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# Modeling of lymph flow in the whole net of lymphatic vessels

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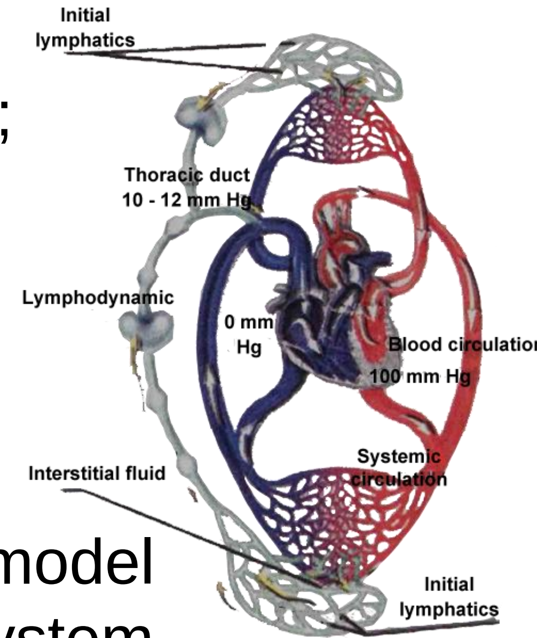
# Goals and tasks

Modeling of lymph flow is actual task because

- lymphatic vessels are tracks for immune cells, infections, cancer metastases, drugs;
- lymphatic system (LS) provide additional drainage to veins, and about 10% of blood go to the lymphatic capillaries from the interstitial space




Our goal is to create quasi-onedimensional model of lymph flow through the whole lymphatic system

Such model must include:

- model of LS;
- models of lymph flow through all parts of the LS with respect to functional features of these parts

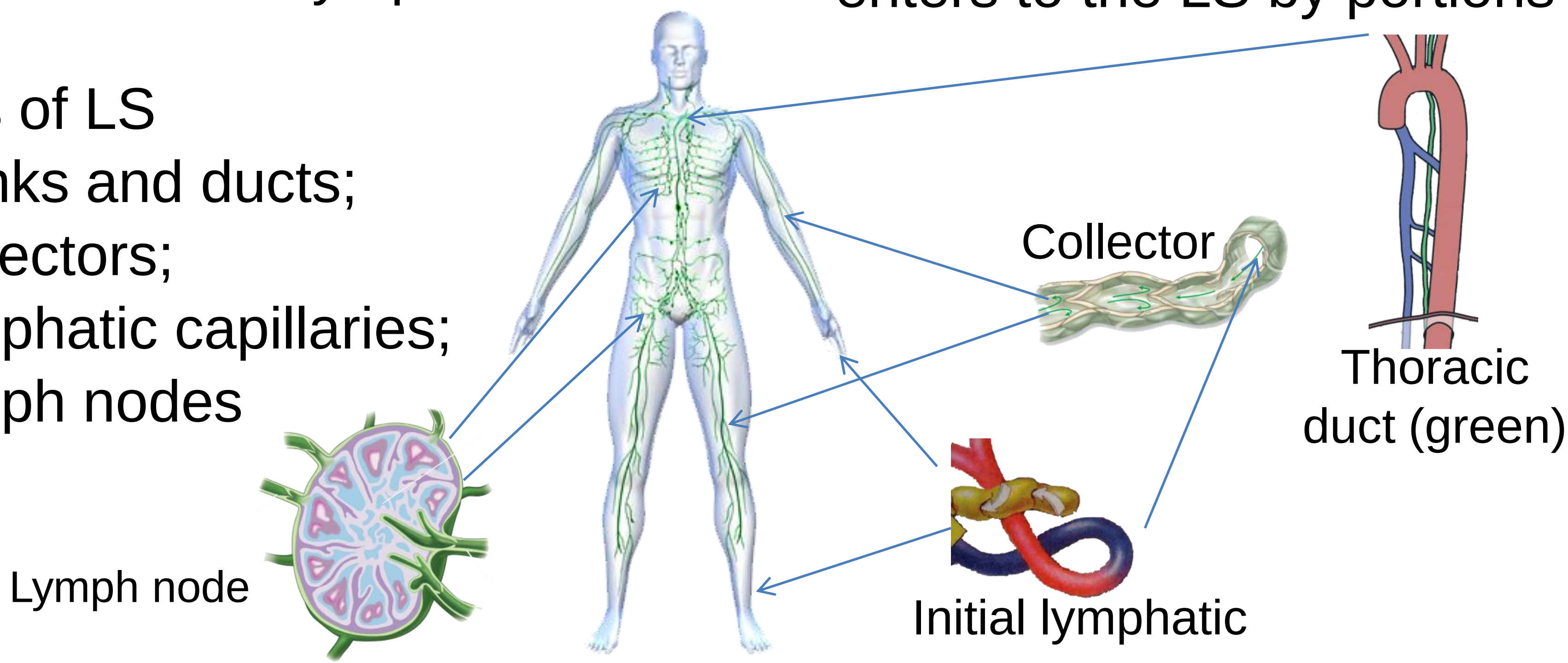
# Anatomy and physiology

LS
- is not closed;
- starts with lymphatic capillaries;
- ends in upper vena cava;
- has no strict hierarchy;
- has numerous lymph nodes

Lymph flow
- low velocity;
- low pressure gradients;
- unidirectional

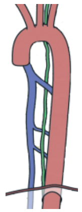
Lymph
- enters to the LS by portions

Parts of LS
- trunks and ducts;
- collectors;
- lymphatic capillaries;
- lymph nodes



# Parameters

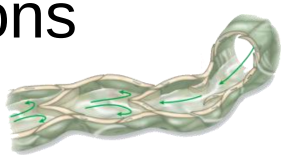
## Trunks and ducts

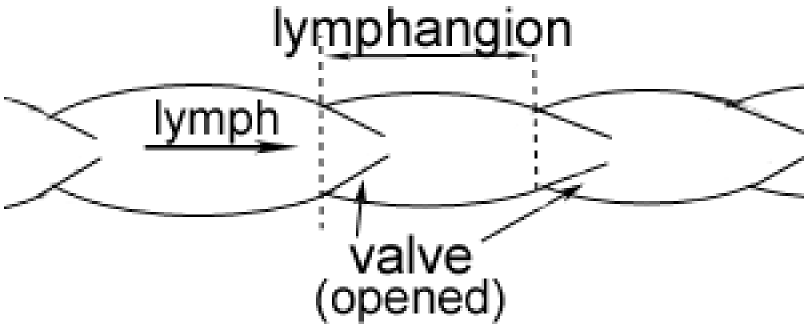


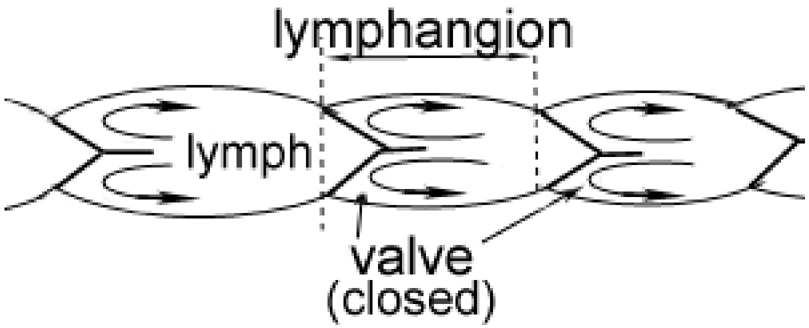
- ∅ 1.5 – 2 mm;
- rare valves, length of lymphangions can reach 5 cm;
- active contractions;
- velocity about 0.5 – 1 cm/s

## Collectors

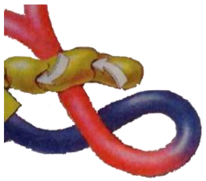
- ∅ 3 – 5 μm to 1 – 2 mm;
- frequent valves;
- active contractions





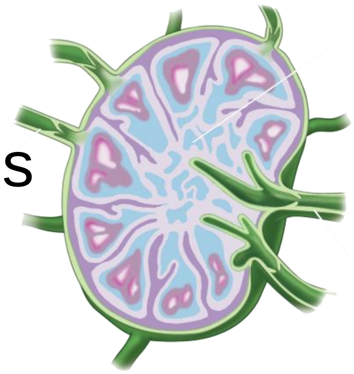

## Initial lymphatics



- ∅ 20 – 200 μm;
- no valves in the lumen;
- “primary” valves

## Lymph nodes

- active contractions

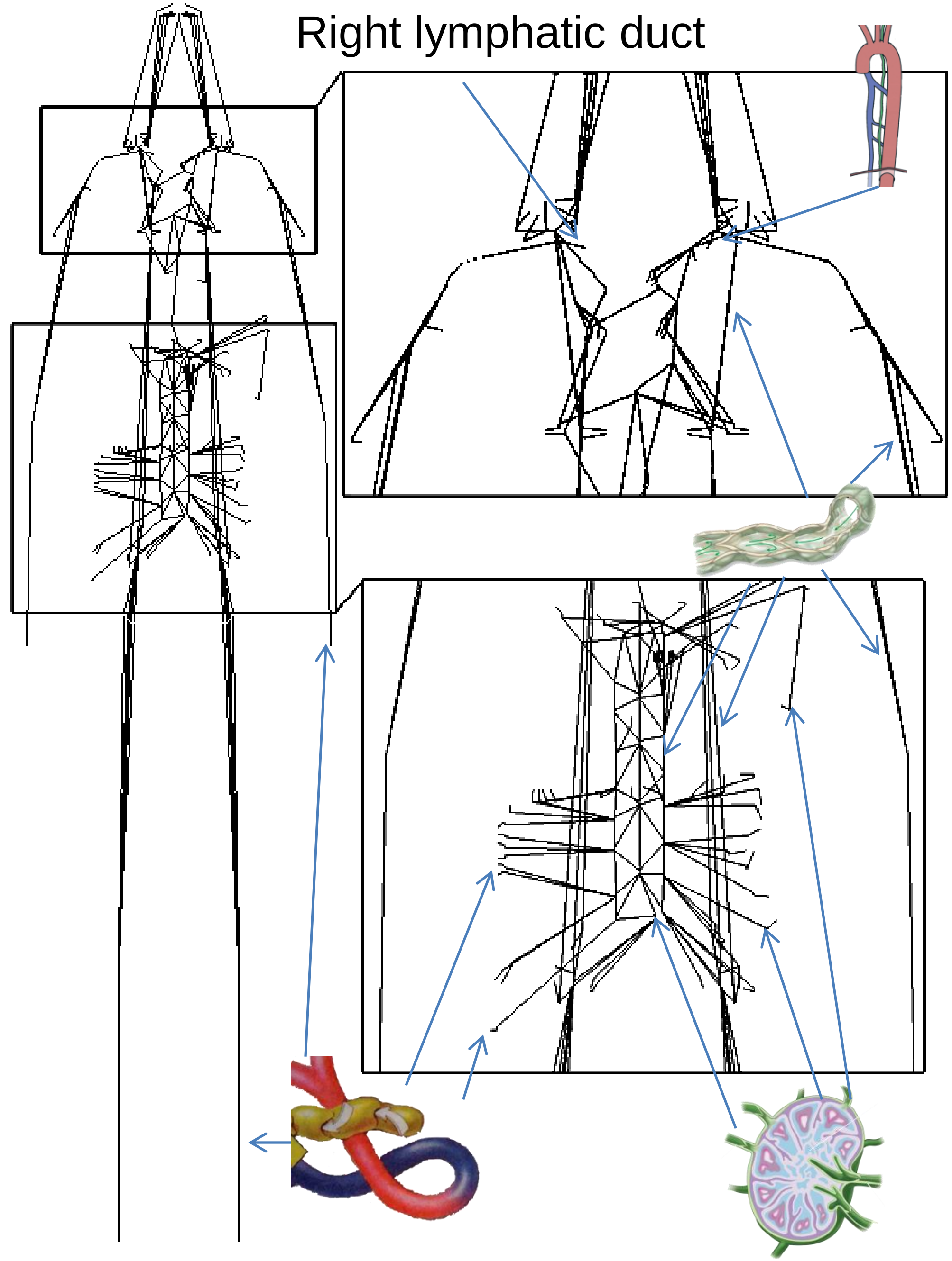


# Graph of the LS

Graph of the LS contains:

- main trunks and ducts;
- main regional groups of lymph nodes;
- afferent and efferent vessels for each node – collectors;
- effective representation of initial lymphatics;
- two exits: to the right and to the left venous angles

There are 543 arcs and 478 vertices in the graph. 161 arcs represent lymph nodes in 46 regional groups

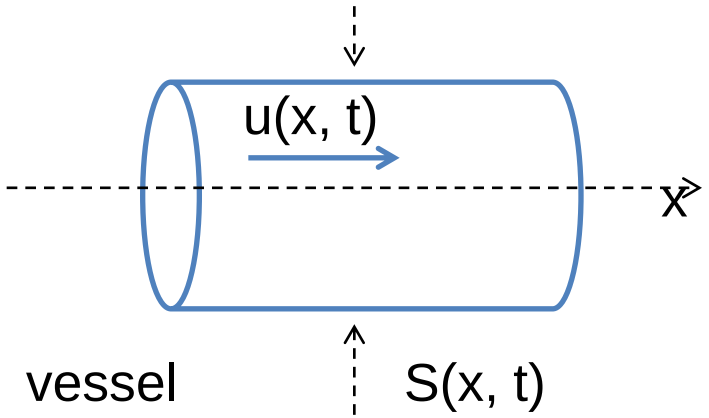


# Graph elements

There are 4 groups of elements in the graph characterized by functional differences and features of lymph flow:

1. Trunks and ducts: rare valves, active contractions.
2. Collectors: frequent valves, active contractions.
3. Initial lymphatics: no valves, no contractions, great number;
4. Lymph nodes: active contractions.

# Basic equations on the vessel




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

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

$$S = S(p)$$

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

# Lymph flow with respect to valves

**1 group**

rare valves -> can be presented directly on the graph with properly boundary condition:

$$\begin{cases} u_i S_i = u_j S_j, \text{ flow is allowed by valve} \\ u_j S_j = 0, \text{ flow is restricted by valve} \end{cases}$$

*i* – number of afferent vessel
*j* – number of efferent vessel

**2 group**

frequent valves -> hard to present directly; very close placement of valves -> valve restriction become the property of media -> it can be modeled by specific function of hydrodynamic resistance $f_{vlv}$ in the movement equation:

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

$$f_{vlv} = \begin{cases} 0, \text{ flow is allowed by valves,} \\ f, \text{ flow is restricted by valves} \end{cases}$$

# Lymph flow with respect to contractions

Such flow in 1, 2 and 4 groups. It can be modeled by following changes in state equation:

$$S(x,t) = S(p,x,t)$$

namely like this:

$$S(x,t) = S(p,pe) = S_0 + \theta(p - p_0) + \theta pe$$

where *pe(x,t)* – function of external pressure

## Problem 1

$$\begin{cases} \dfrac{\partial S}{\partial t} + \dfrac{\partial uS}{\partial x} = 0, \\ \dfrac{\partial u}{\partial t} + u\dfrac{\partial u}{\partial x} + \dfrac{1}{\rho}\dfrac{\partial p}{\partial x} = 0, \\ S(x,\mathrm{t}) = \mathrm{S}(\mathrm{p},\mathrm{x},\mathrm{t}) = S_0 + \theta(p - p_0), \\ 0 < x < +\infty,\ t > 0 \end{cases}$$

$$\begin{cases} u(x,0) = \overline{u} = 0 \\ p(x,0) = \overline{p} \end{cases},\ 0 \le x < +\infty,$$

$$p(0,t) = \overline{p} + A\sin\left(\frac{2\pi}{\lambda}at\right),\ \mathrm{t} \ge 0$$

$$u(x,t) = \overline{u} + \tilde{u}(x,t)$$
$$p(x,t) = \overline{p} + \tilde{p}(x,t)$$
$$S(x,t) = \overline{S} + \tilde{S}(x,t)$$
$$\tilde{p} \ll \overline{p},\ \tilde{S} \ll \overline{S}$$

$$\begin{cases} \tilde{p}_t + \overline{u}\tilde{p}_x + \rho\overline{c}^2\tilde{u}_x = 0 \\ \tilde{u}_t + \dfrac{1}{\rho}\tilde{p}_x + \overline{u}\tilde{u}_x = 0 \end{cases},\ 0 < x < +\infty,\ \mathrm{t}>0$$

$$\overline{c}^2 = \left.\frac{\mathrm{d}S}{\mathrm{d}p}\right|_{p=\overline{p}} = \theta$$

$$\begin{cases} \tilde{u}(x,0) = 0 \\ \tilde{p}(x,0) = 0 \end{cases},\ 0 \le x < +\infty$$

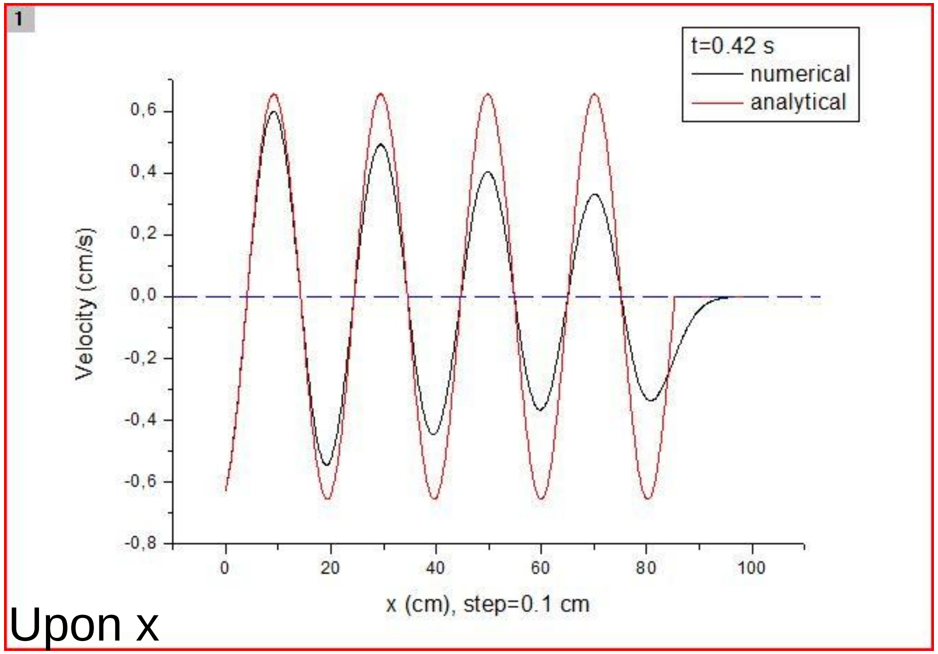
$$\tilde{p}(0,t) = A\sin\left(\frac{2\pi}{\lambda}at\right),\ t \ge 0$$

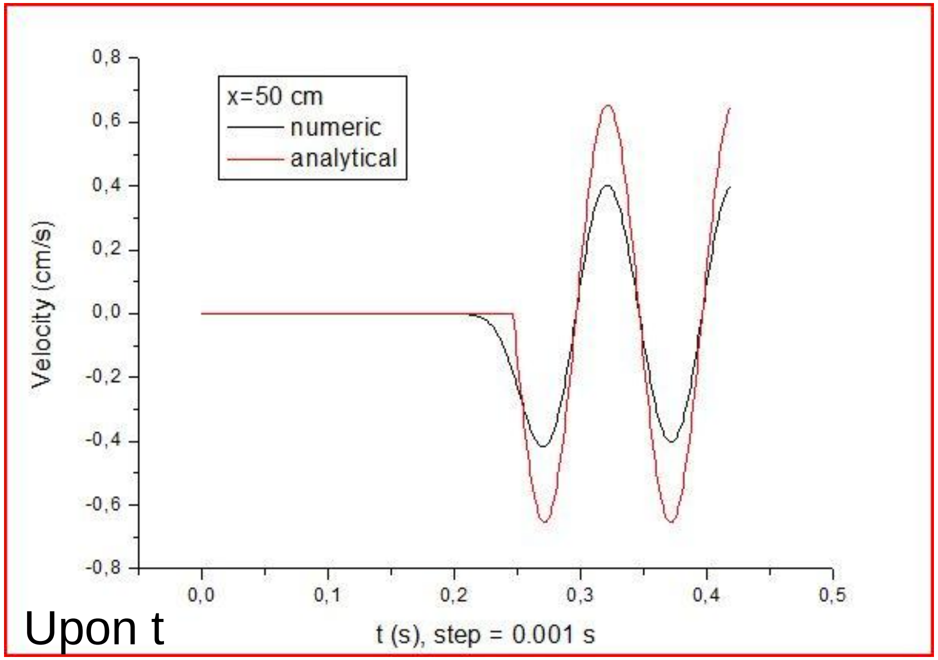
# Exact solution of linear problem

$$\tilde{p}(x,t) = \begin{cases} 0, \; x-(\bar{u}+\bar{c})t \geq 0 \\ A\sin\left(\dfrac{2\pi}{\lambda}a\left(t-\dfrac{x}{\bar{u}+\bar{c}}\right)\right), \; x-(\bar{u}+\bar{c})t < 0 \end{cases},$$

$$\tilde{u}(x,t) = \begin{cases} 0, \; x-(\bar{u}+\bar{c})t \geq 0 \\ \dfrac{A}{\rho\bar{c}}\sin\left(\dfrac{2\pi}{\lambda}a\left(t-\dfrac{x}{\bar{u}+\bar{c}}\right)\right), \; x-(\bar{u}+\bar{c})t < 0 \end{cases}$$

Comparison of exact (red) and numerical (black) solutions of problem 1:



# Problem 2

$$\begin{cases} \dfrac{\partial S}{\partial t} + \dfrac{\partial uS}{\partial x} = 0, \\ \dfrac{\partial u}{\partial t} + u\dfrac{\partial u}{\partial x} + \dfrac{1}{\rho}\dfrac{\partial p}{\partial x} = 0, \\ S = S(p,x,t) = S_0 + \theta(p - p_0) + \theta pe(x,\mathrm{t}), \\ \boxed{pe(x,\mathrm{t}) = -A\cos\left(\dfrac{2\pi}{\lambda}(x - at)\right),} \\ -\infty < x < +\infty,\ t > 0, \end{cases}$$

$$\begin{cases} u(x,0) = \bar{u} = 0 \\ p(x,0) = \bar{p} \end{cases},\ -\infty < x < +\infty$$

$$u(x,t) = \bar{u} + \tilde{u}(x,t)$$
$$p(x,t) = \bar{p} + \tilde{p}(x,t)$$
$$S(x,t) = \bar{S}(x,t) + \tilde{S}(x,t)$$
$$\tilde{p} \ll \bar{p},\ \tilde{S} \ll \bar{S}$$

$$\begin{cases} \tilde{p}_t + \bar{u}\tilde{p}_x + \rho\bar{c}^2\tilde{u}_x = q(x,t) \\ \tilde{u}_t + \dfrac{1}{\rho}\tilde{p}_x + \bar{u}\tilde{u}_x = 0 \end{cases},\ -\infty < x < +\infty,\ t>0$$

$$\begin{cases} \tilde{u}(x,0) = 0 \\ \tilde{p}(x,0) = 0 \end{cases},\ -\infty < x < +\infty$$

$$\boxed{q(x,t) = -\frac{1}{\theta}\left(\bar{S}_t + \bar{u}\bar{S}_x\right) = A\frac{2\pi}{\lambda}(a - \bar{u})\sin\left(\frac{2\pi}{\lambda}(x - at)\right)}$$

## Exact solution of linear problem:

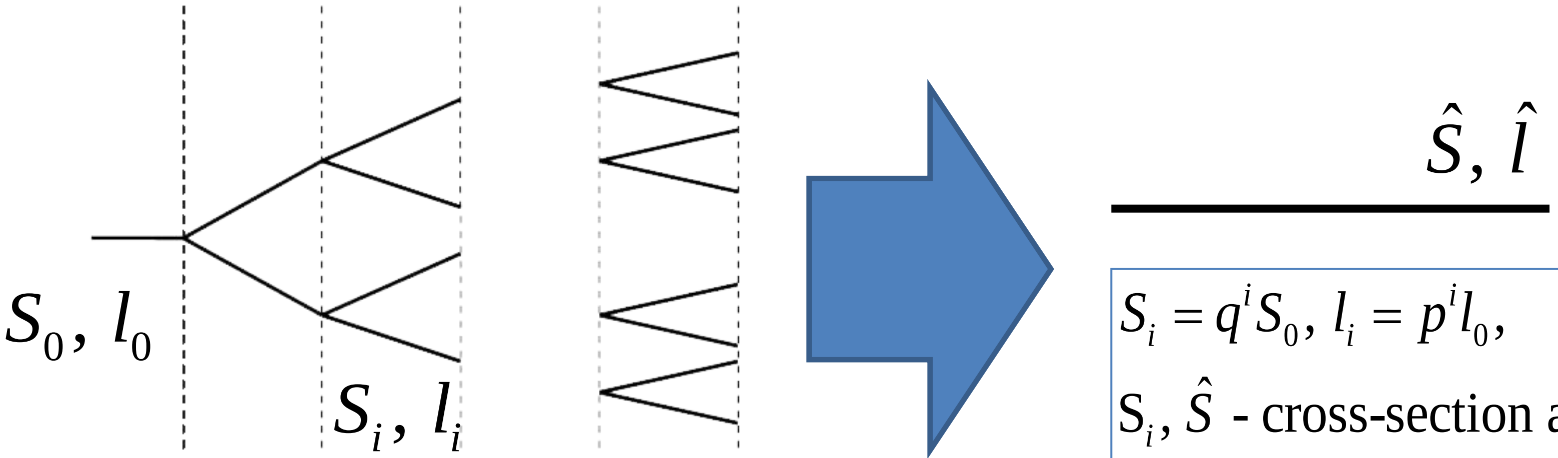
$$\tilde{p}(x,t) = -\frac{A(a-\bar{u})}{2}\left[\frac{\cos\left(\frac{2\pi}{\lambda}(x-at)\right) - \cos\left(\frac{2\pi}{\lambda}(x-\bar{\lambda}^{+}t)\right)}{\bar{\lambda}^{+} - a} + \frac{\cos\left(\frac{2\pi}{\lambda}(x-at)\right) - \cos\left(\frac{2\pi}{\lambda}(x-\bar{\lambda}^{-}t)\right)}{\bar{\lambda}^{-} - a}\right],$$

$$\tilde{u}(x,t) = -\frac{A(a-\bar{u})}{2\rho\bar{c}}\left[\frac{\cos\left(\frac{2\pi}{\lambda}(x-at)\right) - \cos\left(\frac{2\pi}{\lambda}(x-\bar{\lambda}^{+}t)\right)}{\bar{\lambda}^{+} - a} - \frac{\cos\left(\frac{2\pi}{\lambda}(x-at)\right) - \cos\left(\frac{2\pi}{\lambda}(x-\bar{\lambda}^{-}t)\right)}{\bar{\lambda}^{-} - a}\right]$$

$$\bar{\lambda}^{\pm} = \bar{u} \pm \bar{c}$$

# Flow in initial lymphatics

Binary tree of initial lymphatics is substituted with one effective element with parameters that save flux, pressure gradient and lateral area of the net




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

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

$l_i, \hat{l}$ - length

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

# Flux in “horizontal” case

**Goals:**

1. Obtain flux in the system.
2. Get presumable flux 0.023 ml/s ≈ 2 l/day

**Initial data:**

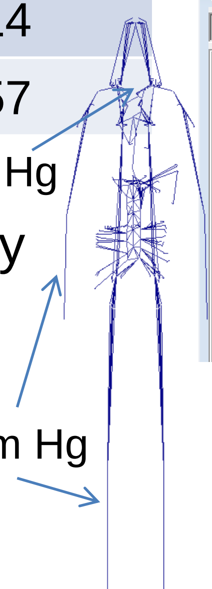
| Name | d (cm) | S (cm^2) |
|---|---|---|
| Effective vessels | 0.02 | 0.00024 |
| Collectors | 0.107 | 0.009 |
| Lumbar trunks | 0.15 | 0.0177 |
| Other trunks | 0.1 | 0.0079 |
| Ducts, lymph nodes | 0.2 | 0.0314 |
| Cisterna Chyli | 0.4 | 0.1257 |

Pressure gradient = 5 mm Hg

No valves, no contractions, no gravity

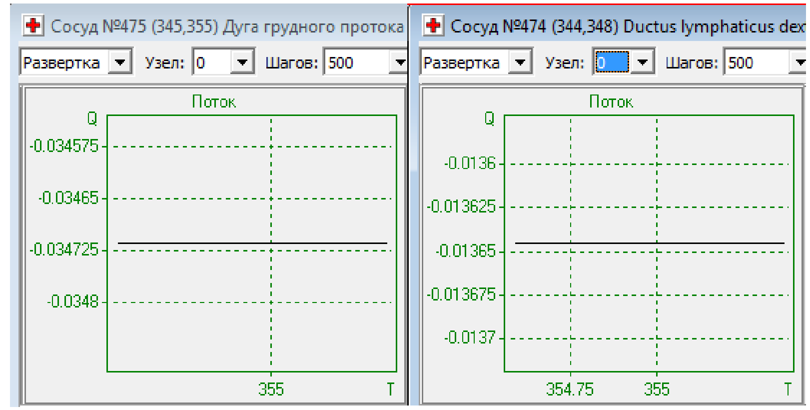
Calculations in CVSS programs until steady flow is established. Get presumable flux by varying parameters of effective elements

0 mm Hg



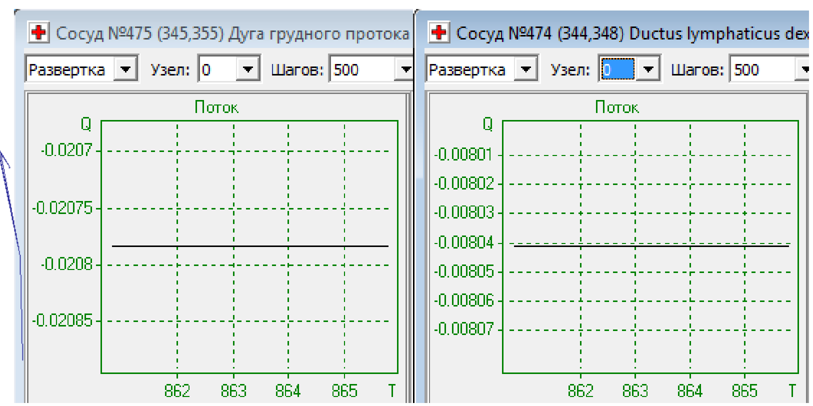
5 mm Hg

**Results**:




Flux upon time

Output flux = 0.0483 ml/s




Flux upon time

Output flux = 0.0288 ml/s – is consistent with physiology value

# Flux in “vertical” case

**Goals:**

1. Investigate model under gravity influence

**Initial data:**

Pressure gradient = 5 mm Hg

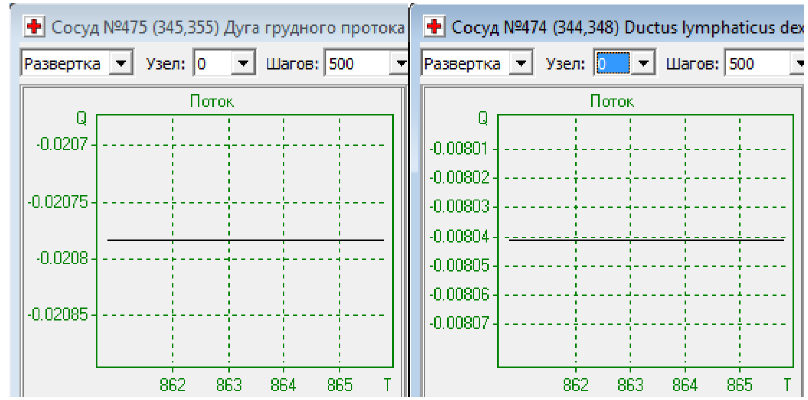
Valves-vertices, no contractions, gravity force influence

**Methods**:

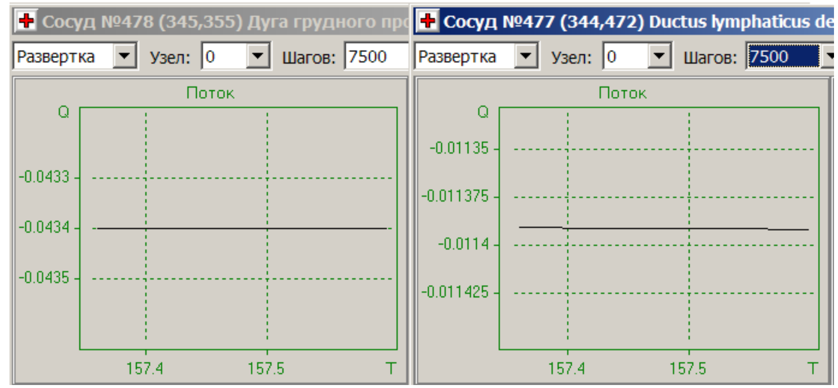
Calculations in CVSS program until steady flow on trunks is established. Gravity factor *g* is consequentially increased from 0 cm/s to 900 cm/s

**Results**:

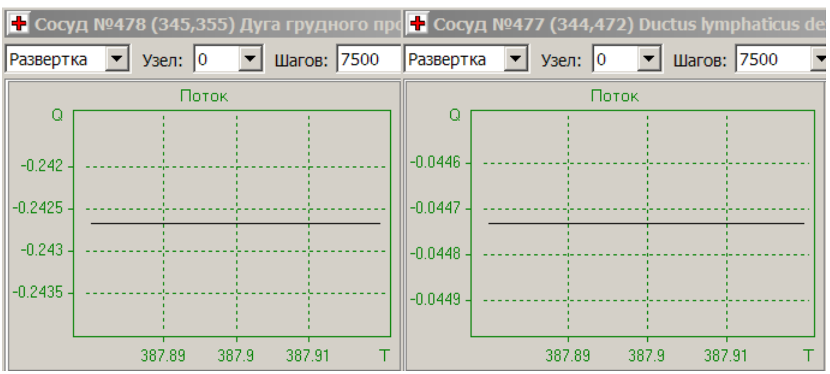
Flux grows with grow of *g*




Flux upon time, *g* = 0. Output flux = 0.0288




Flux upon time, *g* = 100. Output flux = 0.0548




Flux upon time, *g* = 900. Output flux = 0.2872

Further increase of *g* is not possible -> valves are not enough for correct modeling in case of gravity influence (vertical state)

# Volumetric model

Volume of big vessels is 20 ml. Physiological values for LS are 500 – 1500 ml, and main part of these values is given by periphery vessels. So we want to create model with physiological volume reached by increasing volume of peripheral vessels

**Goals:**

1. Obtain flux in the system.
2. Get presumable flux 0.023 ml/s ≈ 2 l/day

**Initial data:**

S of effective vessels = 2.12208 cm^2

Volume of LS = 491 ml

Valves-vertices, no contractions, no gravity

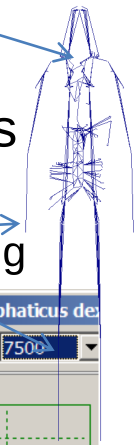
**Methods:**

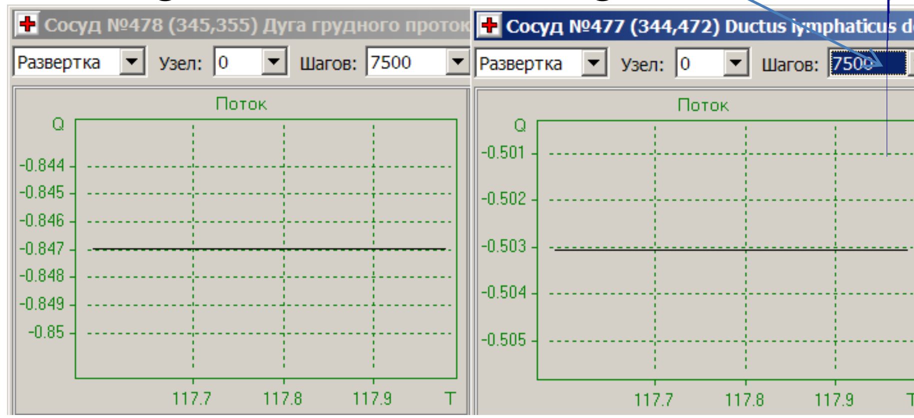
Calculations in CVSS programs until steady flow is established.

Get presumable flux by varying pressure gradient

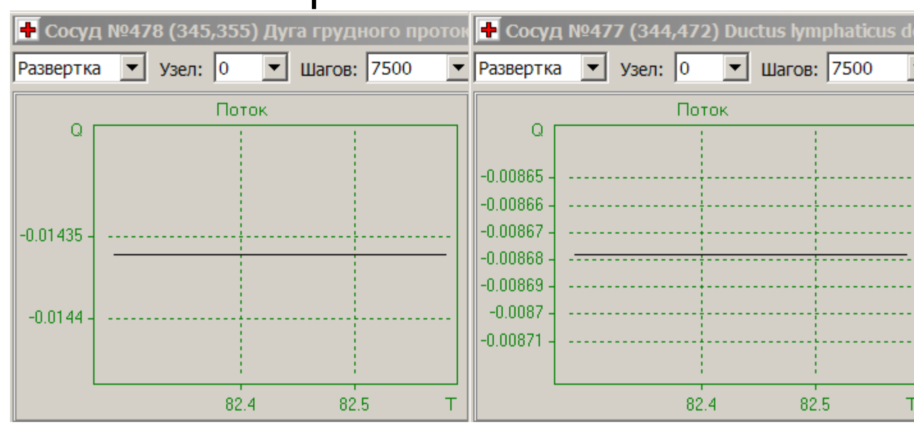
**Results**:

Presumable flux 0.023 ml/s is reached under the pressure gradient 0.1 mm Hg




Flux upon time, $\Delta P$ = 5 mm Hg. Output flux = 1.35 ml/s




Flux upon time. Output flux = 0.023 ml/s - physiological

# Results

- anatomically adequate graph of a whole net of lymphatic vessels was created (!);
- valves in trunks and ducts (valves-vertices) have been implemented in numerical model of lymph flow;
- the model of lymph flow in LS under the pressure gradient has been created. This model gives physiology correct results without gravity influence;
- volumetric model has been created. This model also gives physiology correct results under pressure gradient without gravity;
- analytical solutions have been written to check numerical realization of contraction mechanism;
- it is shown that current mechanisms of regularization are not enough for modeling lymph flow in case of gravity influence

Thank you for attention!