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Modeling of the pump function of the lymphatic vessels

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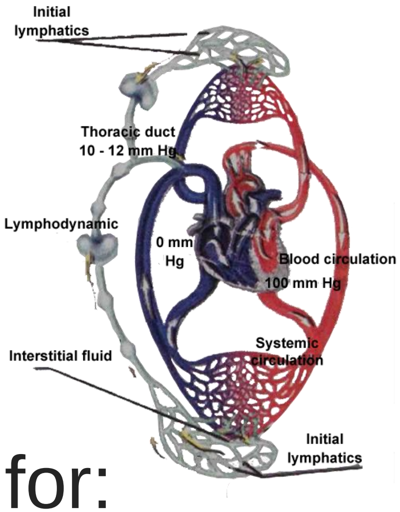
Goals and tasks



- Functions of the lymphatic system (LS):

  drainage, transport, immune

- Model of lymph transport in the LS is basic for:

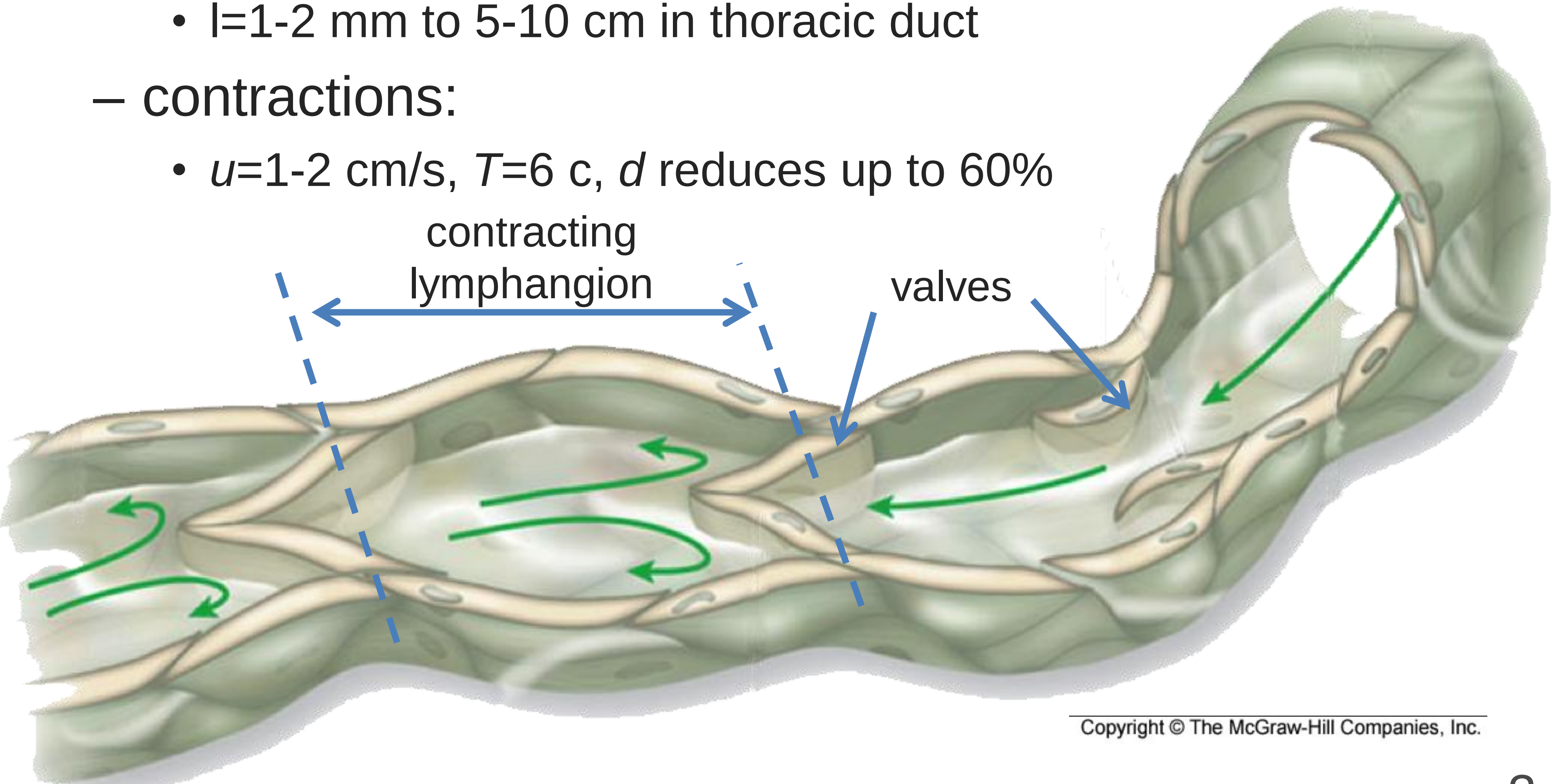
  drug distribution, lymphangiogenesis, coupled flow of blood and lymph, dysfunctions of transport and/or drainage functions of LS, check of the hypotheses and definition of the parameters of lymph flow

- Goal of the current work:

  to create a model of lymph flow in the human lymphatic system with respect to features of the lymphatic vessels in the quasi-onedimentional approach

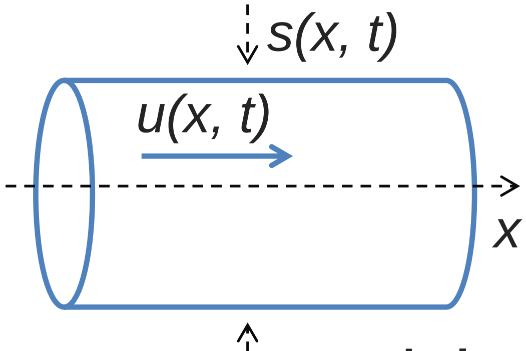
Pump function of lymphatic vessels

- is provided by valves and contractions
  - valves: restrict backward flow
  - lymphangions:
    - l=1-2 mm to 5-10 cm in thoracic duct
  - contractions:
    - u=1-2 cm/s, T=6 c, d reduces up to 60%



Quasi-onedimensional muscle pump

- quasi-onedimensional hemodynamic equations



$$\frac{\partial s}{\partial t}+\frac{\partial us}{\partial x}=0,\ \frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+\frac{1}{\rho}\frac{\partial p}{\partial x}=-8\pi\nu\frac{u}{s},\ s=s(p)$$

  – x – spatial variable, t – time, $p(x,t)$ – pressure, $u(x,t)$ – velocity, $s(x,t)$ – cross-section area, ρ=const – density, ν=const – viscosity

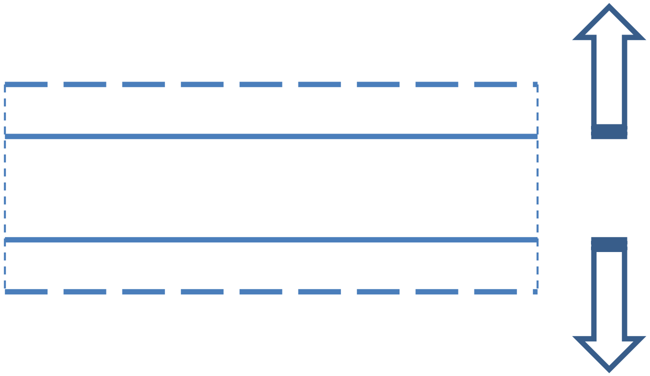
- with respect to valves and contractions

$$\frac{\partial s}{\partial t}+\frac{\partial us}{\partial x}=0,\ \frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+\frac{1}{\rho}\frac{\partial p}{\partial x}=-8\pi\nu(u)\frac{u}{s},\ s=s(p,x,t)$$

  – ν=const -> $\nu=\nu(u)$ – respect to frequent valves
  – $s(p)$ -> $s(p,x,t)$ – respect to lymphangion contractions

Muscle pump with *s=s(t)*

$$\frac{\partial s}{\partial t}+\frac{\partial us}{\partial x}=0,\quad \frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+\frac{1}{\rho}\frac{\partial p}{\partial x}=-8\pi\nu(u)\frac{u}{s},$$



$$s=s(t),\quad 0<x<l,\quad t>0$$

$$p(l,t)=p_l(t),\quad p(0,t)=p_0(t),\quad t>=0$$

solution:

$$u(x,t)=u_0(t)-\frac{s'}{s}x;\quad p(x,t)=p_0(t)+\rho\left[\frac{1}{2}\frac{s''}{s}-\left(\frac{s'}{s}\right)^2\right]x^2+\rho\left[u_0(t)\frac{s'}{s}-u_0'(t)\right]x+$$

$$8\pi\rho\frac{s'}{s^2}Ix-8\pi\rho\frac{u_0(t)}{s}I-8\pi\rho\frac{s'}{s^2}\int_{x_0}^{x}I\mathrm{d}x$$

where:

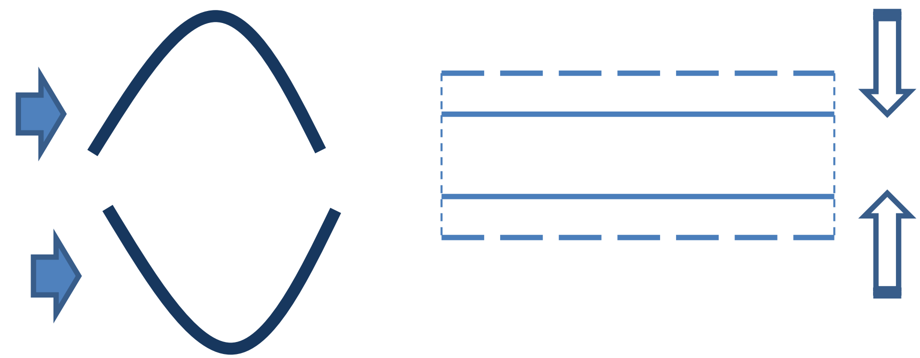
$$I=I(x)=\int_{x_0}^{x}\nu(u)dx$$

$$u_0'(t)=-\frac{p_l(t)-p_0(t)}{\rho l}-\frac{1}{2}U'(t)l-U(t)u\left(\frac{l}{2},t\right)-\frac{8\pi}{s(t)l}\Big(I\big(u(x,t)\big)-I\big(u_0(t)\big)\Big),\quad U(t)=-\frac{s'}{s}$$

Muscle pump with $s=s(t)$: pressure profile

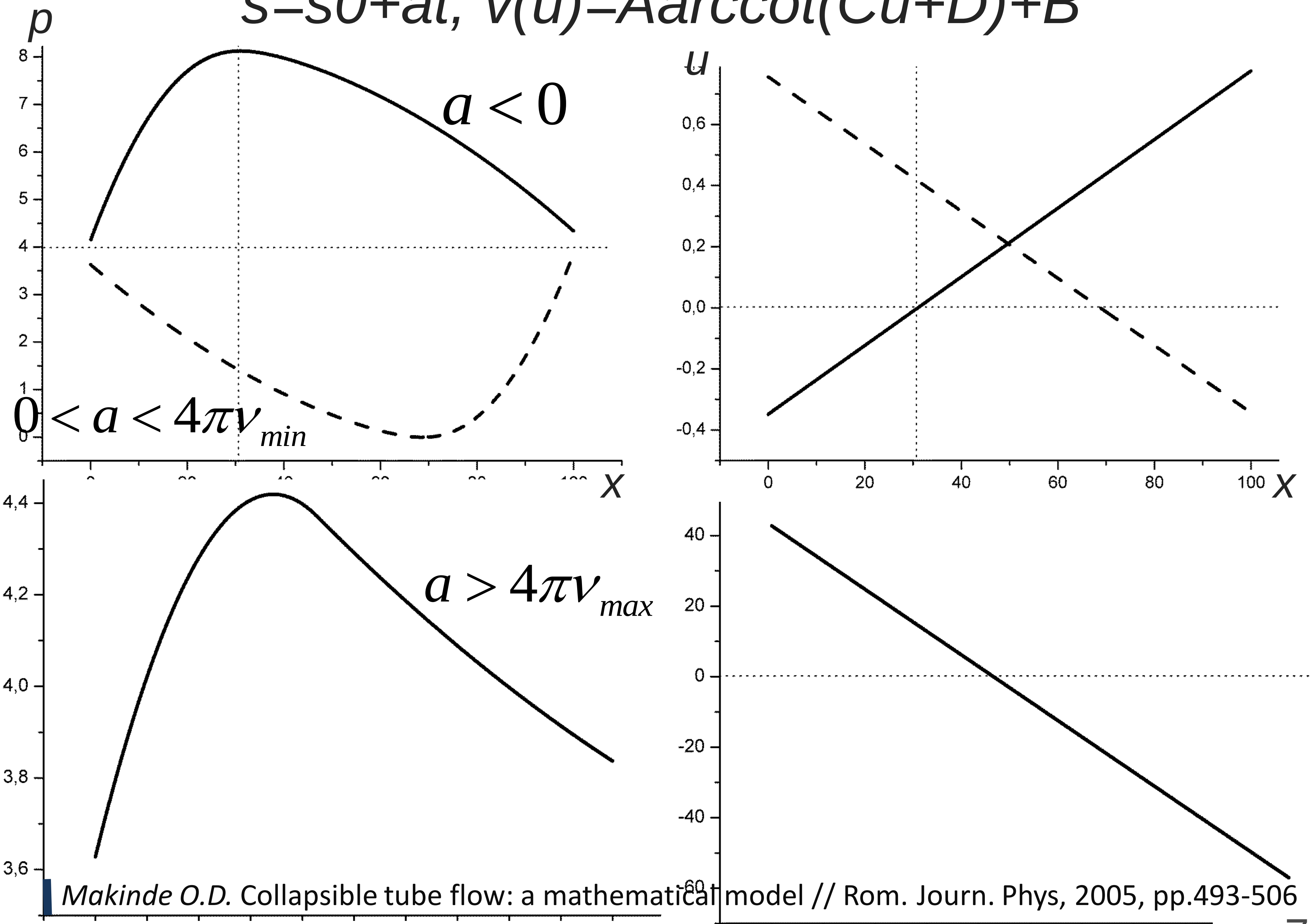
Proposition (sufficient conditions):

- if $v(u)$:
  - monotone bounded function
  - satisfying condition $0 < v_{min} \le \left(uv(u)\right)'_u \le v_{max}$
- then:
  - if $s'(t)<0$
    - if $s''s/s' - 2s' + 8\pi v_{\min} > 0$
    - if $s''s/s' - 2s' + 8\pi v_{\max} < 0$



  - if $s'(t)>0$
    - if $s''s/s' - 2s' + 8\pi v_{\min} > 0$
    - if $s''s/s' - 2s' + 8\pi v_{\max} < 0$

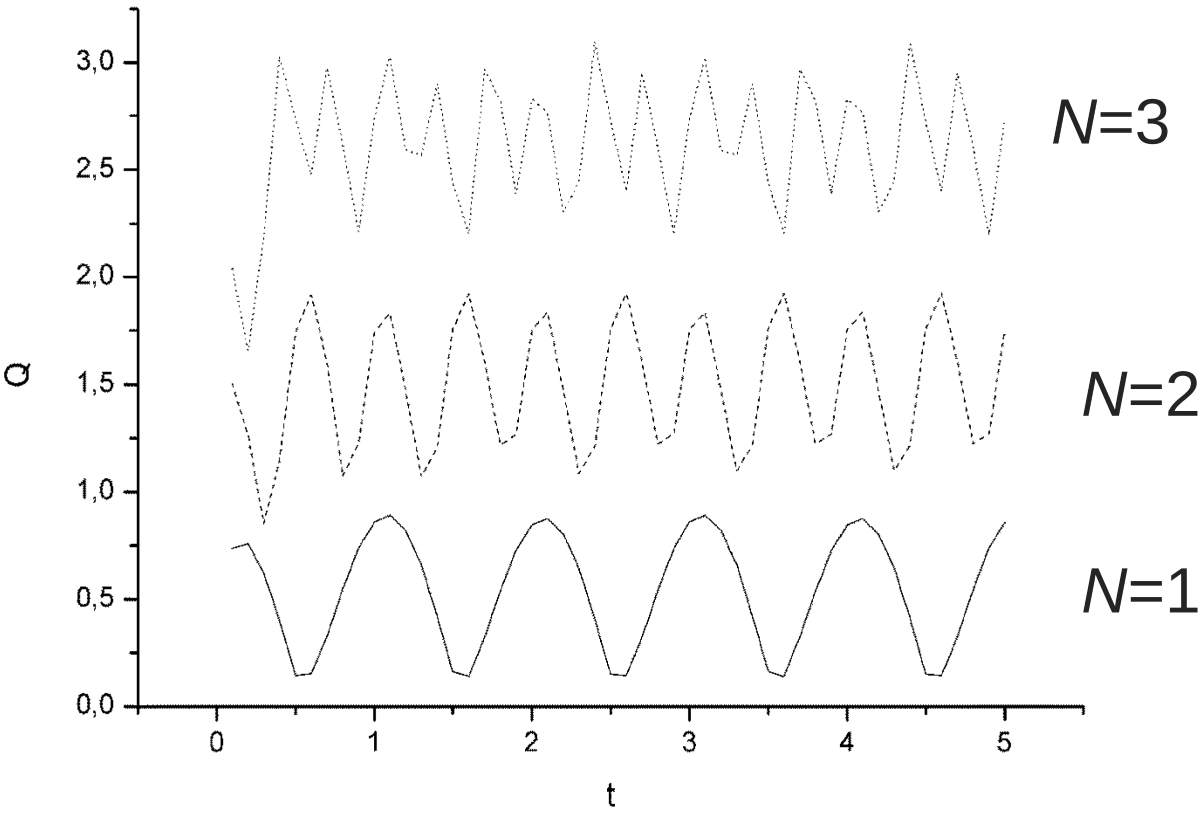
$s = s0 + at$, $v(u) = A\,\mathrm{arccot}(Cu + D) + B$



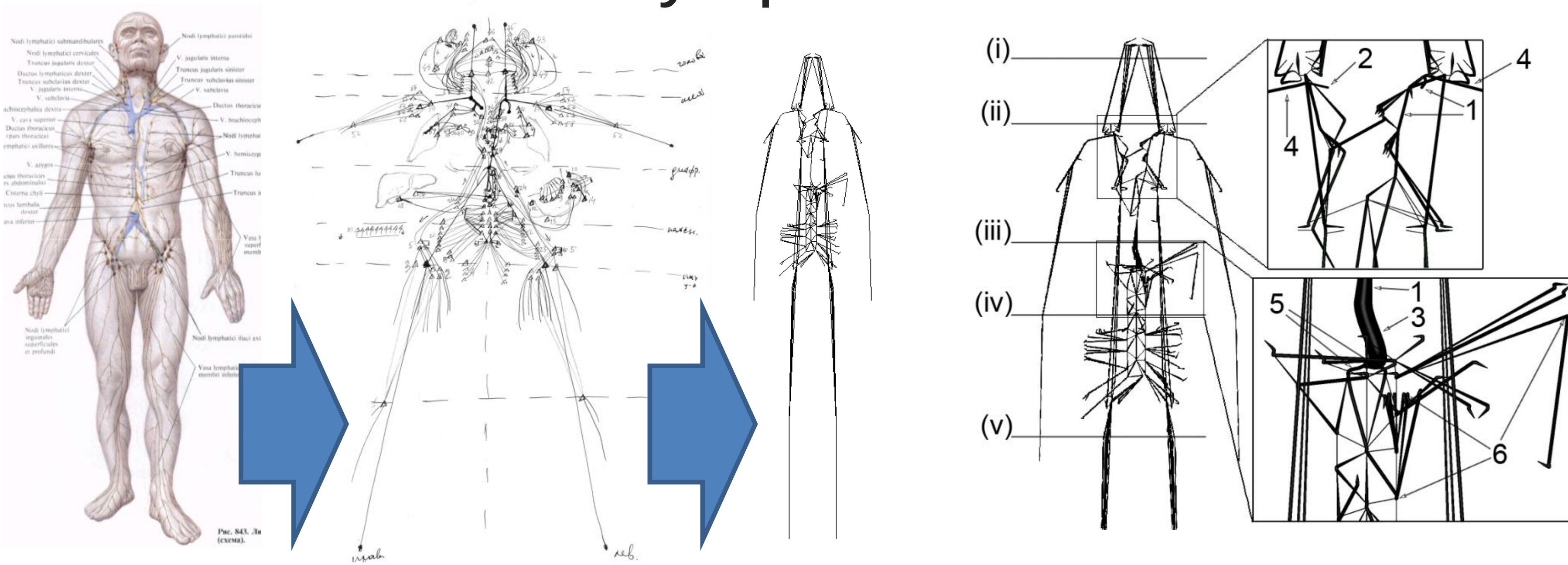
Makinde O.D. Collapsible tube flow: a mathematical model // Rom. Journ. Phys, 2005, pp.493-506

Performance of muscle pump

- *v=v(u)* and *s=s(p,x,t)* – unidirectional flow
- performance: $Q_{out}=Q_{right} - Q_{left}$
- Q_{out} depends on contraction frequency
- results for $s = s_0 + a\sin(N\pi t)$



Model of lymph flow in the LS



- graph of LS:
  - 543 arcs (trunks, ducts, collectors, nets of initial lymphatics, lymph nodes)
    - 225 contracting vessels
    - 186 vessels with anisotropic viscosity
  - 478 vertices (boundaries, points of bifurcations, valves)
- calculations in Cardio Vascular Simulation System (CVSS), h=0.1-0.2 cm, τ=0.01 s
- about 15 000 computational nodes

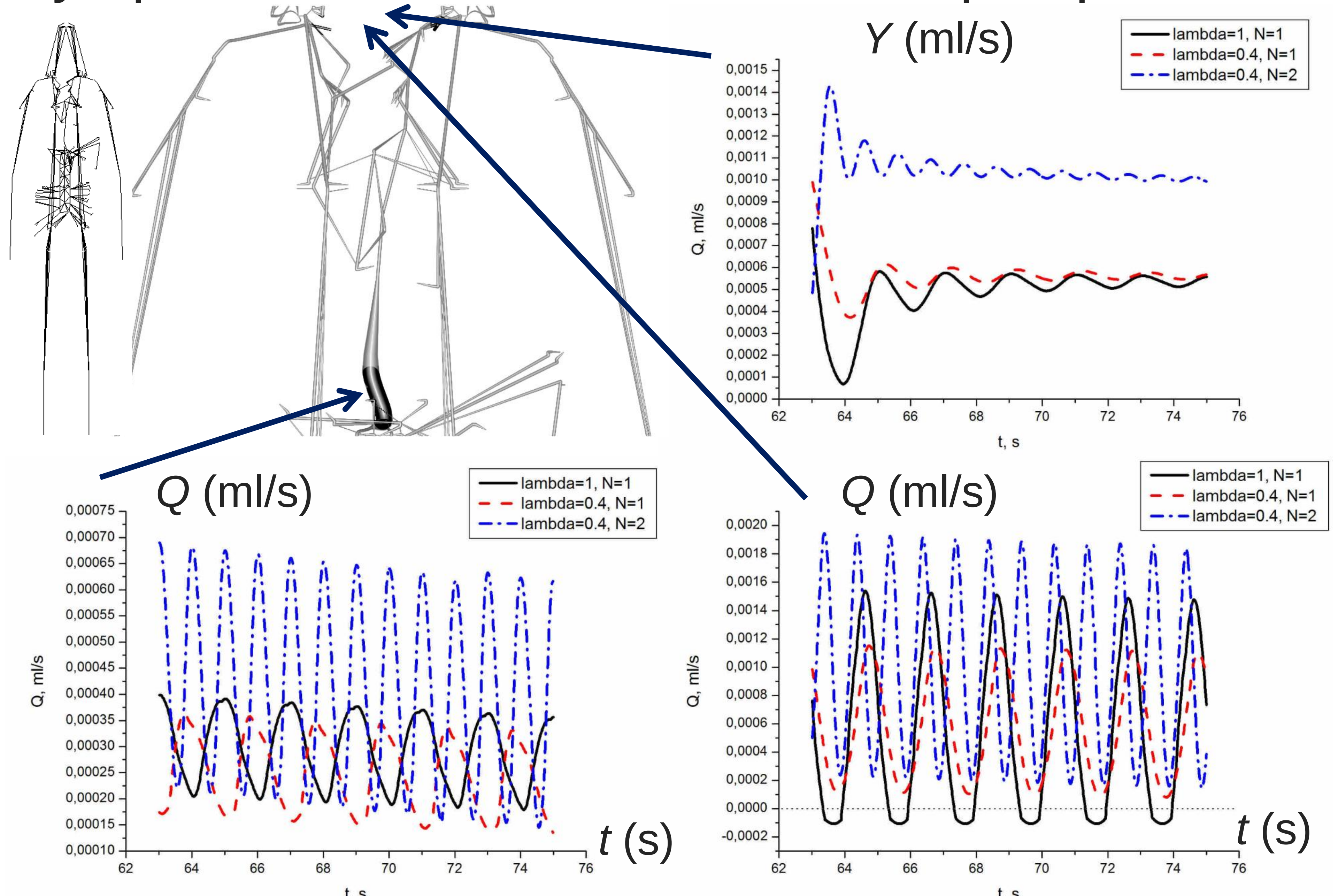
Lymph flow in the LS under muscle pump

- Input parameters:
  - *dp*=0 mm Hg: 1 mm Hg in the inerstitial fluid, 1 mm Hg in the upper vena cava
  - contractions: $s(p,x,t) = s_0 + \theta(p - p_0) + \theta A \sin\left(\frac{2\pi}{\lambda}(x - at)\right)$
  - *A*=0.1 mm Hg ($\Delta S/S_0 \approx 0.33\%$)
- Results:

$$Y = \int_{t_0}^{t_N} Q_{out}(\tau)\,\mathrm{d}\tau / (t_N - t_0)$$

λ	**N**	p_{min}	p_{max}	**dp**	**Y**
1	1	0.41	1.03	0.62	0.00054
0.4	1	0.41	1.03	0.62	0.00056
0.4	2	0.03	1.04	1.01	0.001

Lymph flow in the LS under muscle pump: results



Acknowledges and references

- Acknowledgments: to Prof. Mukhin S.I.
- References:
  - about LS graph and calculations:

    - Mozokhina A.S., Mukhin S.I. (2018) Pressure Gradient Influence on Global Lymph Flow. In: Mondaini R. (eds) Trends in Biomathematics: Modeling, Optimization and Computational Problems. Springer, Cham
    - А. С. Мозохина, С. И. Мухин, and В. Б. Кошелев. Квази-одномерный подход к моделированию течения лимфы по лимфатической системе. *Препринт МАКС-Пресс*, 20 стр., 2017.

  - about solution of contraction problem in a vessel with anisotropic viscosity:

    - A. S. Mozokhina and S. I. Mukhin. Quasi-one-dimensional flow of a fluid with anisotropic viscosity in a pulsating vessel. *Differential Equations*, 54(7):938–944, 2018.
    - the same in Russian: А. С. Мозохина and С. И. Мухин. О квазиодномерном течении жидкости с анизотропной вязкостью в сокращающемся сосуде. *Дифференциальные уравнения*, 54(7):956–962, 2018.

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Thank you for attention!