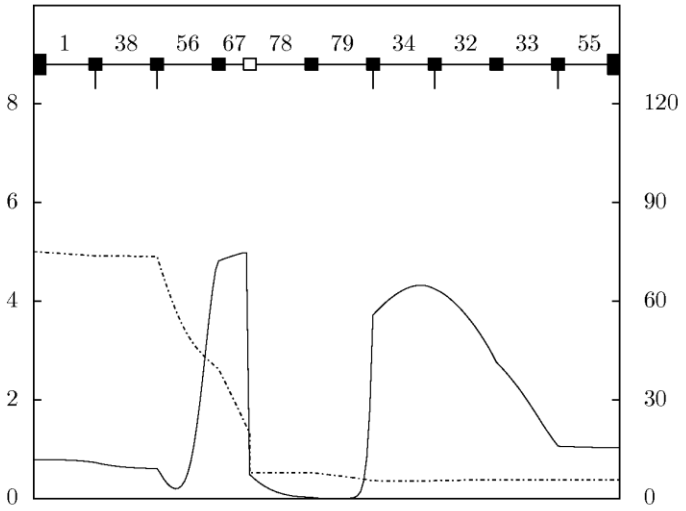


Иллюстрация 7

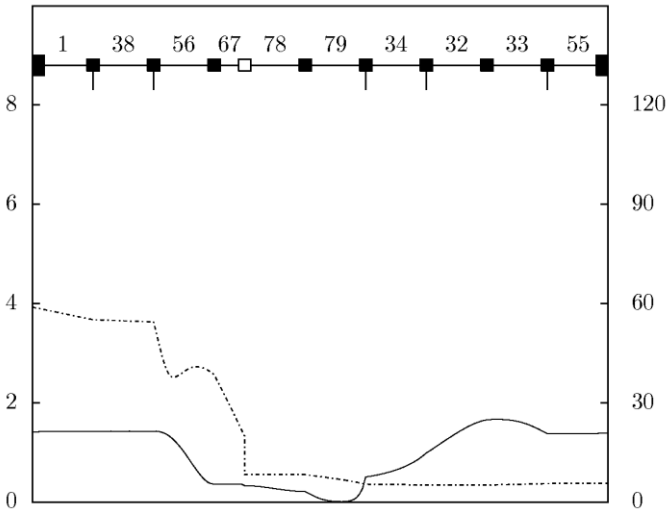
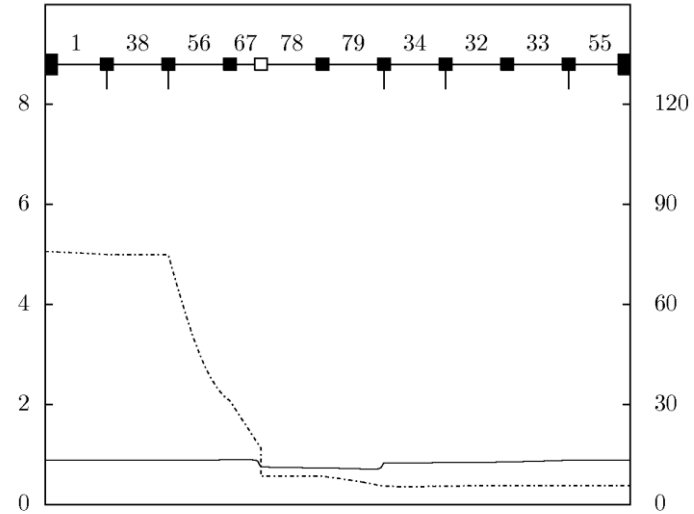
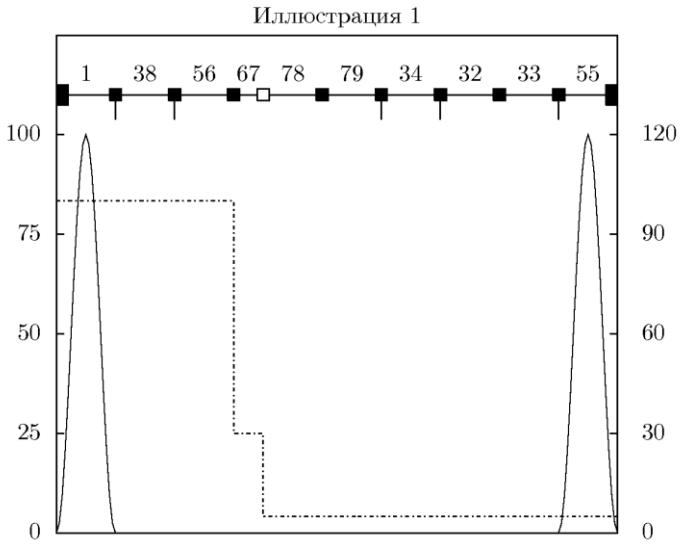
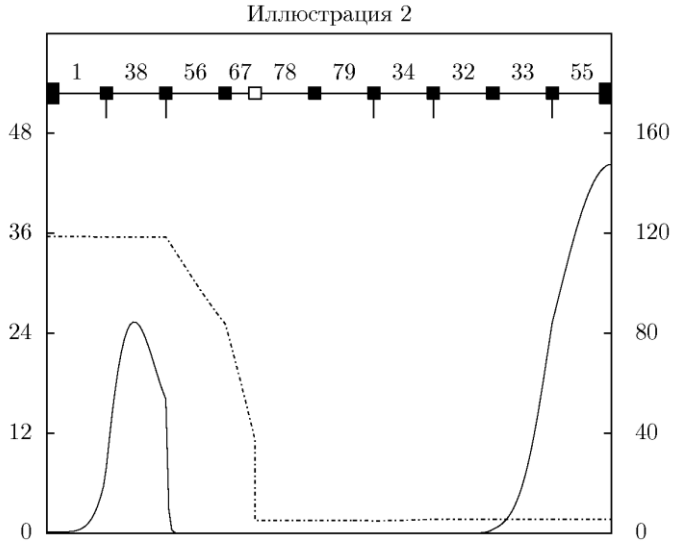


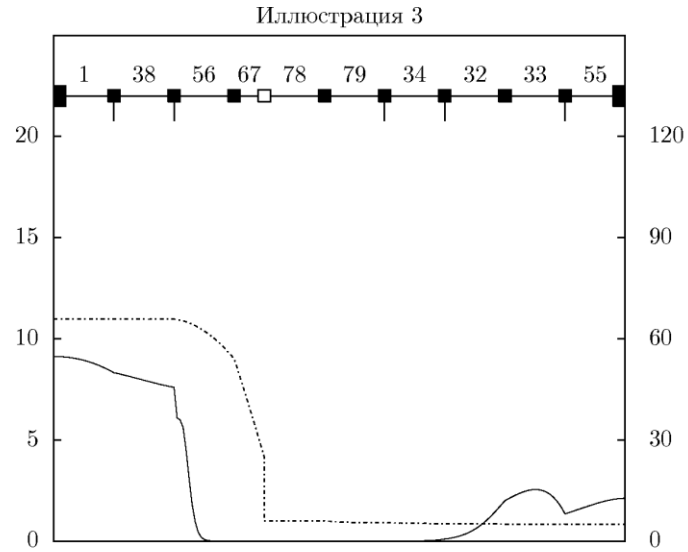
Иллюстрация 8

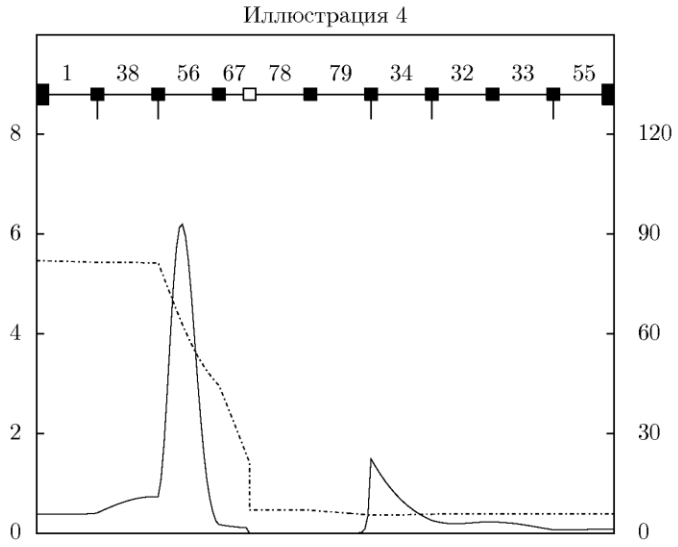


Propagation of the substance through the vessels



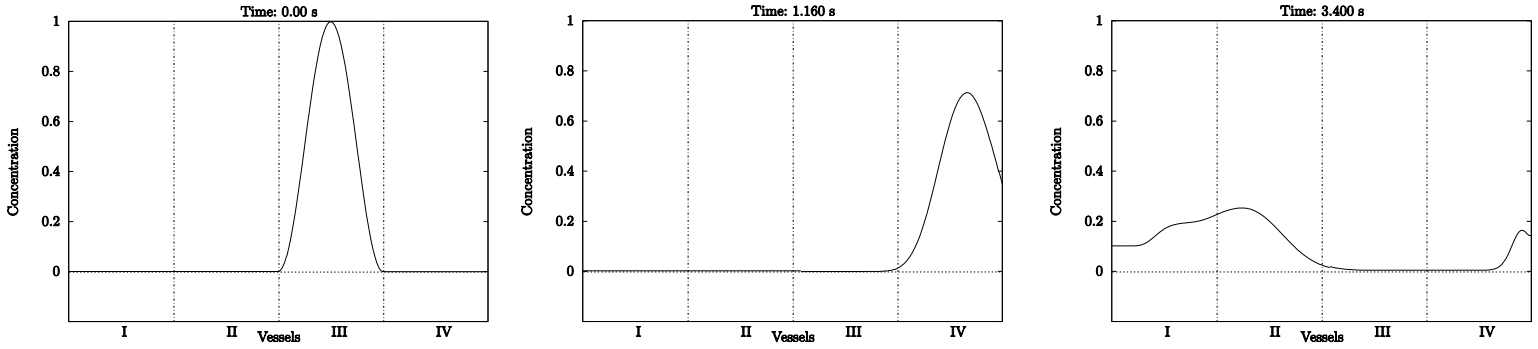






Mass transfer (numerical calculations)

Propagation of concentration wave along circled rout in systemic circulation's vessels



With the help of mass transfer computer modeling a lot of practical problems can be studded

- **Oxygen supply and carbon gas removal**
- **Drug propagation and their influence on blood flow and organs**
- **Distribution of hormones**
- **Humoral regulating mechanisms**
- **Insulin and glucose interference**
- **etc.**

Modeling insulin and glucose dynamics.

For the simulation of the spatial-time dependant dynamics of glucose and insulin we need:

- **To be able to estimate (model) blood flow in the closed CVS (!),**
- **To carry out computation of the process in network vessels for a long time (up to 16-20 hours).**
- **To be able to count (simulate) the transfer of at least of two substances in this system. The algorithm should be conservative (!).**
- **To formalize (to described in mathematical terms) the processes of glucose incom and excretion; to formalize introduction of insulin and excretion of insulin, depending on the level of sugar.**
- **To determine the parameters of the model (!).**

Modeling insulin and glucose dynamics.

On the base of CVSS quasi one-dimensional methodic

- Main organs and tissues are taken into account (the set may be expanded)
- Glucose and insulin sources can be placed anywhere in the system in order to simulate normal and bolus insulin and glucose income.
- Production and interference of both substances can be configured to represent normal or pathological glucose-insulin dynamics.
- Graph of vessels can be designed to suit ordered physiological accuracy, thus allowing to research in details glucose and insulin redistribution, specific to the considered diabetes mellitus.

On the base of endocrinological tests and clamp tests it is possible to tune personal parameters of the model

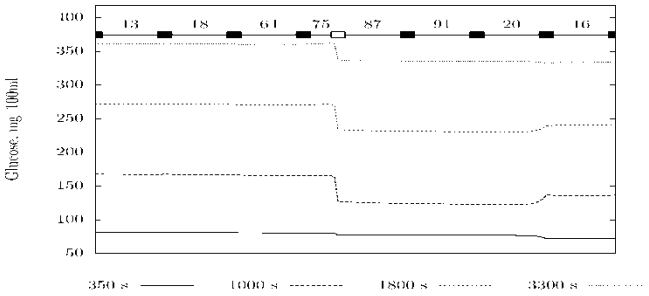
	m	g/h	, mUN/h	, g/h	coeff
Stomach	3	1.6	36,3	—	—
Spleen	4	15.9	837	—	—
Stomach BB	5	23.5	413	0.49	0.02
Leg rt	12	7.2	131	0.5	0.07
Leg lt	13	7.2	131	0.5	0.07
Liver arter.	24	15	264	—	—
Liver vein.	25	48.4	1823	—	—
Liver port.	26	69	2088	1	0.0155
Arms (lf. rt)	34	4.3	81	0.17	0.04
Brain	45	7.4	130	1.46	0.2
Brain	46	7.4	130	1.46	0.2
Brain	48	4.7	77	1.1	0.27
Kidney rt.	55	23.3	119	—	—
Kidney lt.	58	23.5	414	0.2	0.01
Pancrea	85	7.4	838	0.2	0.028

Modeling of insulin and glucose distribution is based on the high accuracy algorithm of their transfer with blood flow, income and elimination.

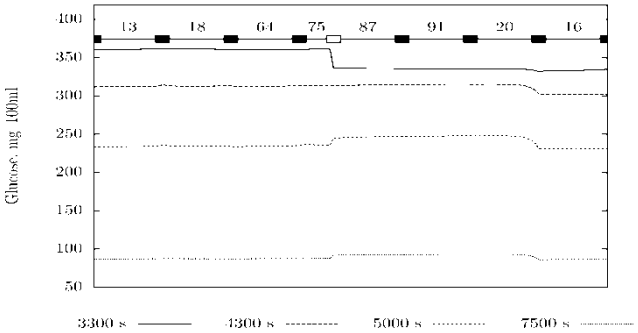
Modeling insulin and glucose dynamics.

The effect of “delay” in the propagation of glucose.

Glucose in femoral artery and vein

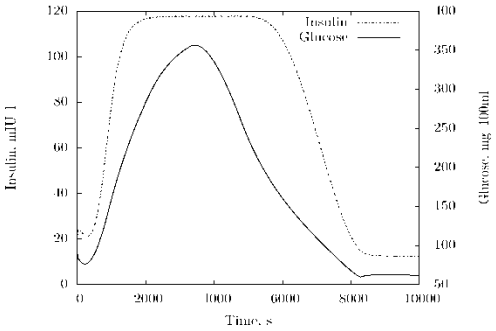


Average level of glucose increase

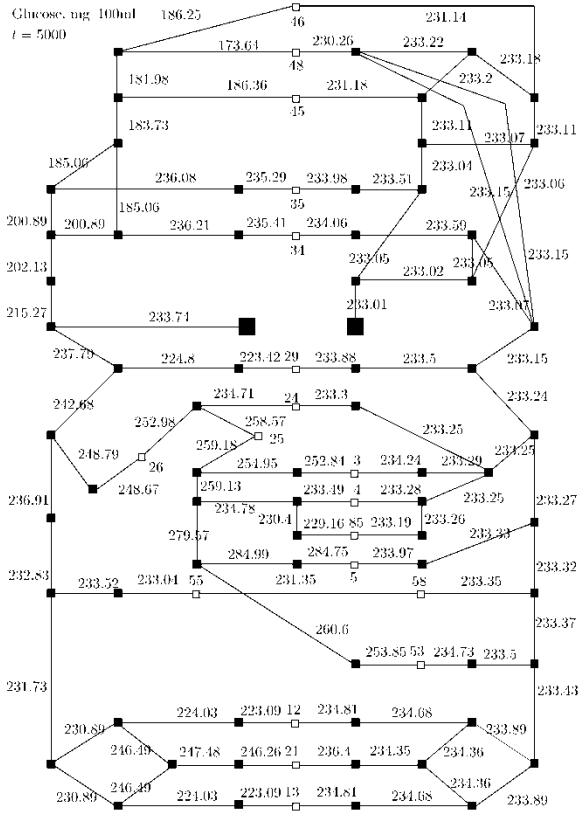


Average level of glucose decrease

Glucose burden



Map of glucose and insulin rate shows the distribution of those substances in every point of vessel at any time



It appears, that concentration of glucose stays on the high level for significant time in femoral veins (and in some other veins) even when the level of glucose in check-points (arms and abdominal wall) is satisfactory.

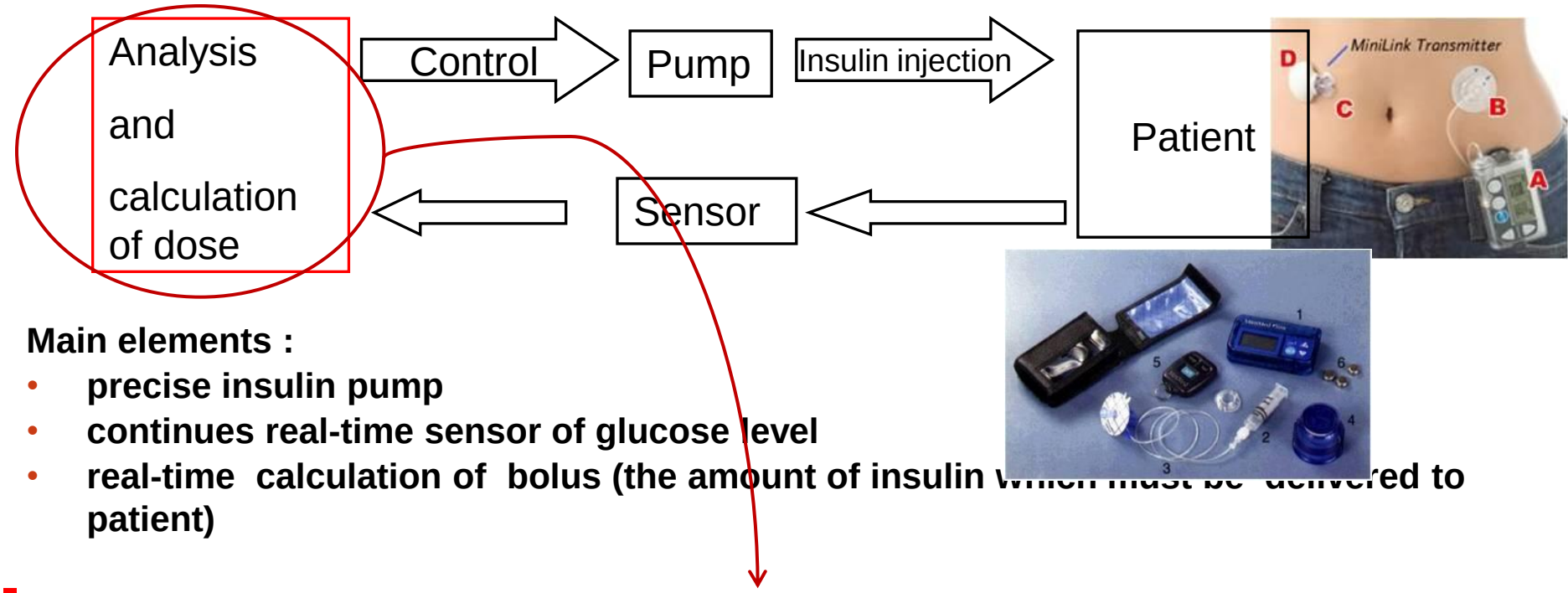
Artificial pancreas

The artificial pancreas is a developing technology which is aimed to provide people with diabetes automatically control of blood glucose level and to provide insulin replacement.

Current project refers to the medical equipment approach:

- using of insulin pump under closed loop control

- using real-time data from a continuous blood glucose sensor



Main elements :

- **precise insulin pump**
- **continues real-time sensor of glucose level**
- **real-time calculation of bolus (the amount of insulin which must be delivered to patient)**

The main attention is paid to the program , which is the key factor. It is necessary to develop a precise algorithm which calculates the right amount of insulin at the right time.

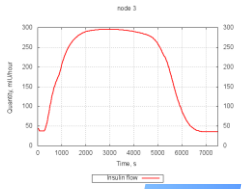
Artificial pancreas

To develop an intelligent and predictive algorithm for computing real-time insulin injection control it is necessary :

To process a huge amount of accumulated physiological data

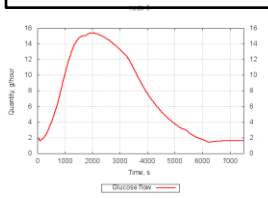
To study qualitative and quantitative characteristics of spatial distribution of insulin and glucose in vessels net

To personalize data (endocrinological tests)



To determine profiles of required bolus according to various peculiarities of the patient under different glucose burden

To specify characteristic times and rates of circulating insulin in system of blood vessels in dependence upon the point of its injection



ETC.

Development of computer simulation and mathematical models of insulin production, intake of glucose and regulation of glicemia can significantly ease the construction of control utility.

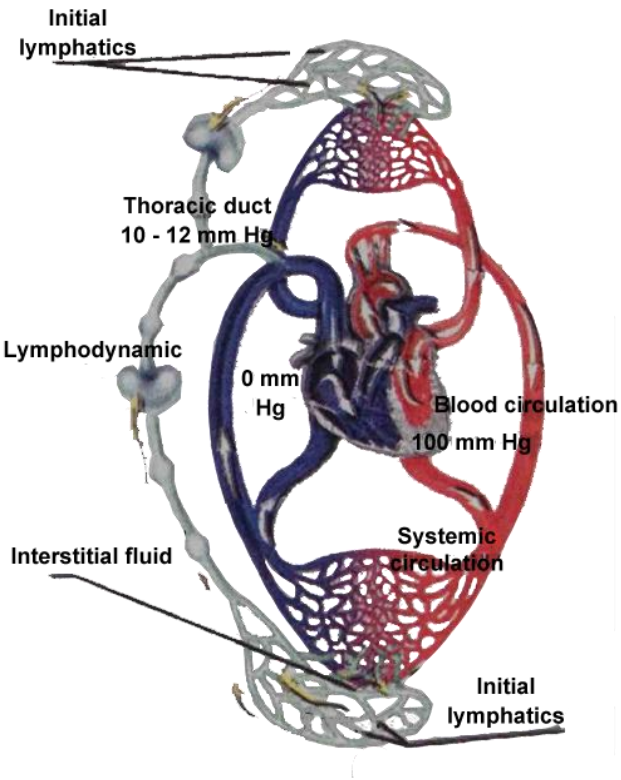
Lymph

Lymphatic system

Lymphatic system modeling is very important task because:

1. big cells and molecules as well as infections are distributed through out the organism by the lymphatic system;
2. it compliments circulatory system: about 10% of blood transforms to lymph and goes to the lymphatic system

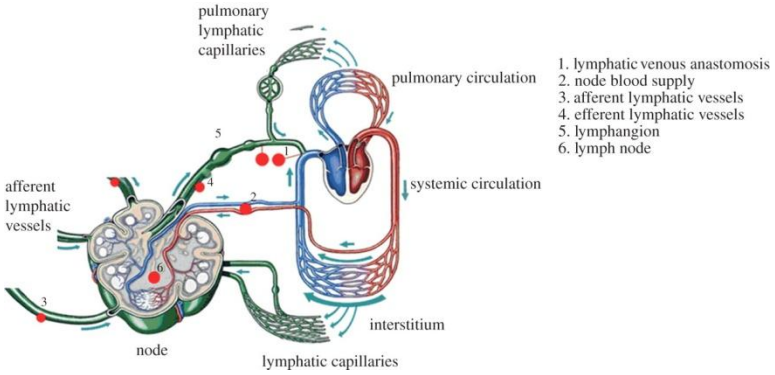
Lymphatic system connected to the cardio-vascular one through the interstitial space

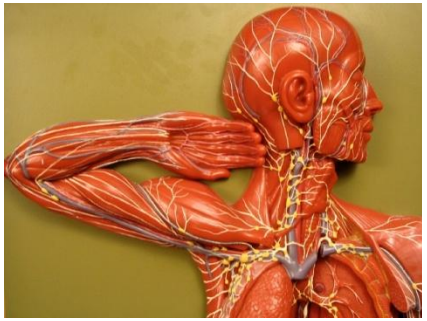


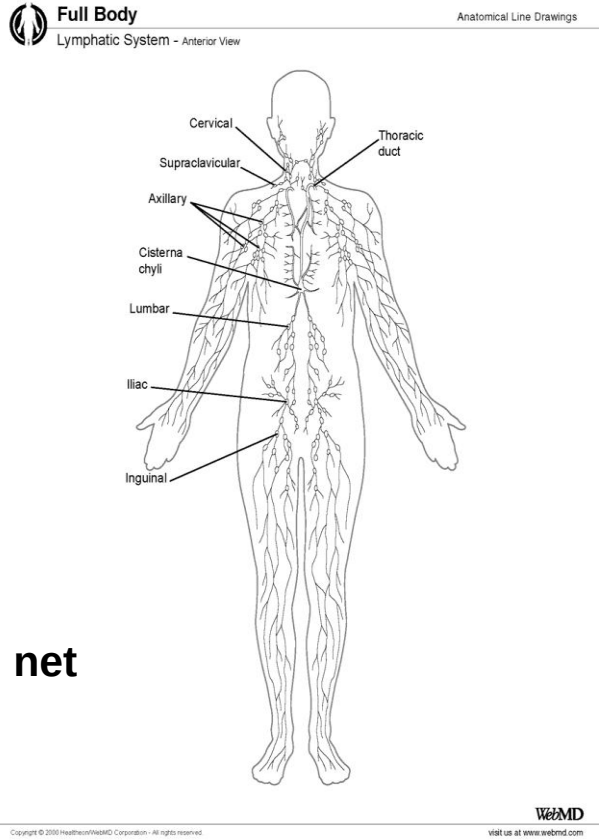
We want to create a model for lymph flow though the whole lymphatic system on the base of the quazi-onedimensional approach

Lymphatic system and quazi 1D approach

Lymphatic system, a subsystem of the cardiovascular system, consists of a network of vessels, tissues, and organs (the same as CV).







- **The topology of lymphatic system is similar to the topology of CV system.**
- **Lymph flow can be described basically with the same hemodynamic equations.**
- **The same, as in case of CV, algorithms used to describe net and to solve the problem numerically.**
- **More over, both nets (CV+L systems) we consider as uniform system from algorithmic point of view.**

Important :

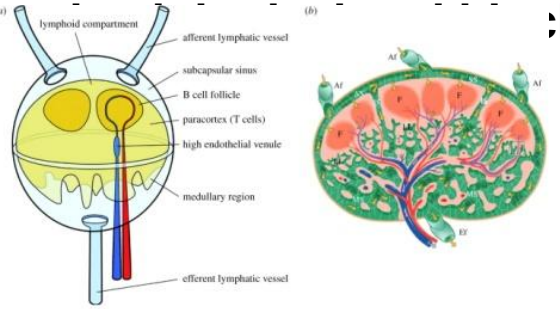
Modeling of mass transfer along lymphatic net.
Connection with CV system via tissues.

Lymphatic system

New features (in comparison with CV)

- **Lymph – contains a lot of components**
- **Lymphatic vessels – specific equation of state, low internal gradient of pressure, valves**
- **New organs – new comple[illegible]chemical models of :**

Lymph nodes
Spleen
Thymus



The main hydrodynamic problem in this case is to investigate why and how lymph moves.
On the first step of research the aim is to verify phisiological hypotheses that lymph flow is caused by:

1) Pressure drop along the system **2)Muscle pump (due to valves)**

The model includes:

- **a graph with arcs representing lymphatic vessels and lymph nodes and nodes representing bifurcations and boundaries;**
- **models for the lymphatic vessels and lymph nodes**

Lymphatic system

Lymphatic system:

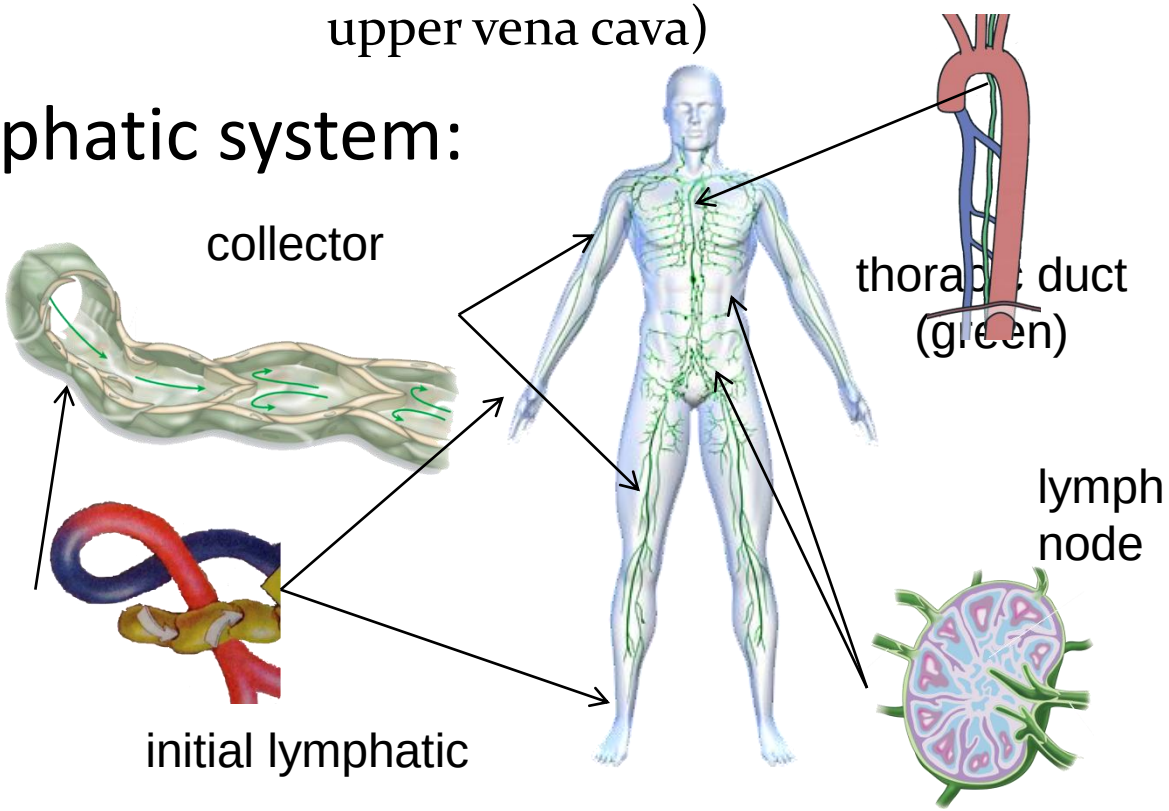
- is not closed;
- is not connected to the heart directly;
- delivers lymph from the interstitial fluid to the upper vena cava

Lymph:

- enters into the lymphatic system through the initial lymphatics;
- flows in one direction (to the upper vena cava)

Elements of the lymphatic system:

1. trunks and ducts;
2. collectors;
3. postcapillaries and initial lymphatics;
4. lymph nodes



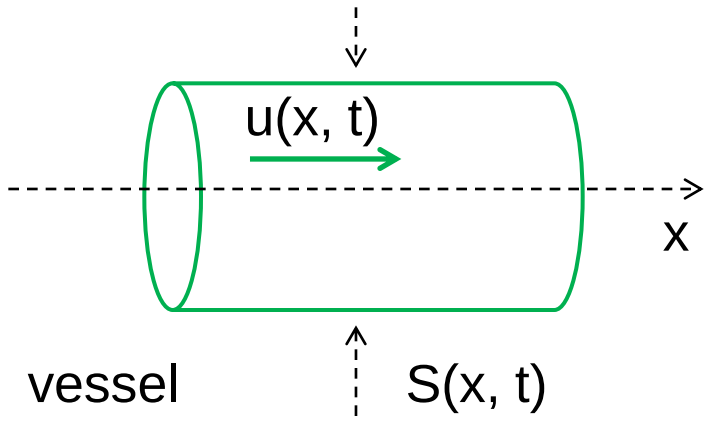
In all of the groups processes are multiscale in velocity and sizes

First group of the vessels

Physiology

includes trunks and ducts:

- the diameters about 1.5 – 2 mm;
- rare valves – can be about 5 cm between adjoint ones;
- active contractions of lymphangions;
- velocity about 0.5 – 1 cm/s



Mathematics

- basic equations:

$$\frac{\partial S}{\partial t} + \frac{\partial uS}{\partial x} = 0,$$

$$\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} + \frac{1}{\rho}\frac{\partial p}{\partial x} = -8\pi\nu\frac{u}{S},$$

$$S = S(p)$$

S(x,t) – cross-section area;
u(x,t) – lymph velocity;
p(x,t) – pressure;
ρ – density, ν – viscosity;
x – axial coordinate, t – time;

- in case of contractions:

$$S = S(p, p_{ext}),\ p_{ext} = p_{ext}(x,t)\ (!)$$

Second group of the vessels

Physiology

includes collectors:

- the diameters from 3 – 5 μm to 1 – 2 mm;
- frequent valves – it can be about 2 mm between adjoint valves with the diameter of the vessel is about 2 mm;
- active contractions of the lymphangions

Mathematics

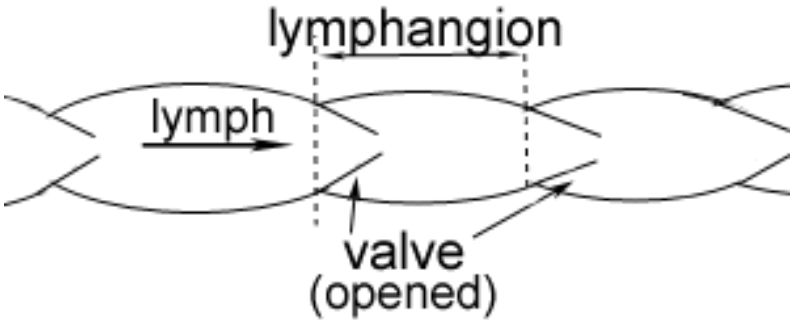
- basic equations with resisting force:

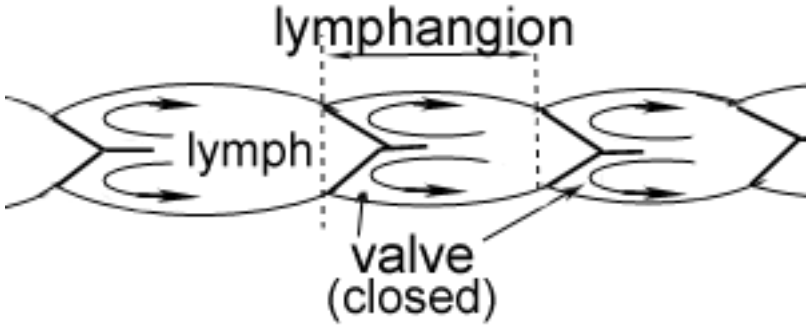
$$\frac{\partial S}{\partial t} + \frac{\partial uS}{\partial x} = 0,$$

$$\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} + \frac{1}{\rho}\frac{\partial p}{\partial x} = -8\pi\nu\frac{u}{S} + F_r,$$

$$S = S(p)$$

- example of : $F_r = k\frac{|u| - u}{S}$
- contractions: $S = S(p, p_{ext})$





Third group of the vessels

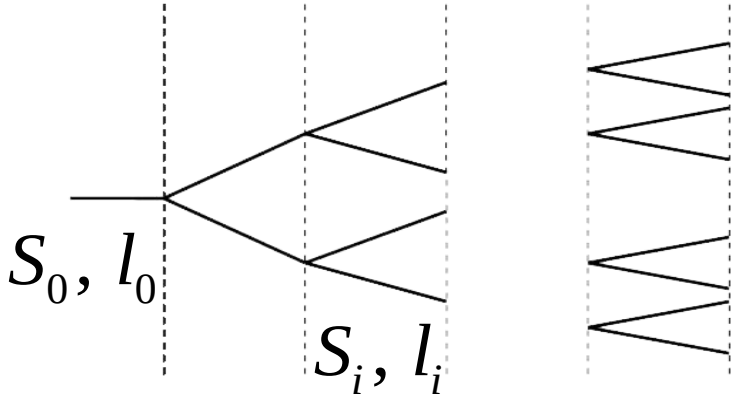
Physiology

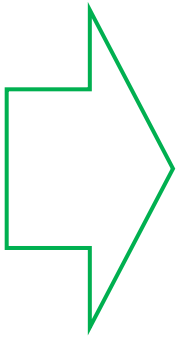
includes initial lymphatics:

- the diameters about 20 – 200 μm;
- no valves

Mathematics

- binary tree net -> an effective vessel with conservation of flux, pressure gradient and lateral area





$\hat{S}, \hat{l}$

$S_i = q^i S_0,\ l_i = p^i l_0,$

$S_i, \hat{S}$ - cross-section area,

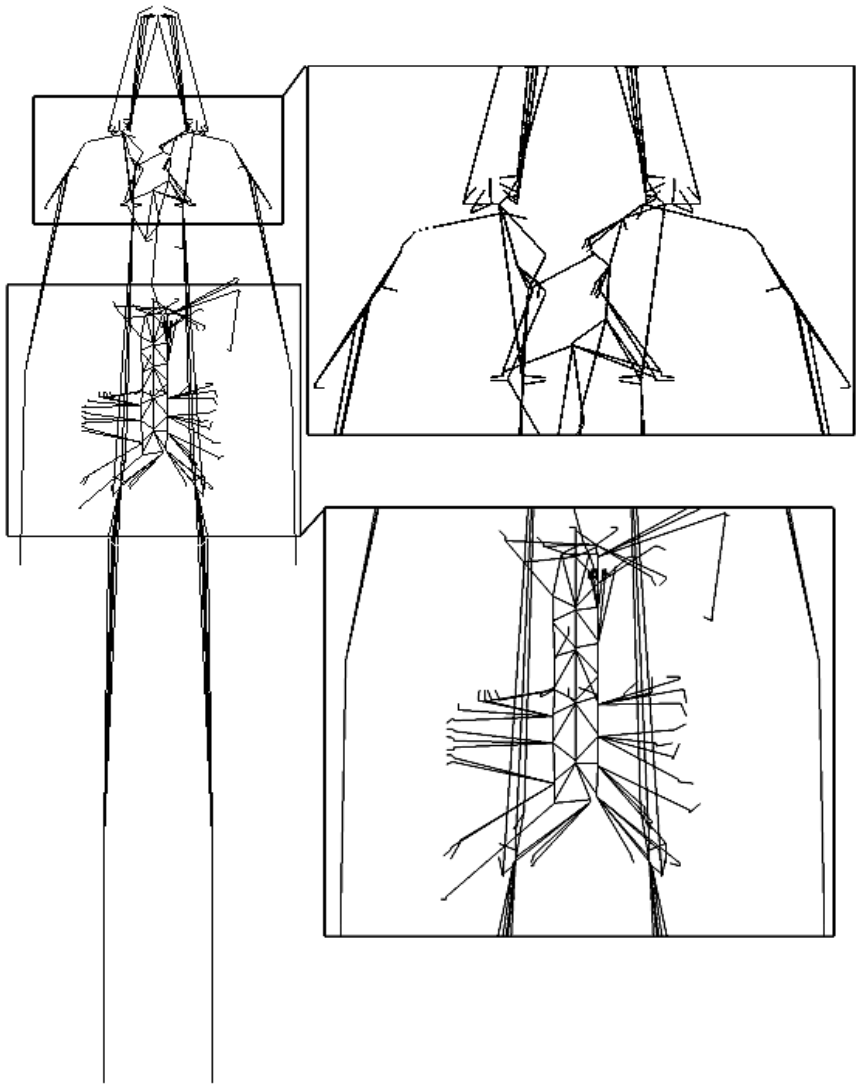
$l_i, \hat{l}$ - length

$$\hat{S} = S_0 \left(\frac{\sum_{i=0}^{n} (2p\sqrt{q})^i}{\sum_{i=0}^{n} \left(\frac{p}{2\sqrt{q}} \right)^i} \right)^{2/5} \to S_0 \left(\frac{2q^2 - p}{2q^2 \left(1 - 2p\sqrt{q}\right)} \right)^{2/5}, \text{ when } 2p\sqrt{q} < 1,\ \frac{p}{2\sqrt{q}} < 1,\ n \to \infty$$

The lymphatic system graph

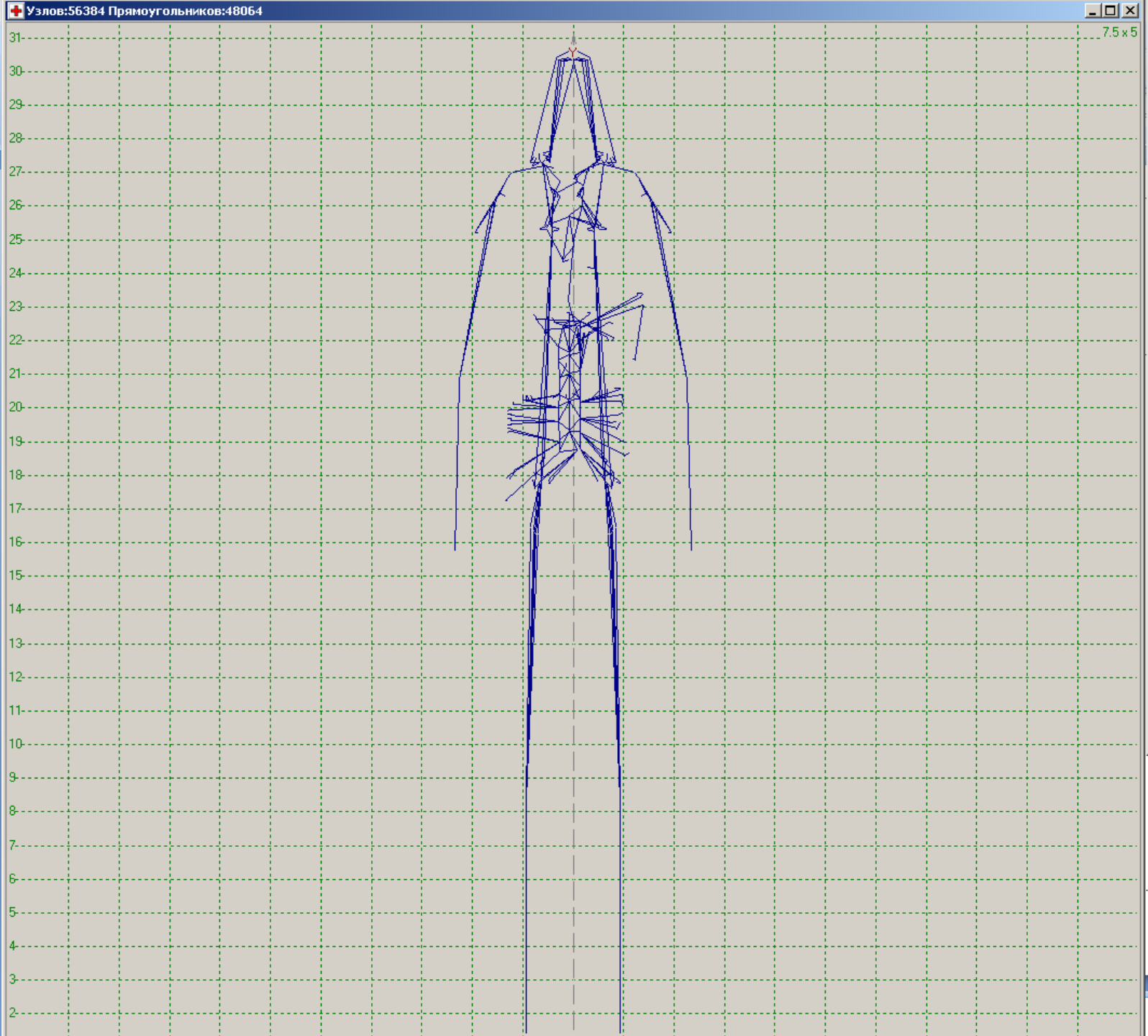
To create the graph for the lymphatic system follow steps had been done:

1. the set of vessels and nodes sufficient for lymphatic system description had been determined;
2. the vessels and nodes had been topologically attached to the graph of the cardio-vascular system.



The lymphatic graph has 520 arcs and 455 nodes.

163 arcs of the graph represent lymph nodes



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Сосуды (текущий №1)

Beg	End	Type	AV
1	2	1300	2
1	27	1400	2
1	33	1400	2
1	35	1400	2
1	115	1400	2
1	121	1400	2
2	125	1400	2
2	157	1400	2
3	4	1300	2

Add Del Edit Data

Узлы (текущий №1)

№	X	Y	Z
1	1.01	94	15.01
2	1.01	94.2	15.01
3	0.6	93.8	15.01
4	0.6	93.6	15.01
5	0.5	110.8	16.8
6	0.5	111	16.8
7	0.7	110.9	16.8
8	0.7	111.1	16.8
9	1	110.9	16.8

Add Del Edit Turn

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Вычисления CVSS

Вычисления ЛГД

Example of some initial parameters

Group Type	ID	Name	d (cm)	Sinit (cm^2)
3	1410	Effective vessels	do = 0.02	0.00024
2	1400	Collectors	-	0.009
1	1401	Cisterna chyli	0.4	0.1257
1	1402	Lumbar trunks	0.15	0.0177
1	1403	Thoracic duct	0.2	0.0314
1	1404	Jugular trunks	0.1	0.0079
1	1405	Right lymphatic duct	0.2	0.0314
1	1406	Bronchomediastinal trunks	0.1	0.0079
1	1407	Subclavian trunks	0.1	0.0079
-	all	Lymph nodes	0.2	0.0314

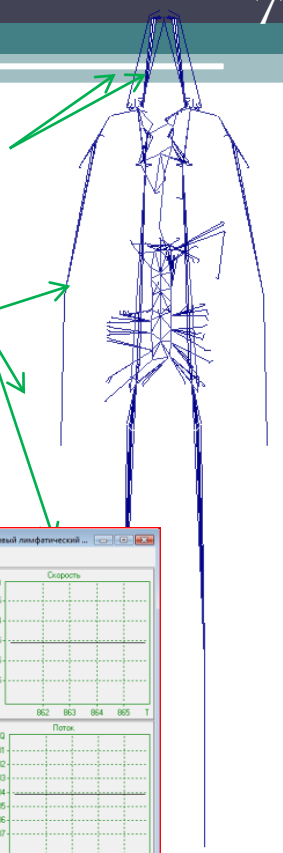
Calculations

Calculations were performed to determine:

1. if there is any flux in the model under given pressure gradient;
2. if there can be reached presumable flux (0.023 ml/s – about 2 l/day)

p = 0 mm Hg
(upper vena cava)

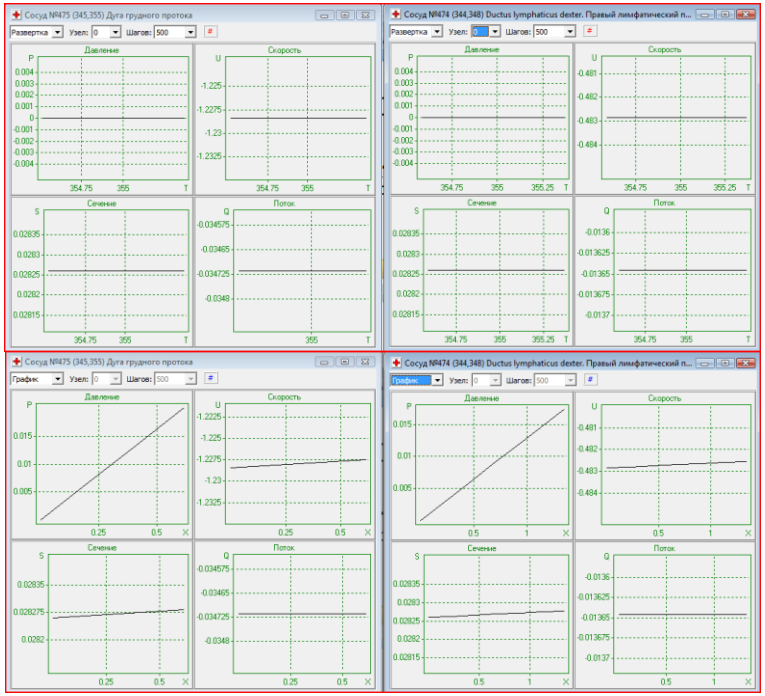
p = 5 mm Hg
(initial lymphatics)

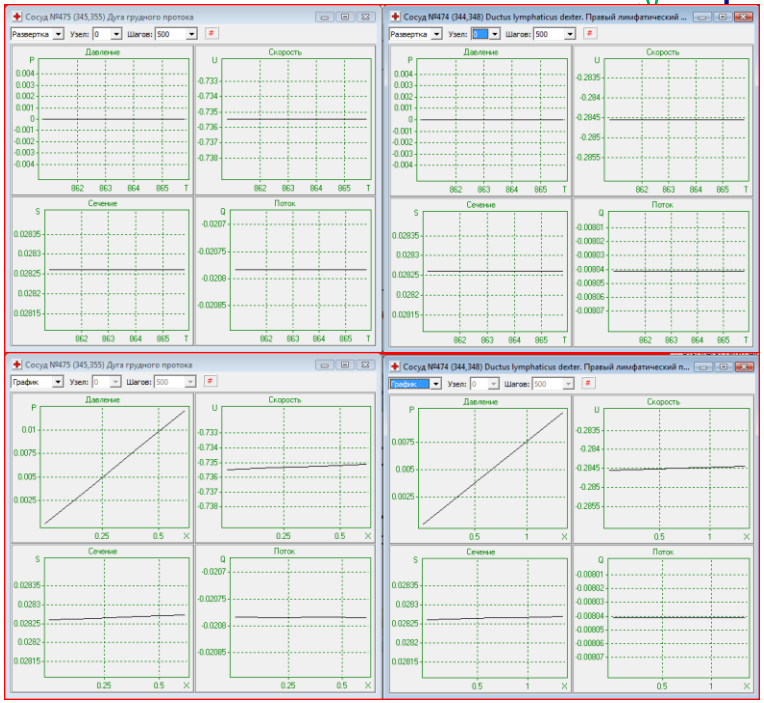


Calculations had been performed in the CVSS program until a steady flow had been established

Upon time

Upon space

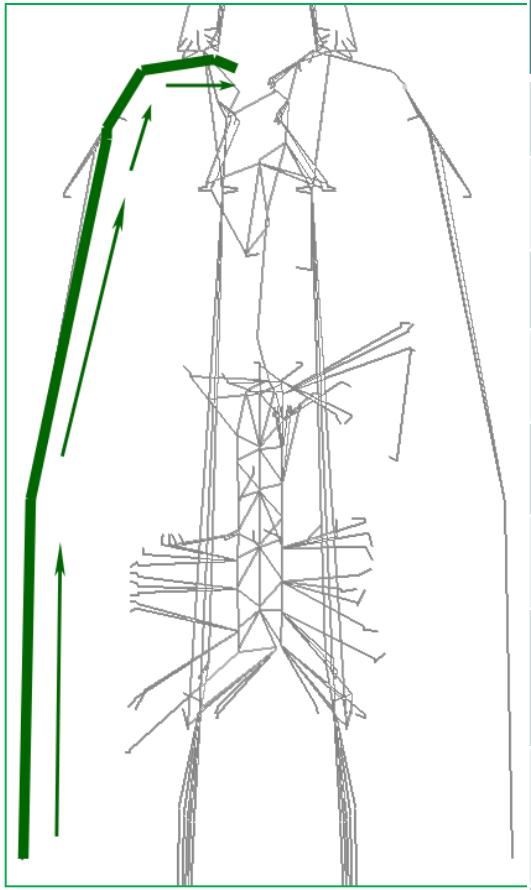




Output flux = 0.0483 ml/s

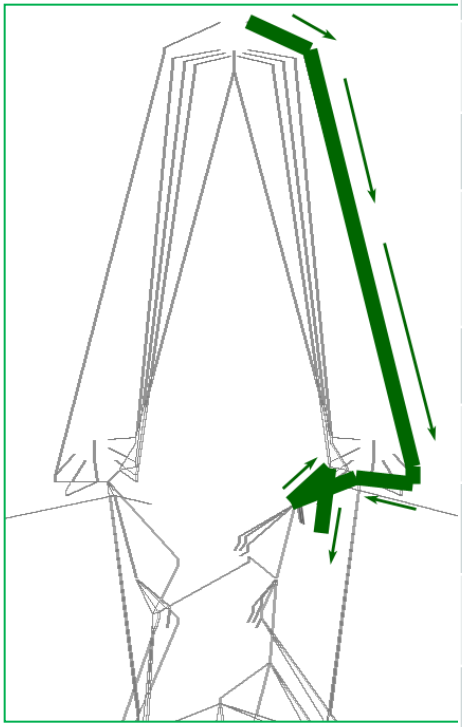
Output flux = 0.0288 ml/s

Track 1: right palm to the right venous angle



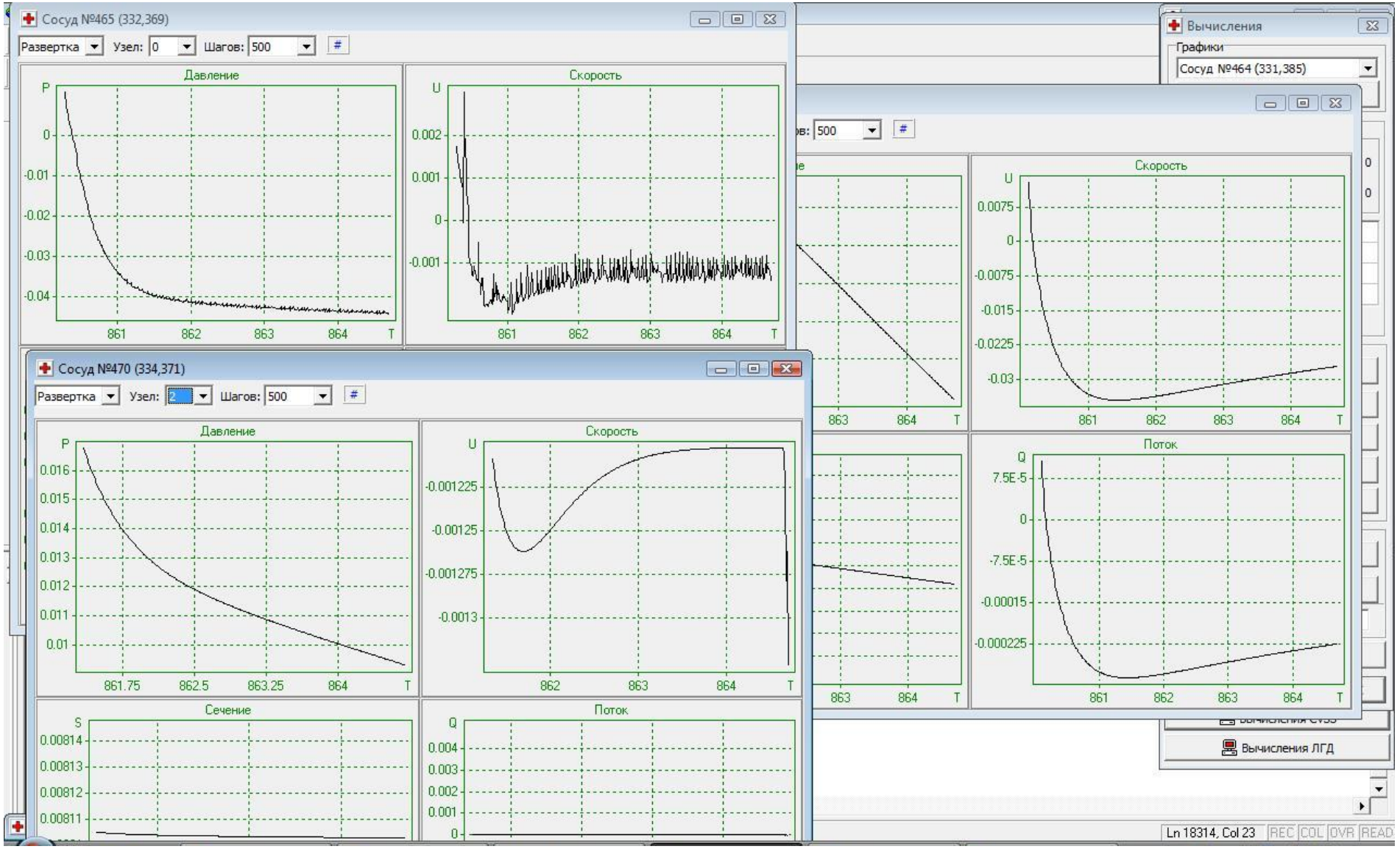
№	Body Region	Leng (cm)	Sinit (cm^2)	p (mm Hg)	|u| (cm/s)	Group Type
464	Right palm	25.329	0.00018	5.000000	0.045779	3
463	Cubital lymph node	0.200	0.03140	0.083414	0.000293	4
466	Right forehand	27.358	0.00900	0.083412	0.000700	2
517	Central axillary lymph node	0.200	0.03140	0.081631	0.003000	4
493	Right shoulder area	3.287	0.00900	0.081615	0.010468	2
489	Apical axillary lymph node	0.200	0.03140	0.078414	0.024052	4
495	Right subclavian area	1.204	0.00900	0.078285	0.083915	2
483	Right subclavian trunk	5.768	0.00790	0.068880	0.095632	1
474	Right lymphatic duct	1.349	0.03140	0.010264	0.284443	1
-	Right venous angle	-	-	0.000000	0.284551	-

Track 2: back of the head (left) to the left venous angle



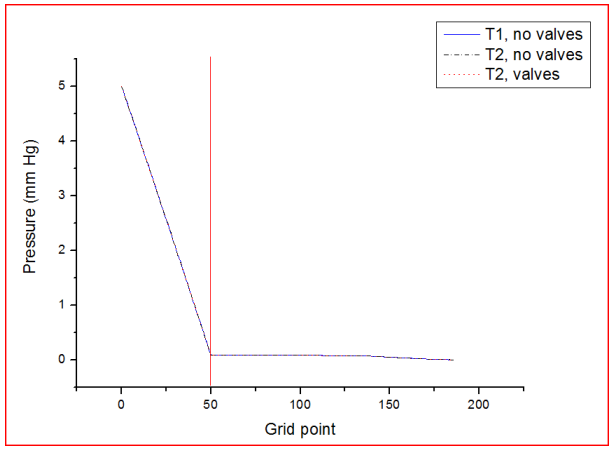
№	Body Region	Leng(cm)	Sinit (cm^2)	p (mm Hg)	|u| (cm/s)	Group Type
349	Back of the head (left)	2.19317	0.00018	5.00000000	0.51547460	3
347	Cervical lymph node	0.20000	0.03140	0.20860548	0.00327959	4
348	Head (left)	16.98530	0.00900	0.20858807	0.01144214	2
457	Lateral deep cervical lymph node	0.20000	0.03140	0.19057910	0.00943150	4
458	Neck (left)	3.44384	0.00900	0.19052900	0.03290553	2
480	Neck (left)	0.40000	0.00900	0.18002417	0.10038180	2
479	Left jugular trunk	2.67208	0.00790	0.17630153	0.36601905	1
485	Arc thoracic duct	1.28063	0.03140	0.07260521	0.69503687	1
487	Arc thoracic duct	1.87083	0.03140	0.04884073	0.73413698	1
475	Arc thoracic duct	0.61644	0.03140	0.01212108	0.73513374	1
-	Left venous angle	-	-	0.00000000	0.73546245	-

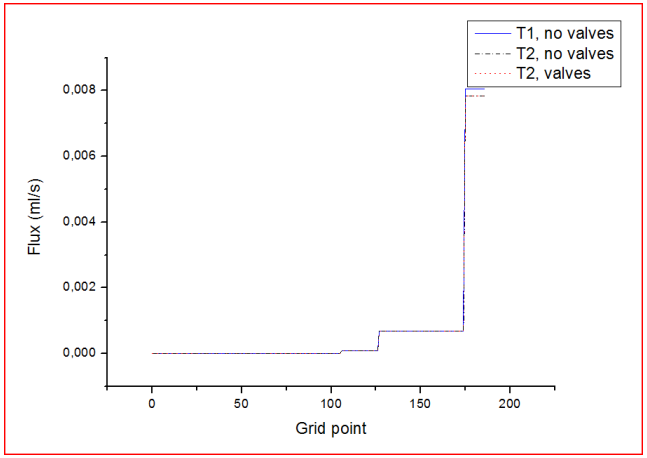
Calculations under gravity

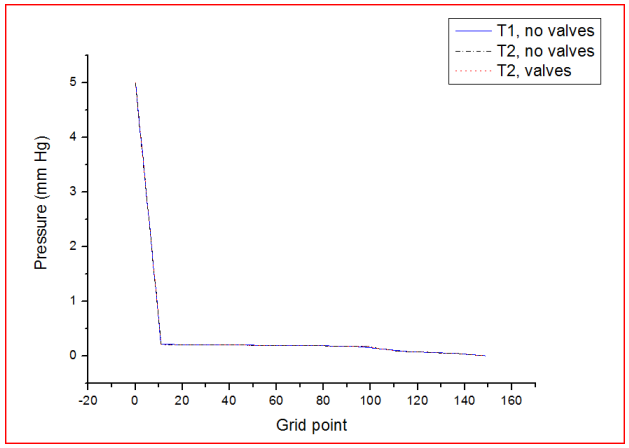


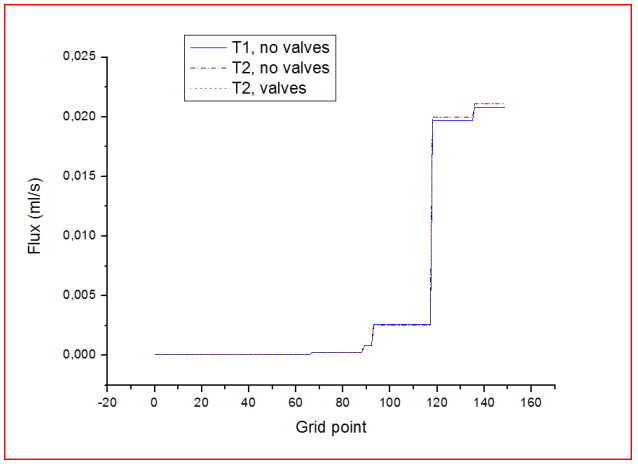
Valves Yes/No without gravity

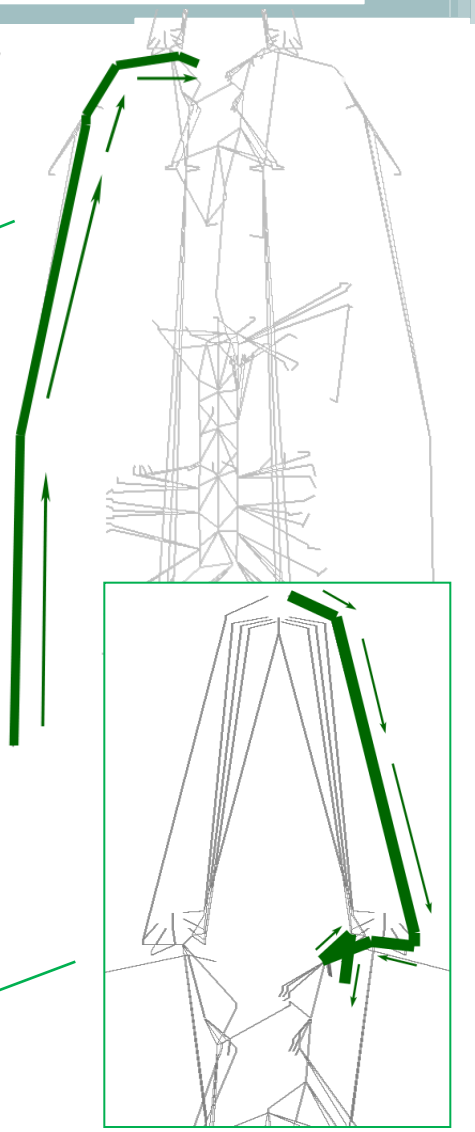
- Is there are any influence of the presence of valves in vessels of first type on the lymph flow without gravity ;
- 2 models (with and without valves) with the same topology
- Calculations were performed in the CVSS program until a steady flow was reached.





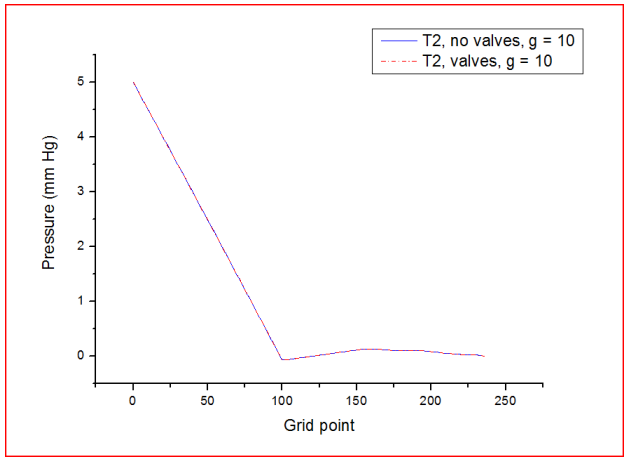


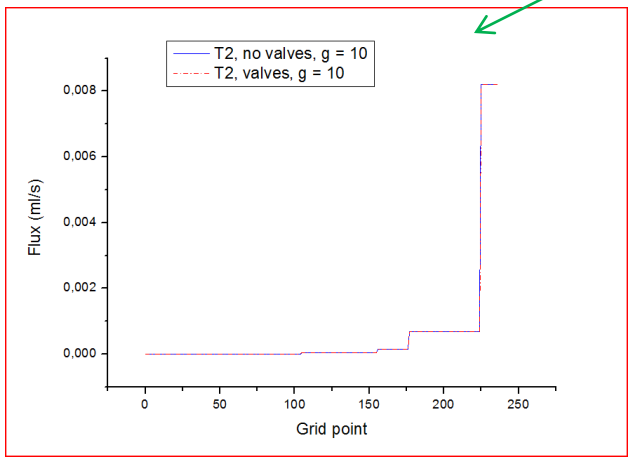


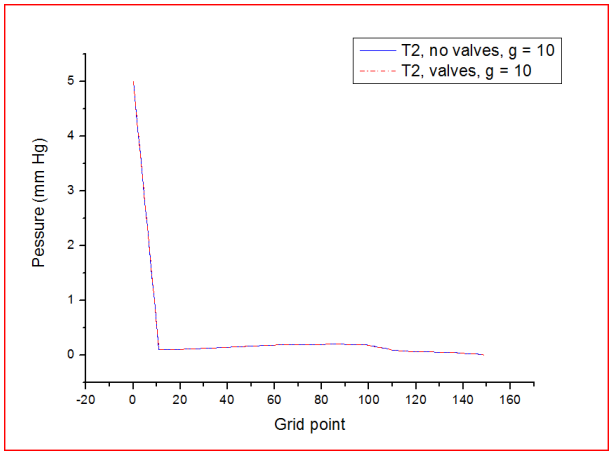


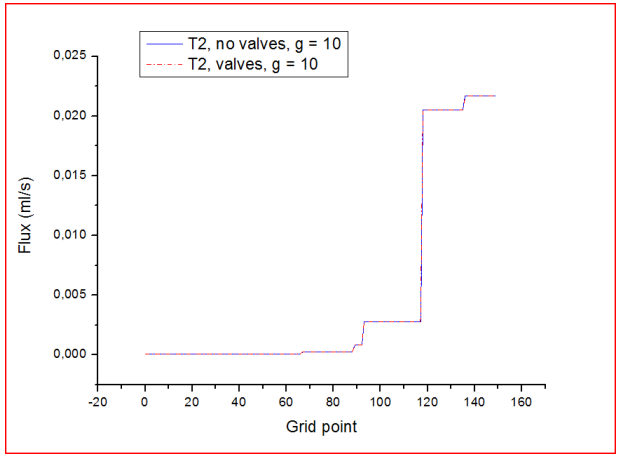
Valves Yes/No with gravity

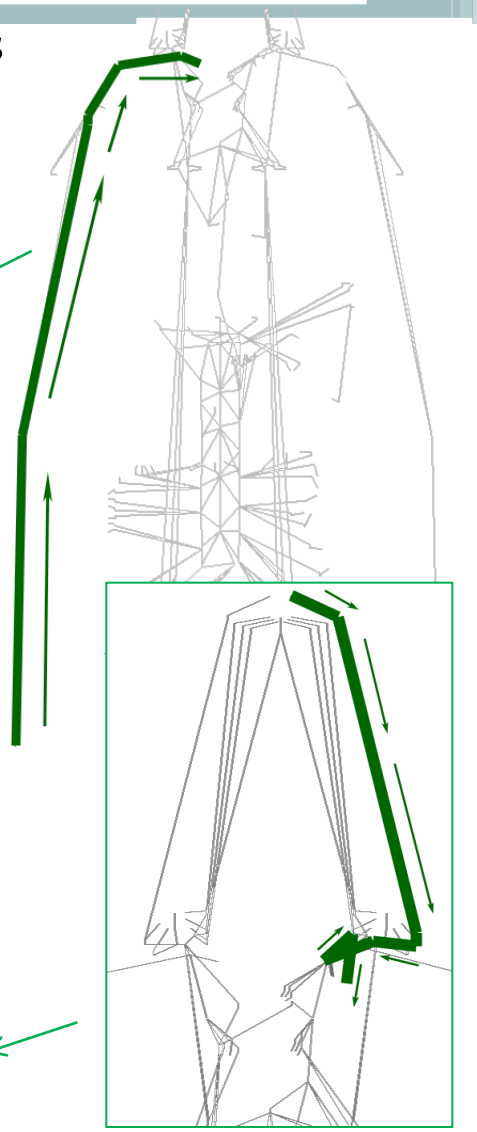
- Is there are any influence of the presence of valves in vessels of first type on the lymph flow with gravity 1g ;
- 2 models (with and without valves) with the same topology
- Calculations were performed in the CVSS program until a steady flow was reached.



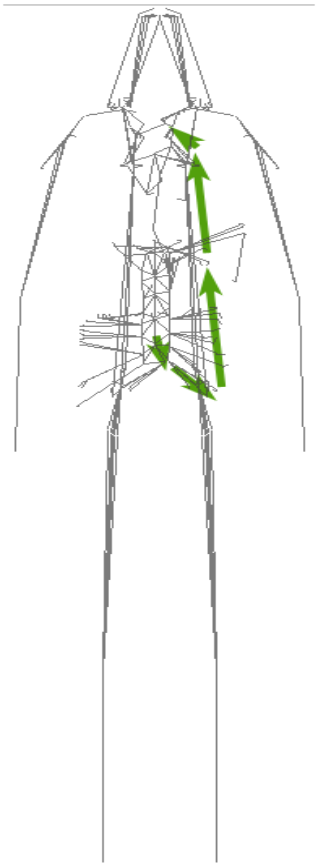




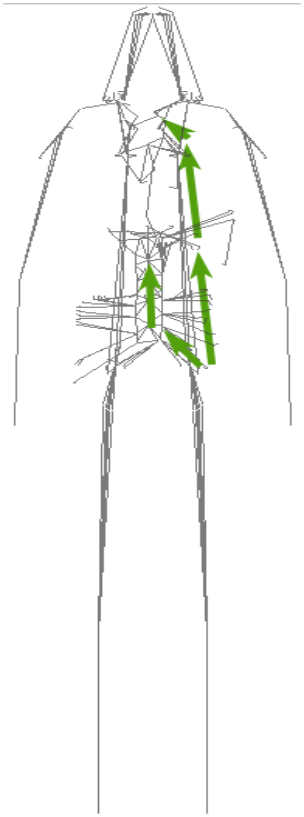




Calculated flow



Expected flow

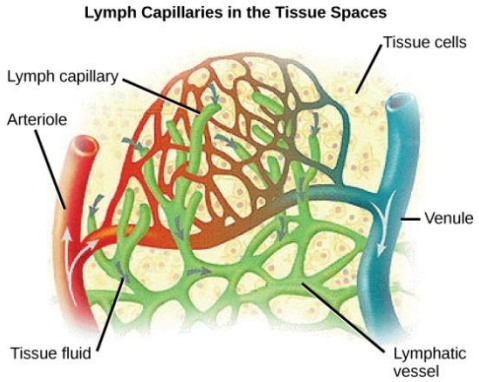


Valves in vessels of the first type do not compensate the influence of gravitation

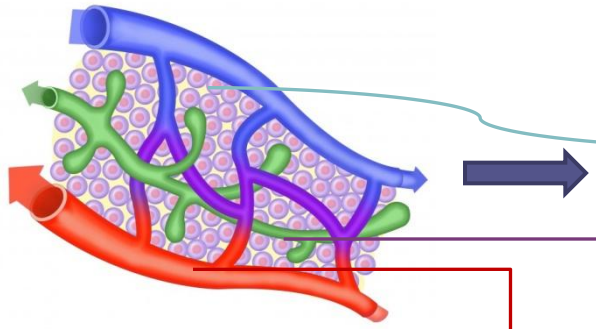
Perhaps the situation will change after accounting valves in vessels of the second type

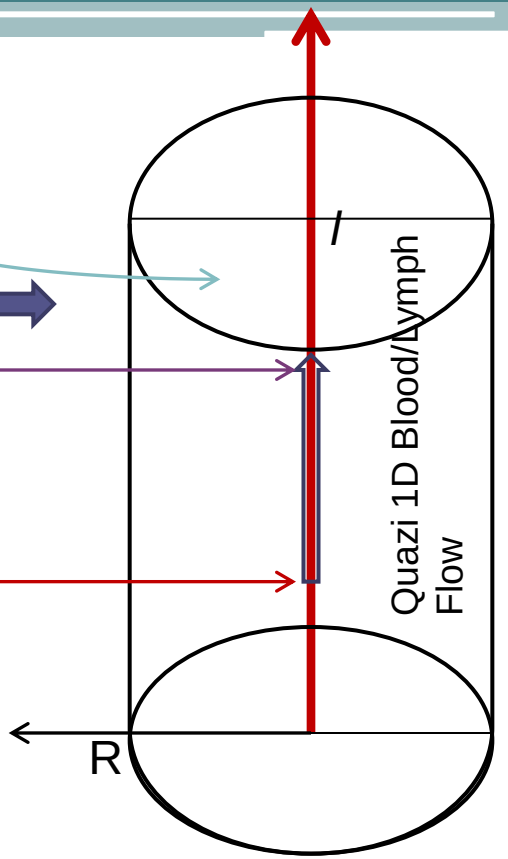
Interstitial

Exchange of 1D flow in vessel with interstitial (+ diffusion and sorption in tissue).



Human Anatomy & Physiology . Elaine N. Marieb and K.Hoehn, published by Pearson

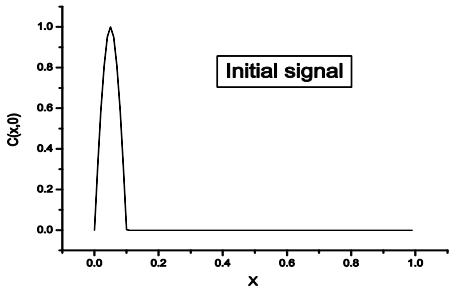


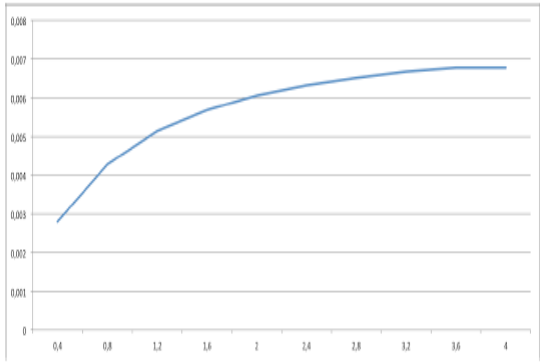


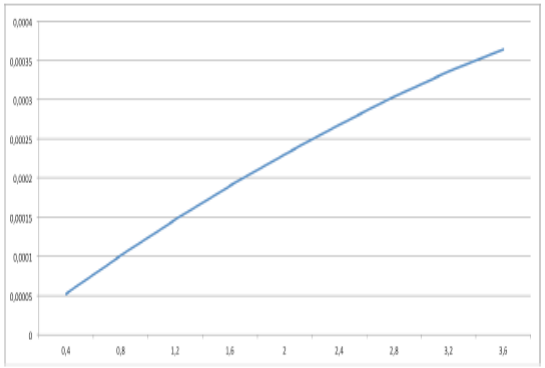
$$\begin{cases} \frac{\partial c}{\partial t} + v\frac{\partial c}{\partial x} = D\frac{d^2c}{\partial x^2} + F(x,t),\ 0 < x < l,\ 0 < t \\ c(0,t) = \mu(t),\ o \le t \\ \frac{\partial c(l,t)}{\partial x} = 0,\ 0 \le t \\ c(x,0) = 0,\ \ 0 < x < l \end{cases}$$

C(x,t) – concentration of substance in vessel
u(x,r,t) – concentration of substance in interstitial

$$F(x,t) = -\left(c(x,t) - u(x,0,t)\right) \times KC \times \lambda \times Mn$$







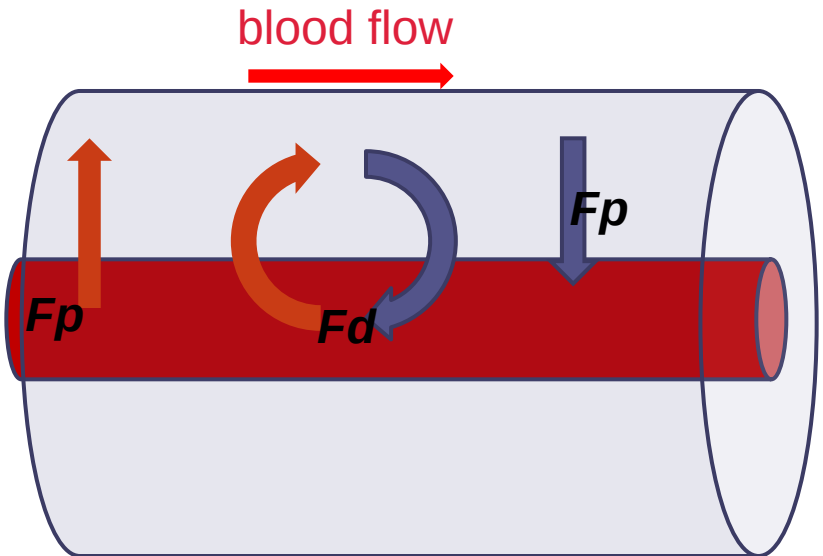
Exchange with interstitial.

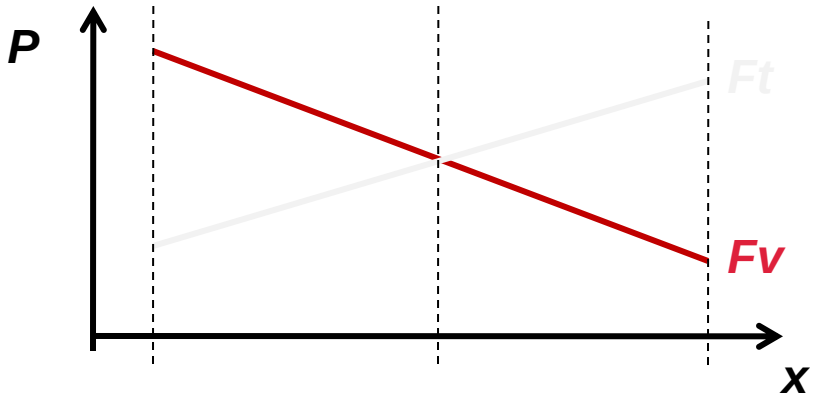
$$\begin{cases} \dfrac{\partial u}{\partial t} = k\triangle u + F(r,x,t),\ r_0 < r < R;\ 0 \le t \le T;\ 0 < x < l \\ \dfrac{\partial u}{\partial r}\overset{r=R}{=} 0 \\ u(r=r_0) = u_{const} \\ \dfrac{\partial u}{\partial x}\overset{x=0,x=l}{=} 0\,, \qquad u(r,x,t) = ? \end{cases}$$

$$u_{const} = u(r_0,x,t) = \frac{F1}{S_{st}}$$

u(x,r,t) – mass concentration in interstitial fluid,
C(x,r,t) - mass concentration in blood
F – sorption flow,
F1- flow from/to the vessel.
F1=Fd +Fp,
Fd – diffusion flow,
Fp – “pressure” flow

In general
Fd= λ(C-u)κ, ***Fp=σ(u,c)ΔP***

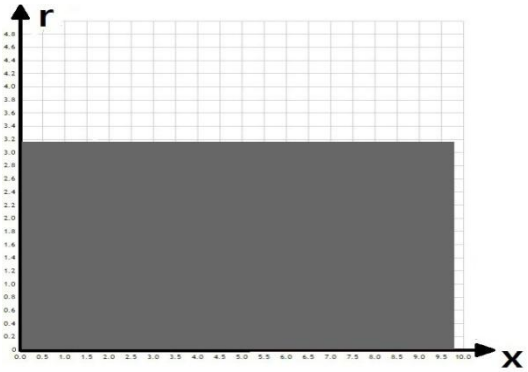


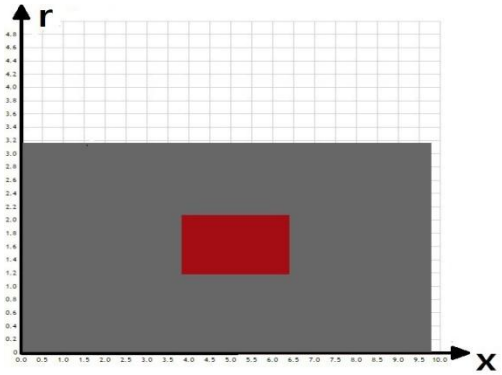


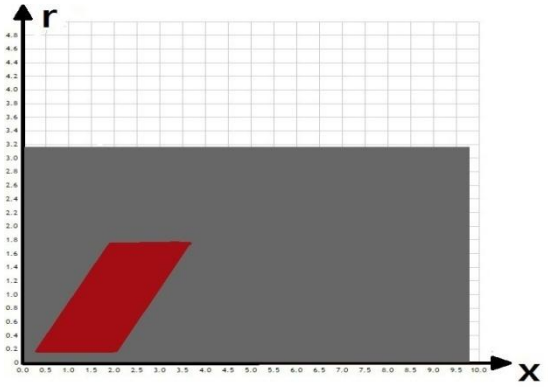
Fv - Pressure in vessel
Ft - Pressure in tissue
ΔP=Fv-Ft

Exchange with interstitial.

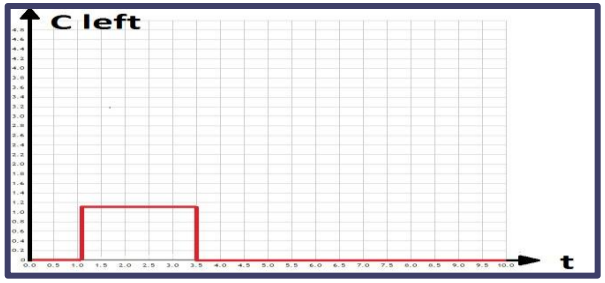
Form of «impenetrable» area

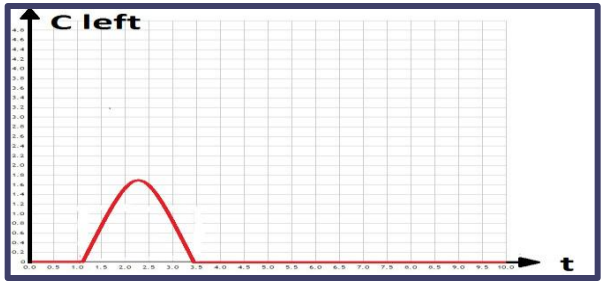


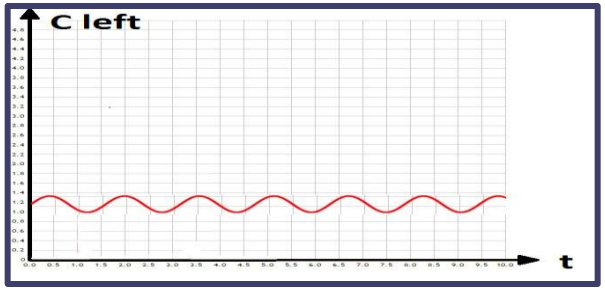




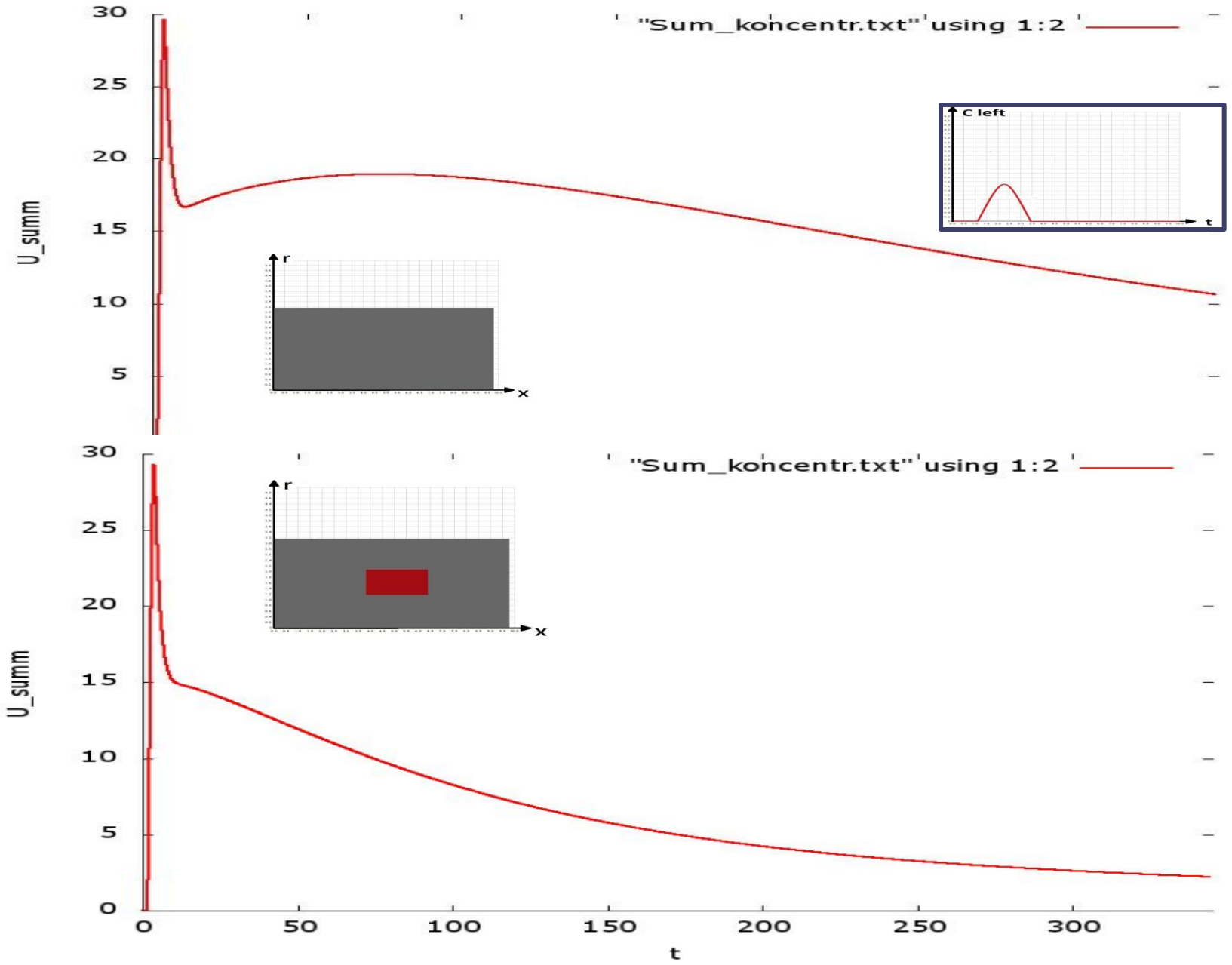
Form of «signal»



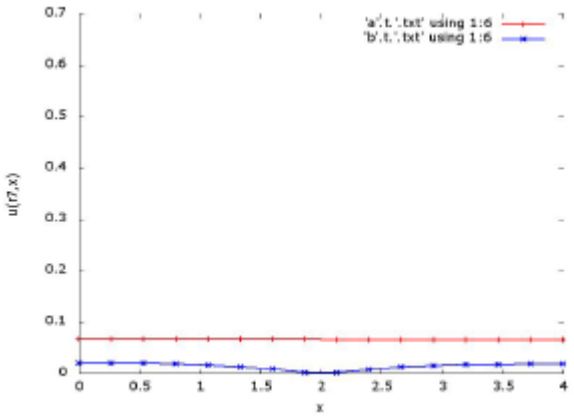


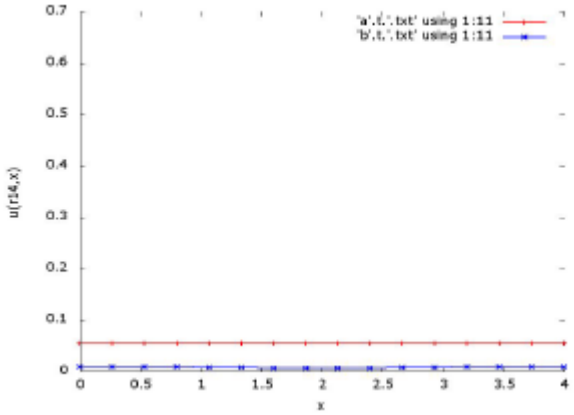


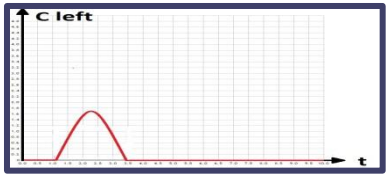
Exchange with interstitial.



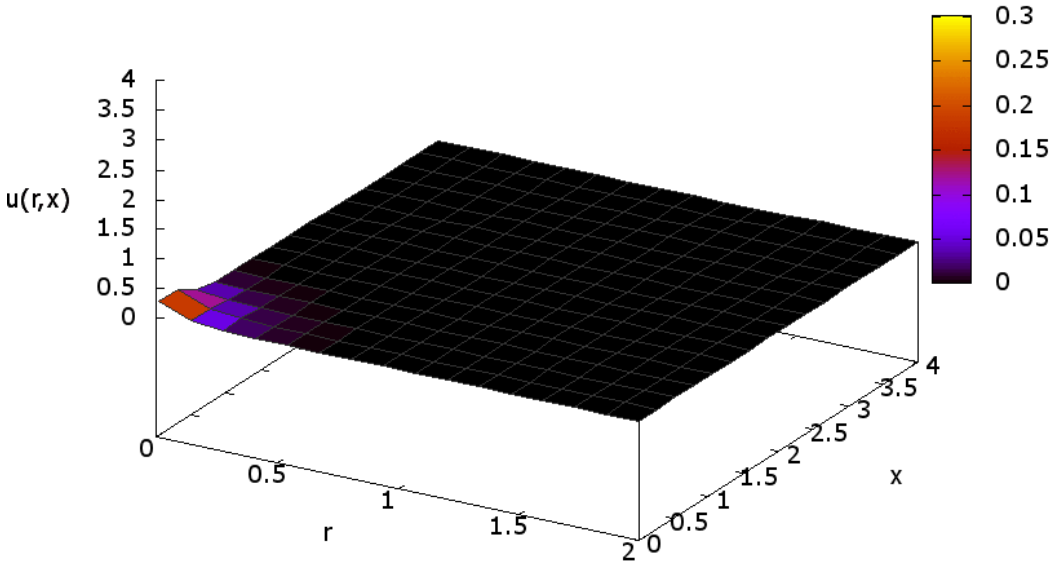
Exchange with interstitial.



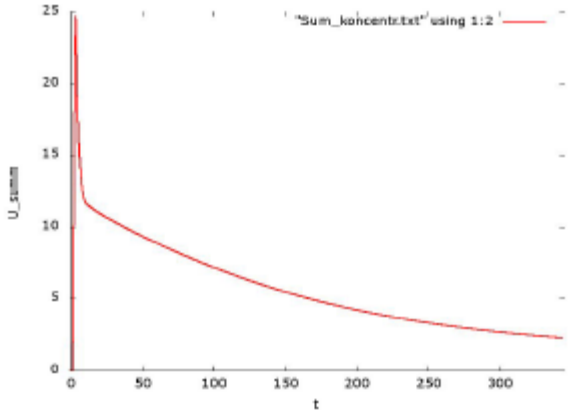


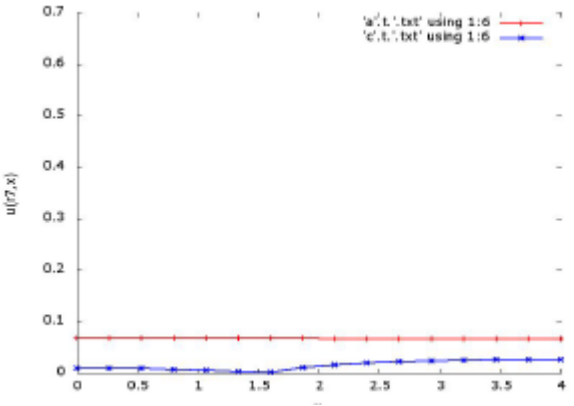


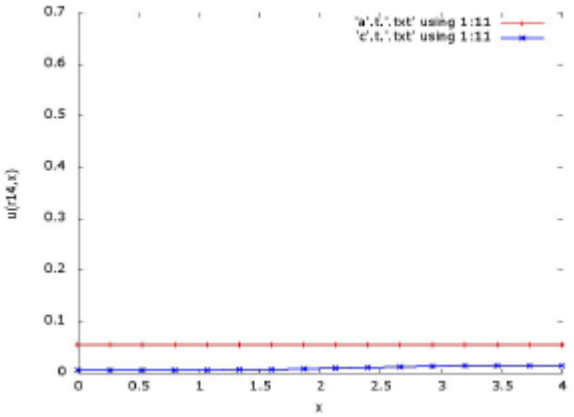
u(r,x)_n2

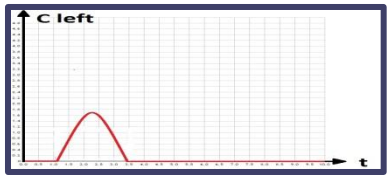


Exchange with interstitial.

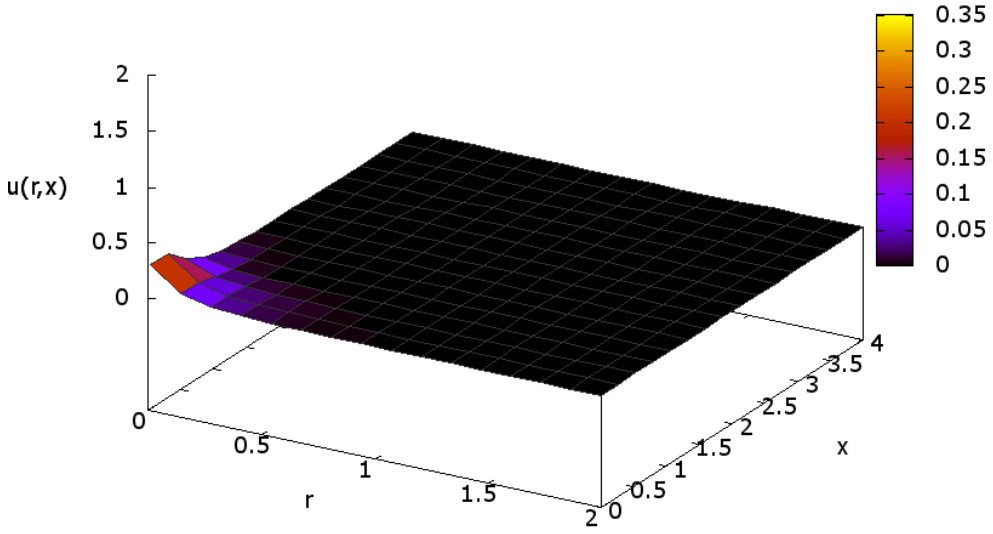




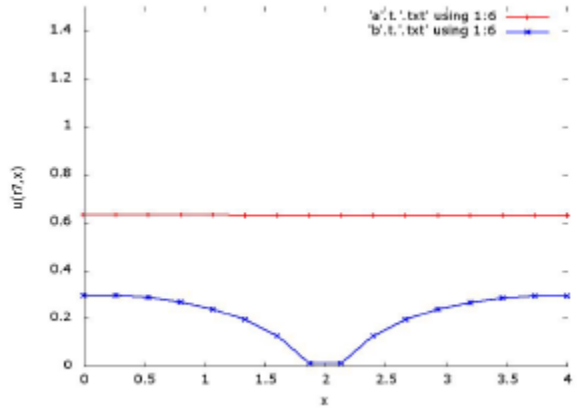


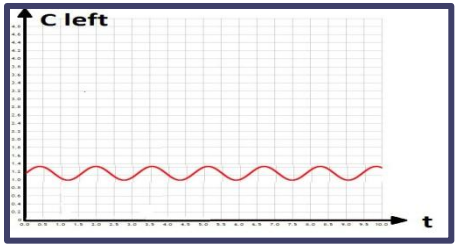


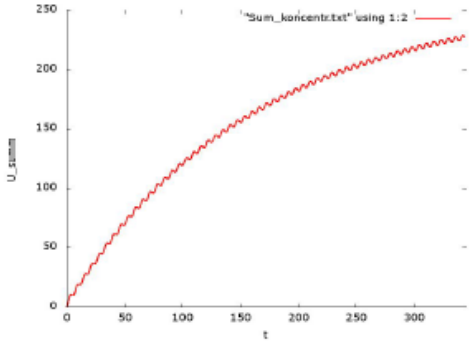
u(r,x)_n1

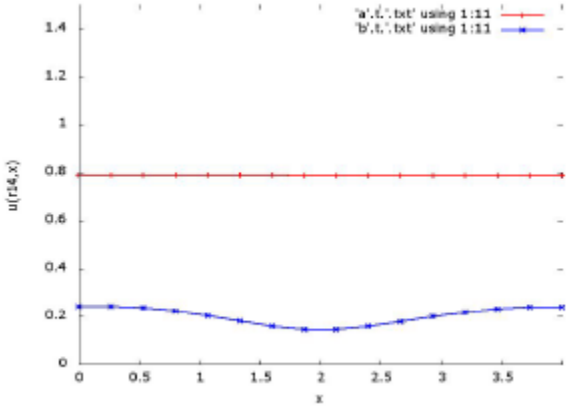


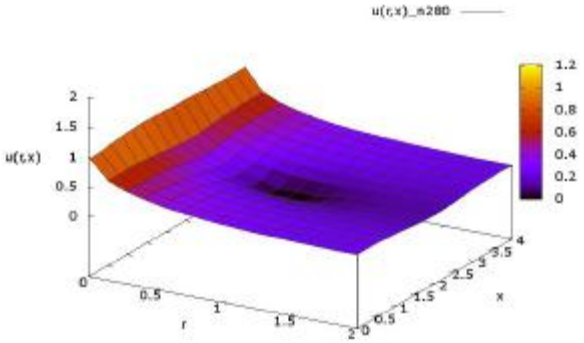
Exchange with interstitial.

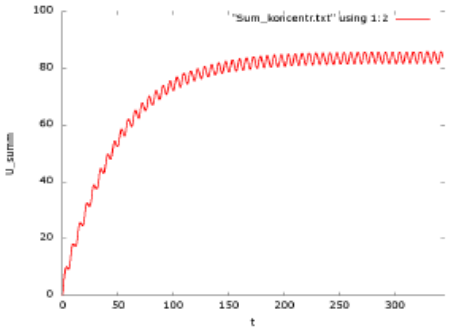




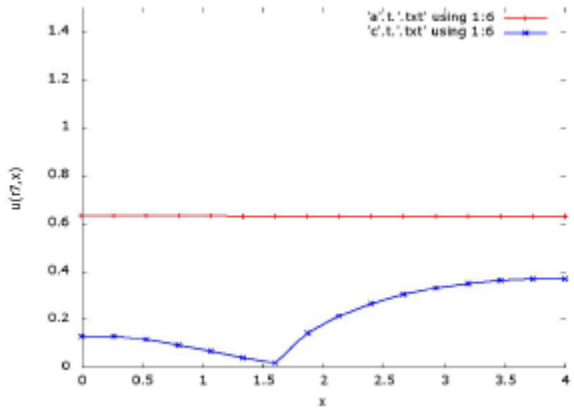


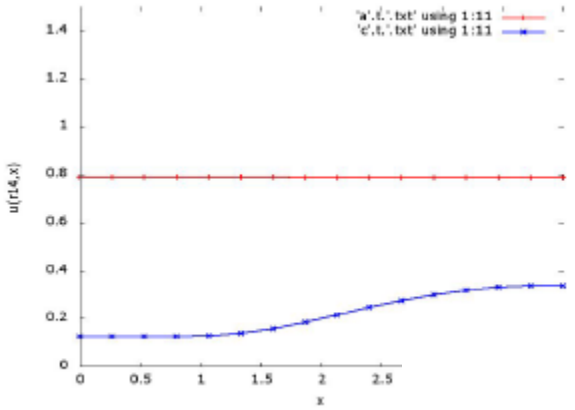


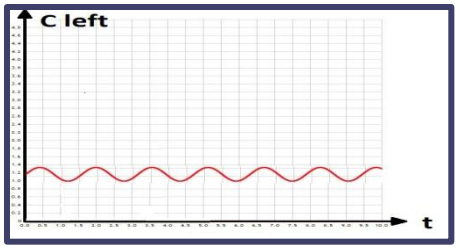


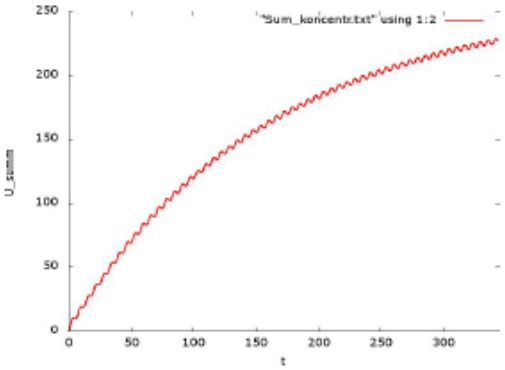


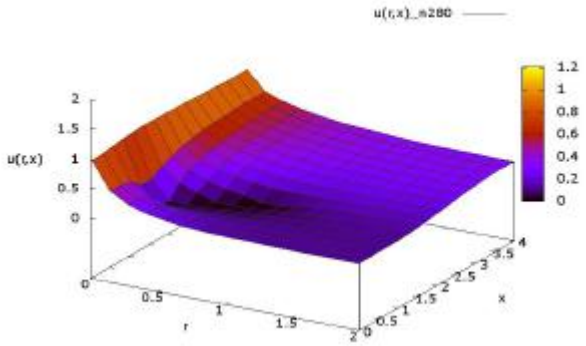
Exchange with interstitial.

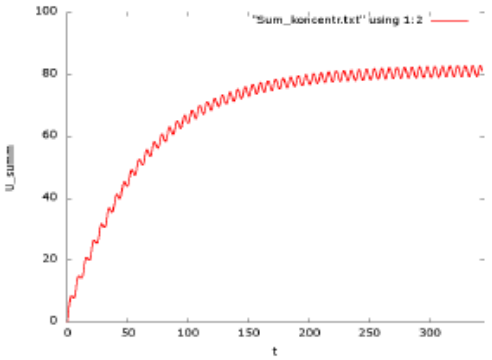




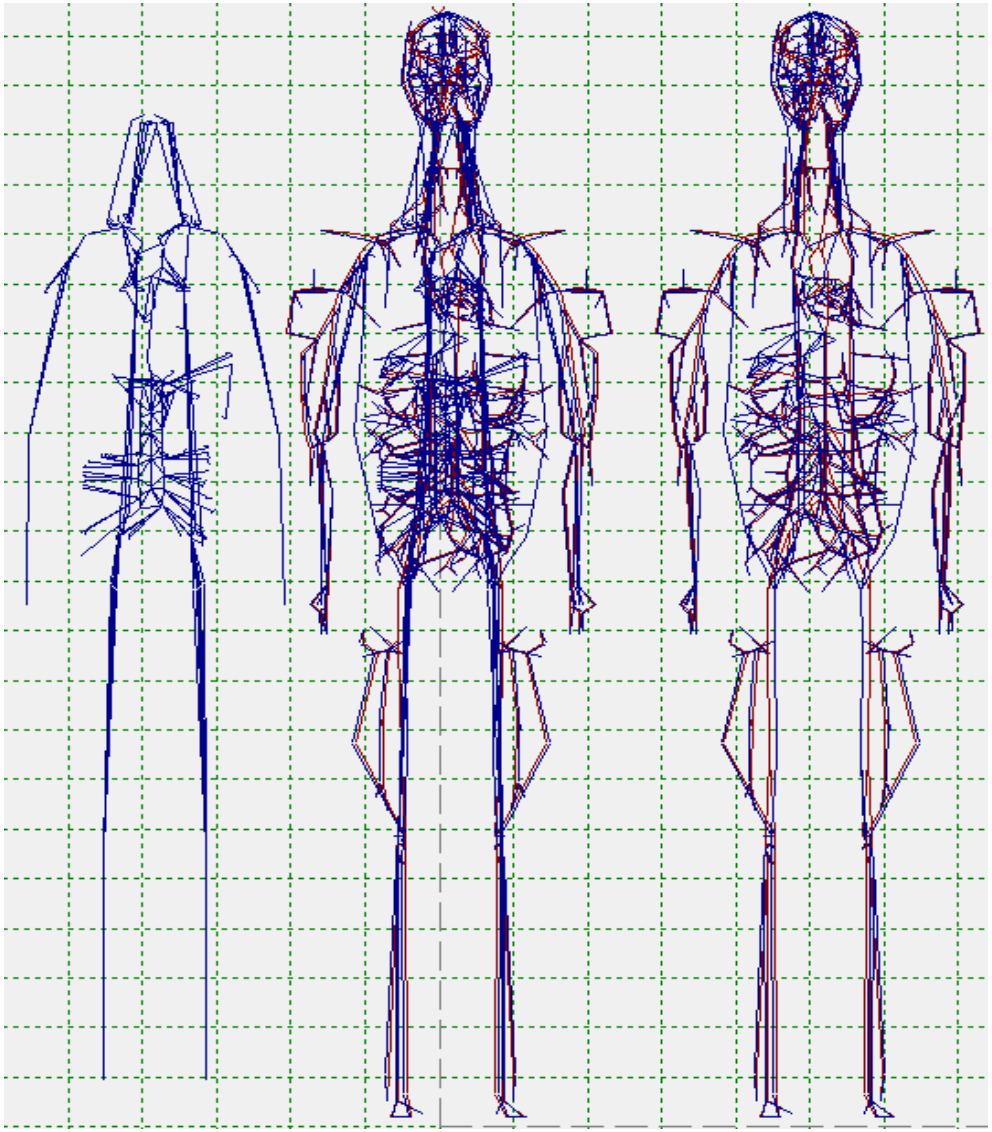








Conjunction of cardiovascular and lympatic system:



- 3D topological correspondence
- quazi 1D hemodynamic equations for liquid flow in big vessels
- mixed Darcy-diffusion models for tissue and areas of conjuction
- specific models for organs
- common simultaneous calculation

- Mathematical model of haemodynamics of cardio-vascular system / M. Abakumov , K. Gavriluk, N.Esikova et al. // *Differential Equations (in Rus.)*— 1997. — Vol. 33, № 7. — p. 892–898.
- Analysis and comparison of some analytic and numerical solutions of hemodynamic problems / I. Ashmetkov, A. Khrulenko, S. Mukhin et al. // *Differential Equations*. — 2000. — Vol. 36, no. 7. — P. 1021–1026.
- An averaged nonlinear model of hemodynamics on the vessel graph / A. Bunicheva, S. Mukhin, N. Sosnin, A. Favorskii // *Differential Equations*. — 2001. — Vol. 37, no. 7. — P. 949–956.
- Mathematical modeling of some applied problems in haemodynamics / A. Bunicheva, S. Mukhin, N. Sosnin et al. // *Computational Mathematics and Modeling*. — 2002. — Vol. 13, no. 4. — P. 382–412.
- Numerical experiment in hemodynamics / A. Bunicheva, S. Mukhin, N. Sosnin, A. Favorskii // *Differential Equations*. — 2004. — Vol. 40, no. 7. — P. 984–999.
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