ИГиЛ
СО РАН

The properties of Van der Pol - Duffing hemodynamics mathematical model for the clinical applications

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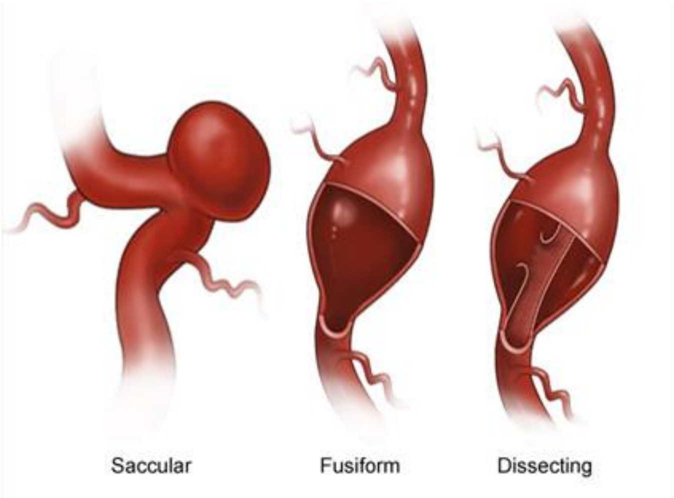
Outline

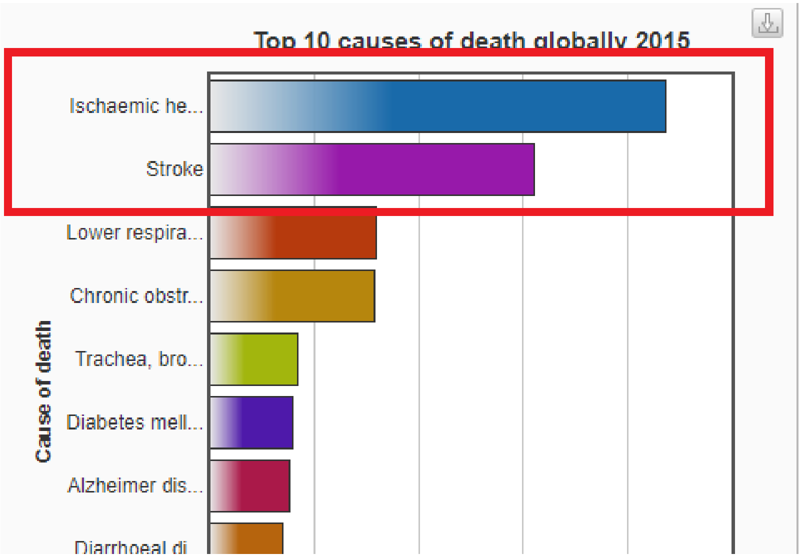
- Introduction
- Clinical measurements
- Mathematical model
- Results
- Conclusions
- References

Introduction. Cerebral aneurysms



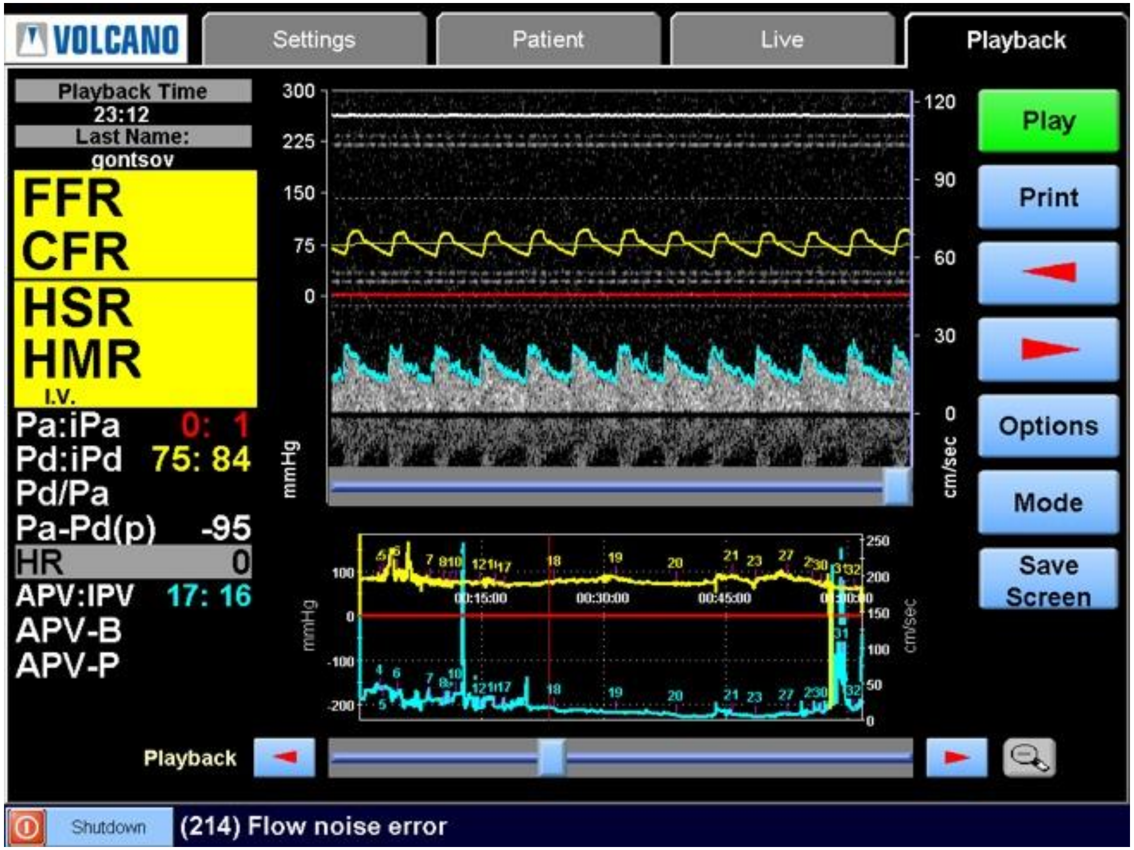
Cerebral aneurysm varieties

- Each one of 50 people has cerebral aneurysm. Multiple aneurysms are also widespread.



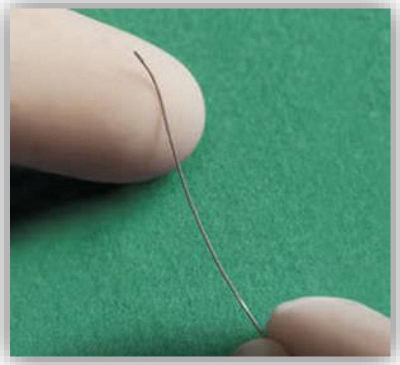
- In **top-10** death cause diseases WHO (January 2017)

Clinical measurements



Measurements performed via Combo Map© unit and Combo Wire© sensor.

During the treatment



Pressure – Velocity investigation of cerebral circulation

Blood flow pressure and velocity can be presented like a combination of “fast” and “slow” variables:

$$p(t) = p_{ave}(t) + a_p(t)\, \boldsymbol{q(t)}$$

$$v(t) = v_{ave}(t) + a_v(t)\, \boldsymbol{u(t)}$$

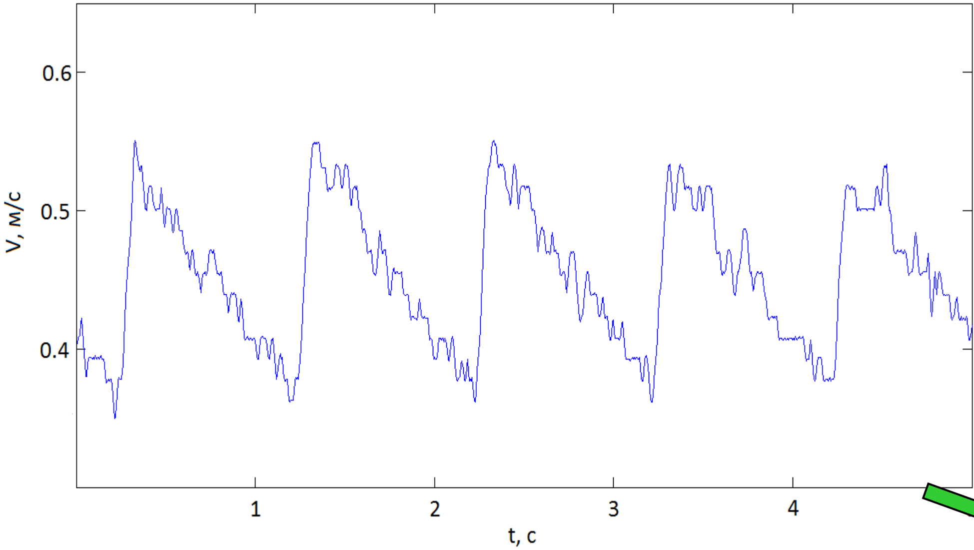
Slow variables

Fast variables

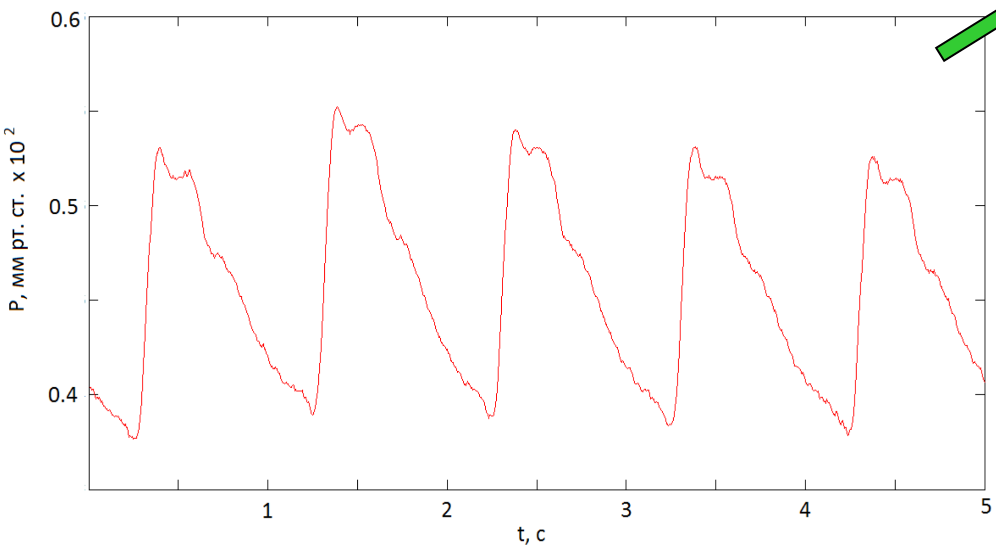
Phisiological interpretation: The reaction of muscles on a pulse wave is local – the signal goes from the blood flow, not controlled by CNS and conducting at the place.

Clinical data

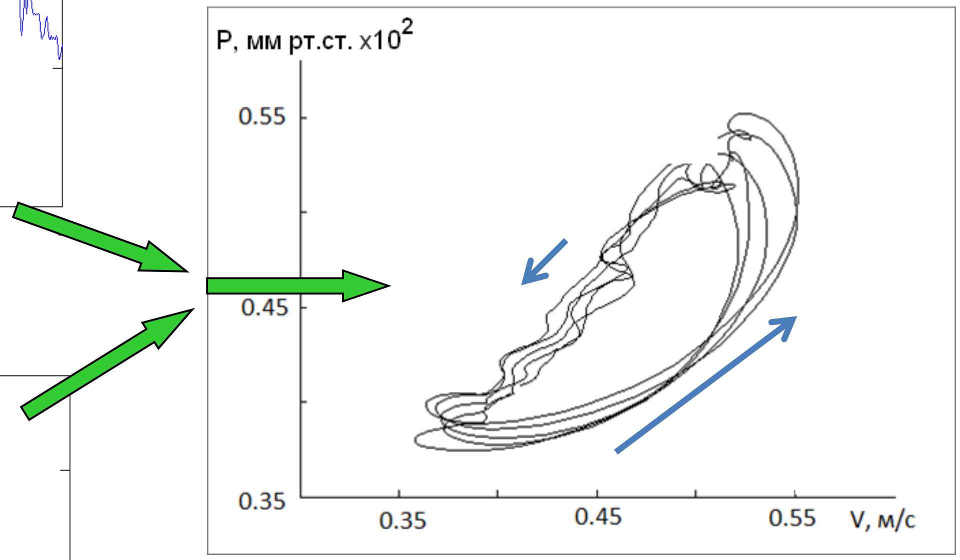
Velocity, m/s



Pressure, mm.Hg.*100

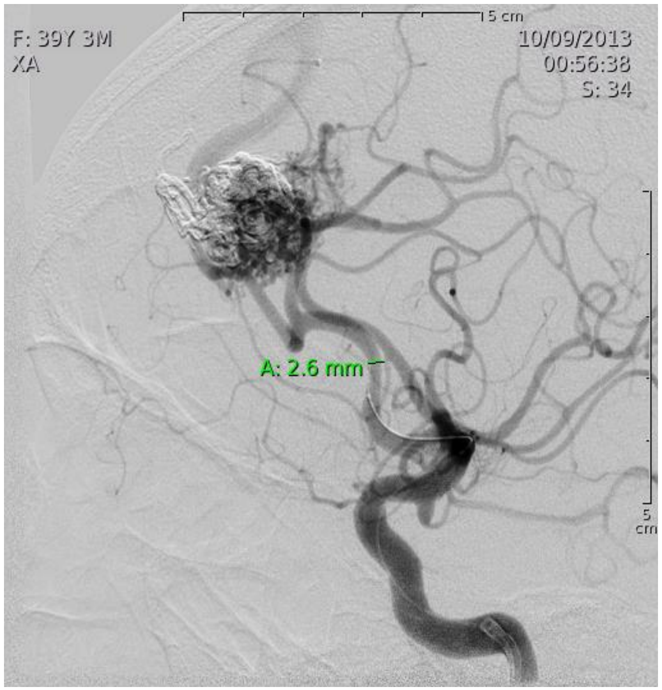


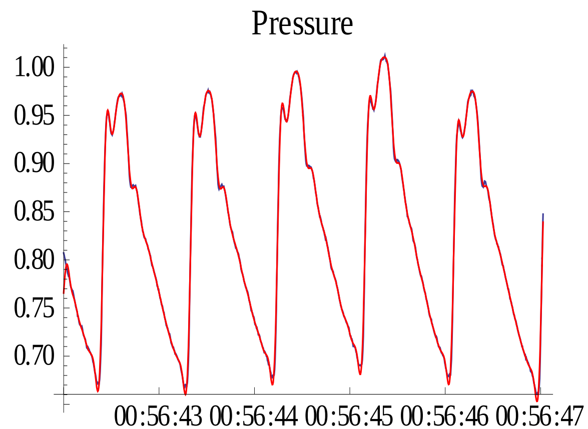
Slow variables define the shape of VP-diagrams

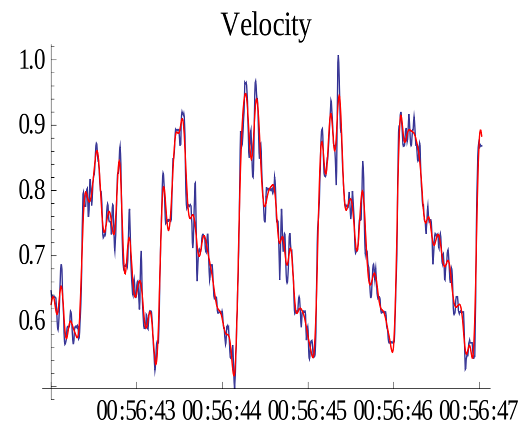


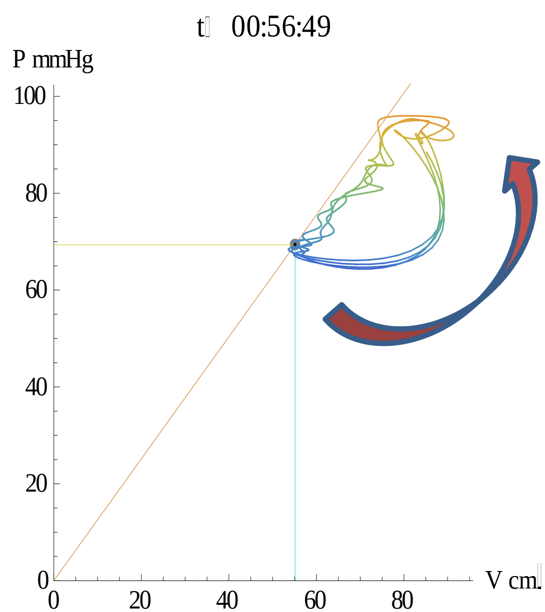
V,P-diagram

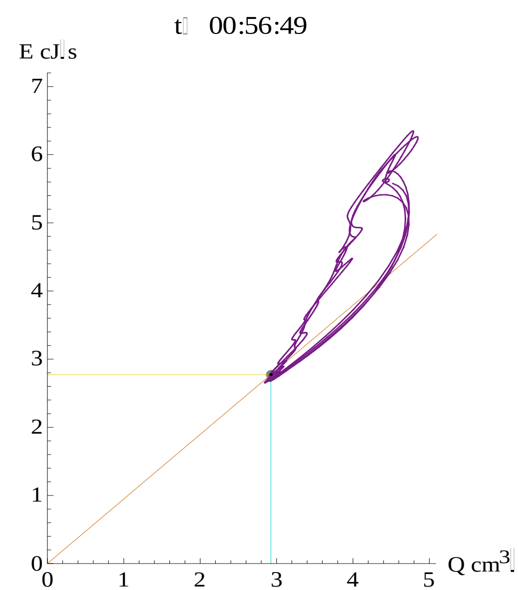
Inside an artery



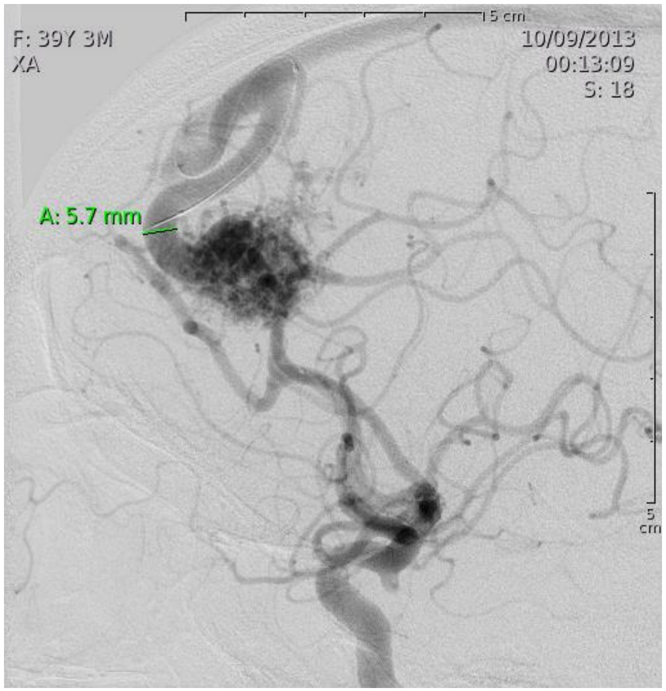


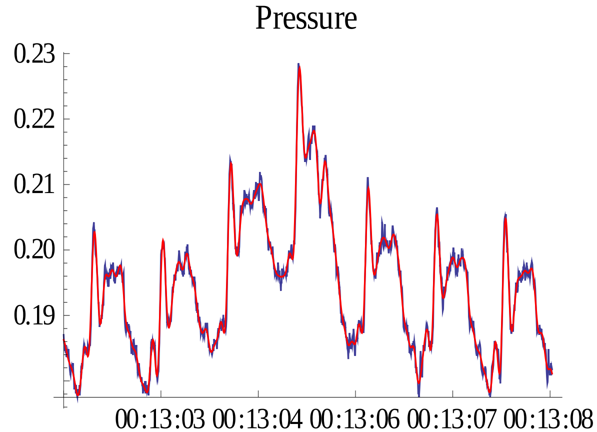


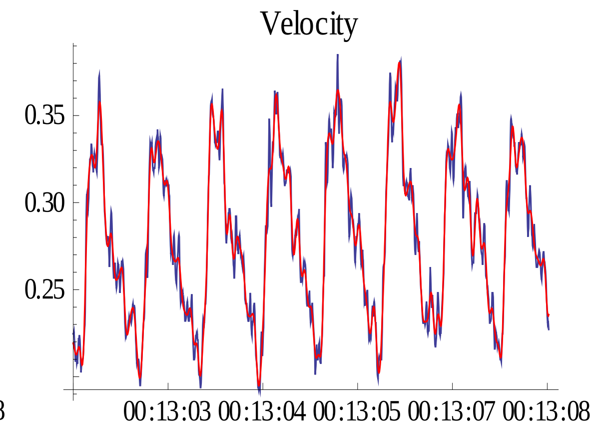


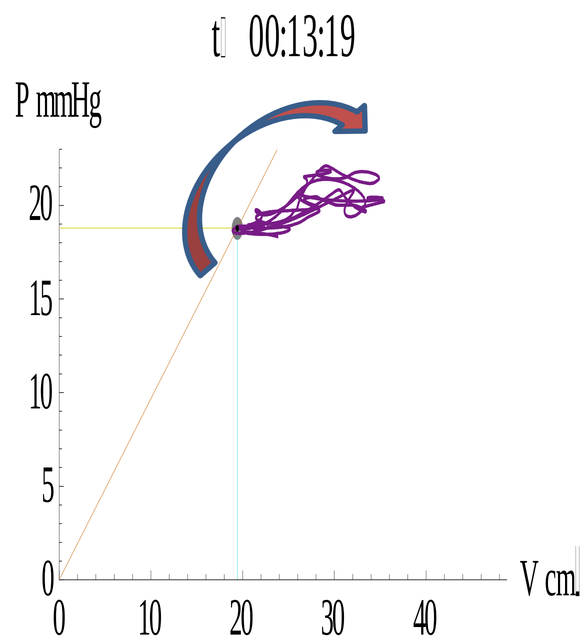


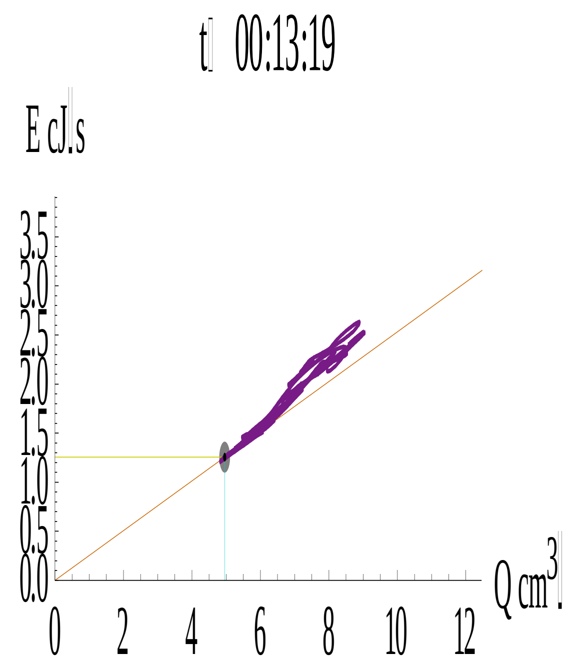
Inside a vien











Phenomenological mathematical models of cerebral circulation

Austin G, 1971	$v'' + Av - Bv^2 + Cv^3 = RHS(p)$
Cronin J, 1973	$v'' + Av - Bv^2 + Cv^3 = RHS(p)$
Austin G, 1974	$v'' + Av' + Bv + Cv^2 = RHS(p)$
Cronin J, 1974	$v'' + Av' + B = RHS(p)$
Nieto, 2000	$v'' + Av' - Bv^2 + Cv^3 = RHS(p)$

Generalized Van der Pol – Duffing equation

- Allow to define a character of fast hemodynamical parameters near with a pathology:

$$\varepsilon q'' + \left(a_1 + a_2 q + a_3 q^2\right) q' + b_1 q + b_2 q^2 + b_3 q^3 = ku,$$

$$a_i, b_i, k \in R; \qquad i = 1,2,3;$$

- here u is the velocity, q is the pressure. For the arterial compartment velocity is defined by a clinical data and manage the pressure values which can be found from the equation.
- Coefficients a_i, b_i, k fit by inverse problem methods on the clinical data. Coefficients b_i are responsible for the elastic properties of a vessel and a_i are responsible for the damping, ε corresponds to a relaxation oscilations in the system.

The existence of the solution

Let us consider an equaition: $\varepsilon x'' + f(x)x' + g(x) = e(t),$ (2)

The equivalent system(3) takes a form:

$$\begin{cases} x' = -F(x) + v \\ v' = -g(x) + e(t) \end{cases}, \qquad (3)$$

where $f(x)$, $g(x)$ –are continuous for all x, $F(x) = \int_0^x f(s)ds,$
$e(t)$ – periodical function with period θ. Hence the conditions of Opyal theorem are satisfied[1].

1 – R.Reysig, G.Sansonet, R.Konti, Qualitative theory of nonlinear differential equations.

Normalization of a clinical data

$$p,v \longrightarrow q,u$$

For the interval I_5 the pressure and the velocity could be made dimensionless by the formulas :

$$q = \frac{p_{I_5} - \xi}{\max\limits_{I_5} \left| p_{I_5} - \xi \right|}, \qquad u = \frac{v_{I_5} - \eta}{\max\limits_{I_5} \left| v_{I_5} - \eta \right|}.$$

With respect to the method of such procedure, ξ and η take the values:

- $\xi = \overline{p_{I_5}}, \eta = \overline{v_{I_5}}$ - average integral values for p_{I_5}, v_{I_5} respectively
- $\xi = \dfrac{\min p_{I_5} + \max p_{I_5}}{2}, \eta = \dfrac{\min v_{I_5} + \max v_{I_5}}{2}$

Discretization of the equation

We use discrete analogue of differential equation (1) :

$$q(t-0)+\tilde{c}_1 q(t-\Delta t) + \tilde{c}_2 q(t-2\Delta t)+\tilde{c}_3 (q(t-\Delta t)-q(t-2\Delta t))q(t-\Delta t)^2 + \\ +\tilde{c}_4 q(t-\Delta t)^2+\tilde{c}_5 (q(t-\Delta t)\text{-}q(t-2\Delta t))q(t-\Delta t)^2+\tilde{c}_6 q(t-\Delta t)^3=\tilde{c}_7 u(t-\Delta t)\ , \qquad (7)$$

Here $\Delta t = \frac{1}{m}$ – is a time step.

To calculate 7 parameters values we use 1000 points from the experiment (5-second time interval). Hence we deal with an overdefined system (1000x7 matrix). To find out the coefficients of the equation we used Matlab System Identification Toolbox.

Coefficients identification

Let $q \in R^n,\ f \in R^m,\ A$ – a matrix of $m \times n$ size.

“Pseudo” solution of a system

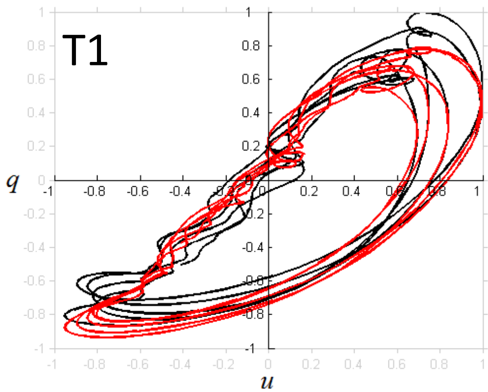
$$Aq = f \qquad (8)$$

is a vector $q_{\Pi} \in R^n$, which minimize the norm of the discrepancy

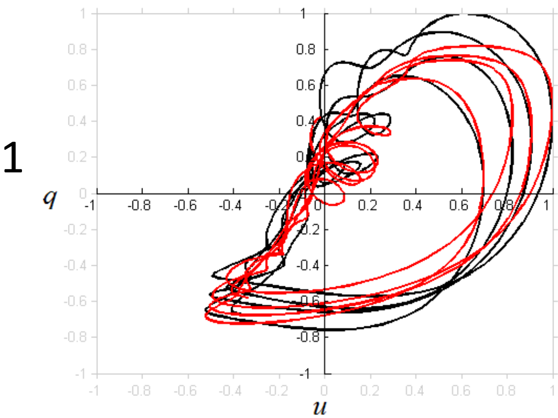
$$J(q) = \left\| Aq - f \right\|^2 \to \min .$$

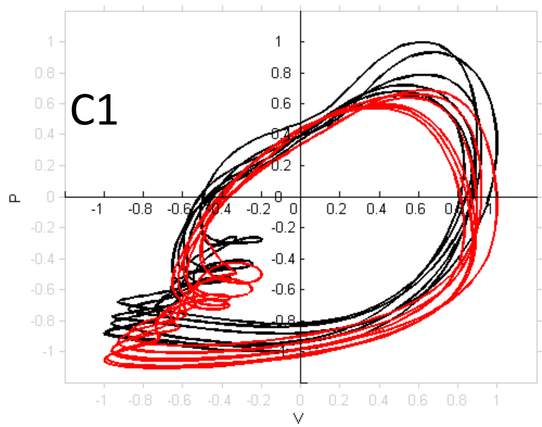
System (8) has no a classical solution due to it’s overdifinition.

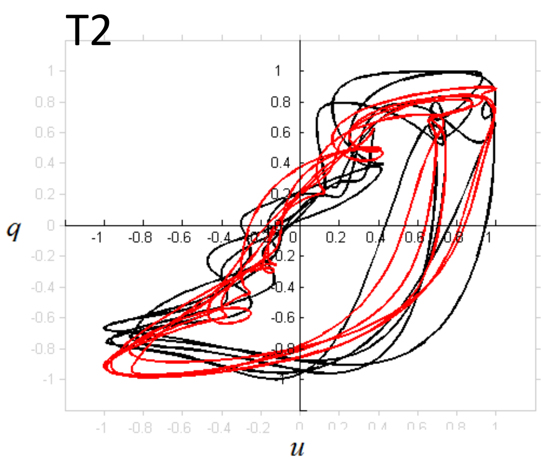
Q,U diagrams (results for 5 patients)

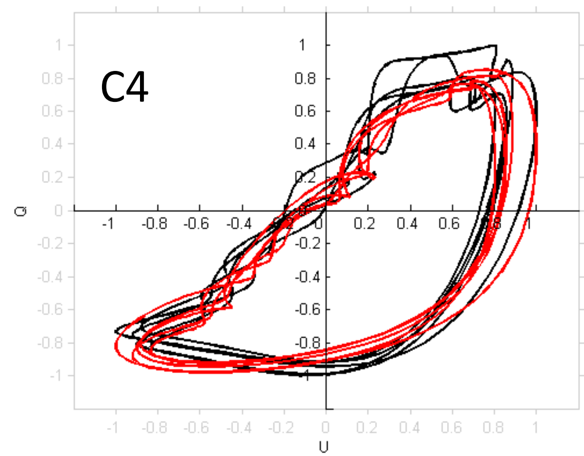


Sh1



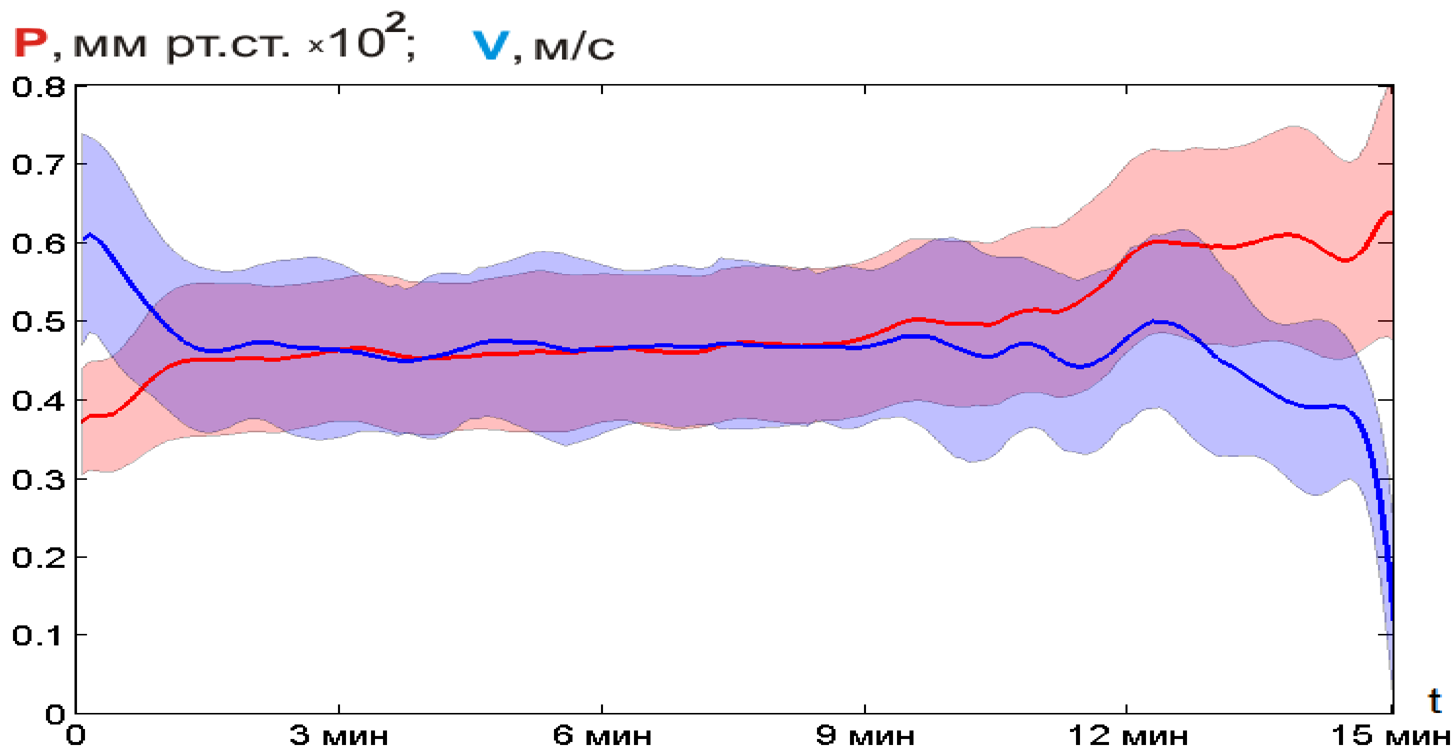






qu-diagrams

The model constructed by 5 sec time interval has a good prediction up to 10 minutes.



Analysis of the system via harmonic probing

For the further investigation we used a method of harmonic probing. This method is widely spread in medicine and enterprise technology:

Harmonic probing – is a base of any kind of Ultra sound diagnostic.

This technique is commonly adopted for the testing of complex mechanical systems.

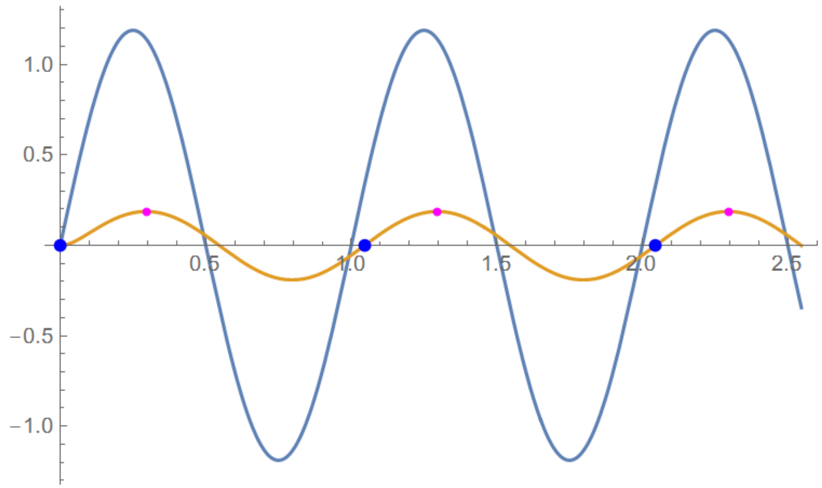
Probing of the system by harmonic signal

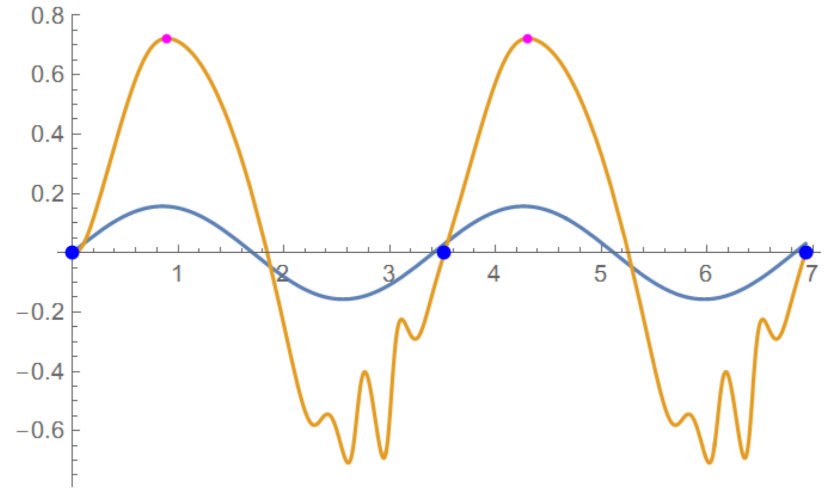
$$\varepsilon q'' + (a_1 + a_2 q + a_3 q^2) q' + b_1 q + b_2 q^2 + b_3 q^3 = k B \sin(\omega t)$$

Hypothesis

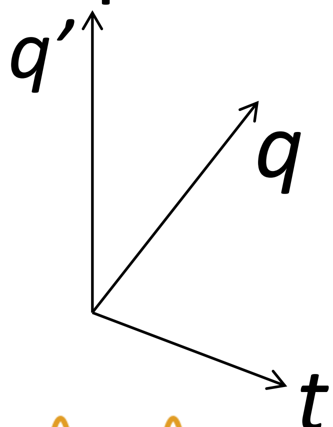
«Healthy» vessels ⟶ «simple» dynamics

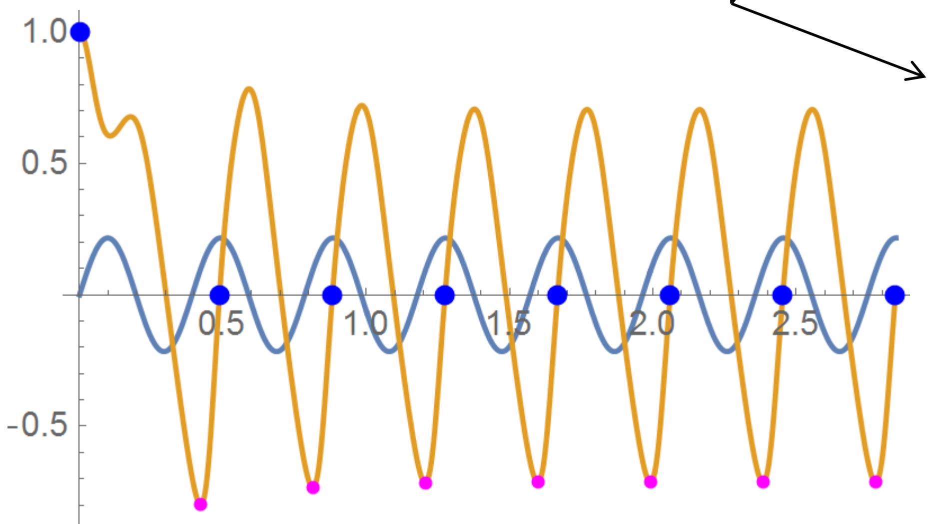
«Sick» vessels ⟶ «complex» dynamics





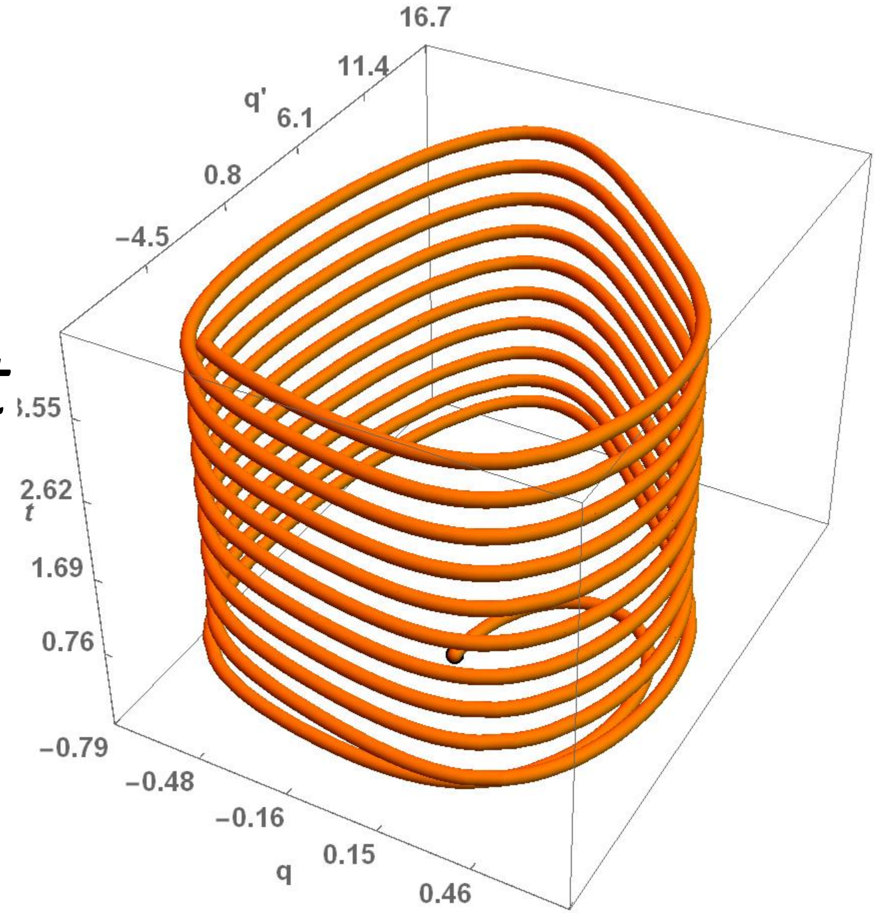
The behavior of the solution when right hand side of equation (1) is harmonic





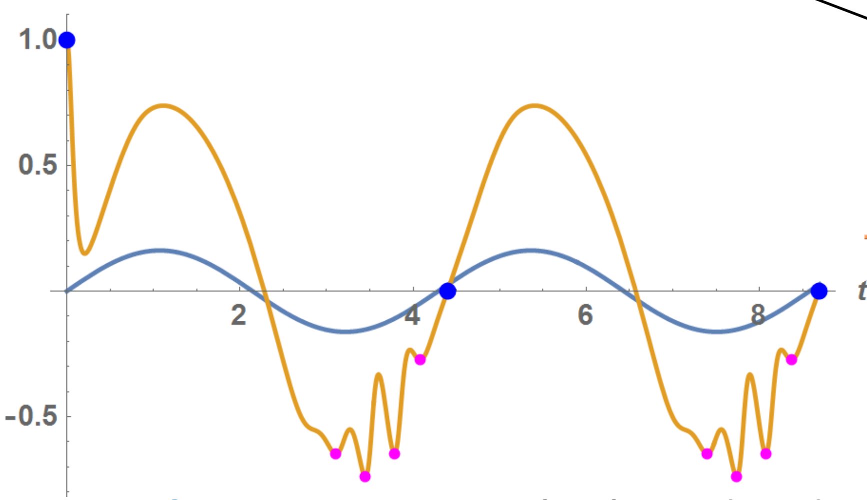
Blue curve – Right hand side

Yellow curve - solution

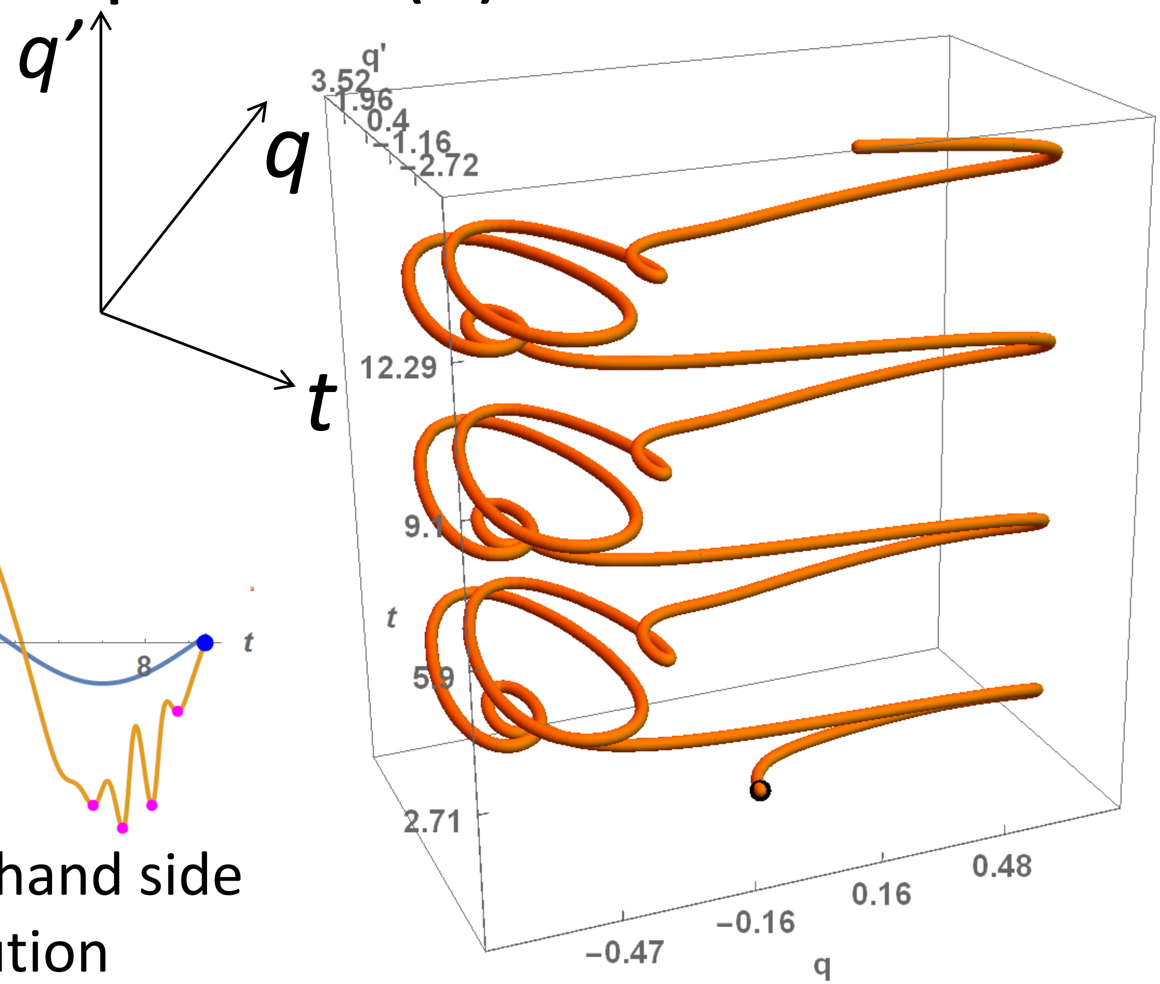


Integral curve in an expanded phase space

The behavior of the solution when right hand side of equation (1) is harmonic



Blue curve – right hand side
Yellow curve - solution

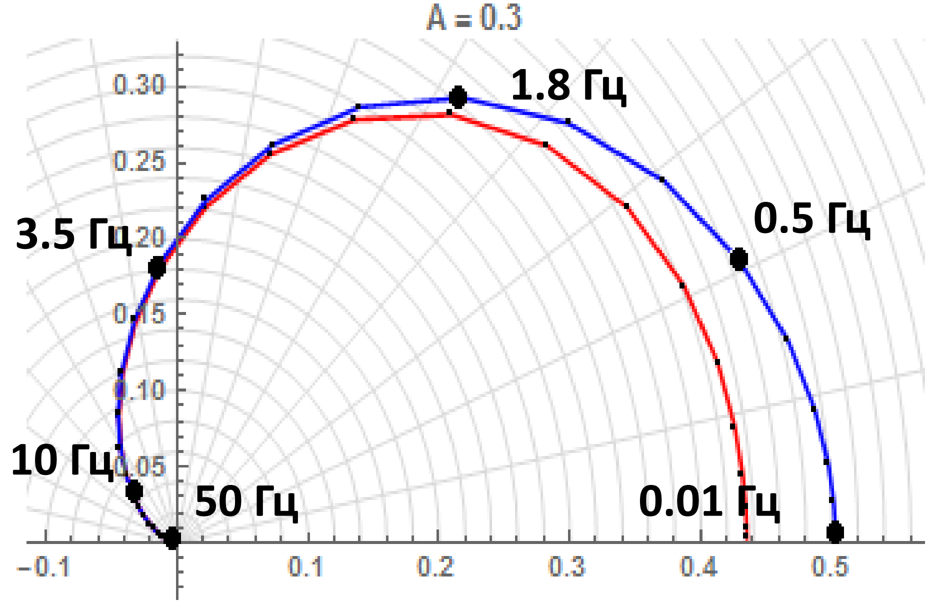


Integral curve in an expanded phase space

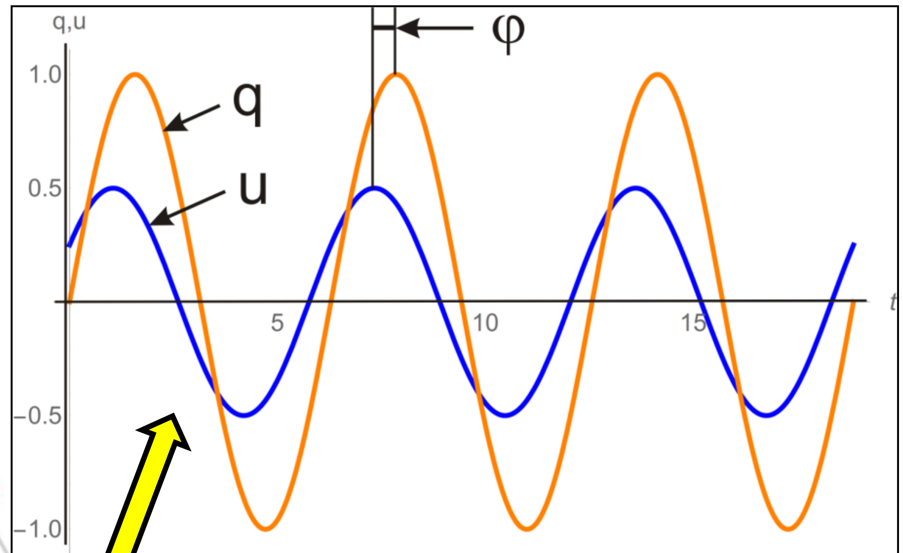
Approach 1. Nyquist plot(NP)

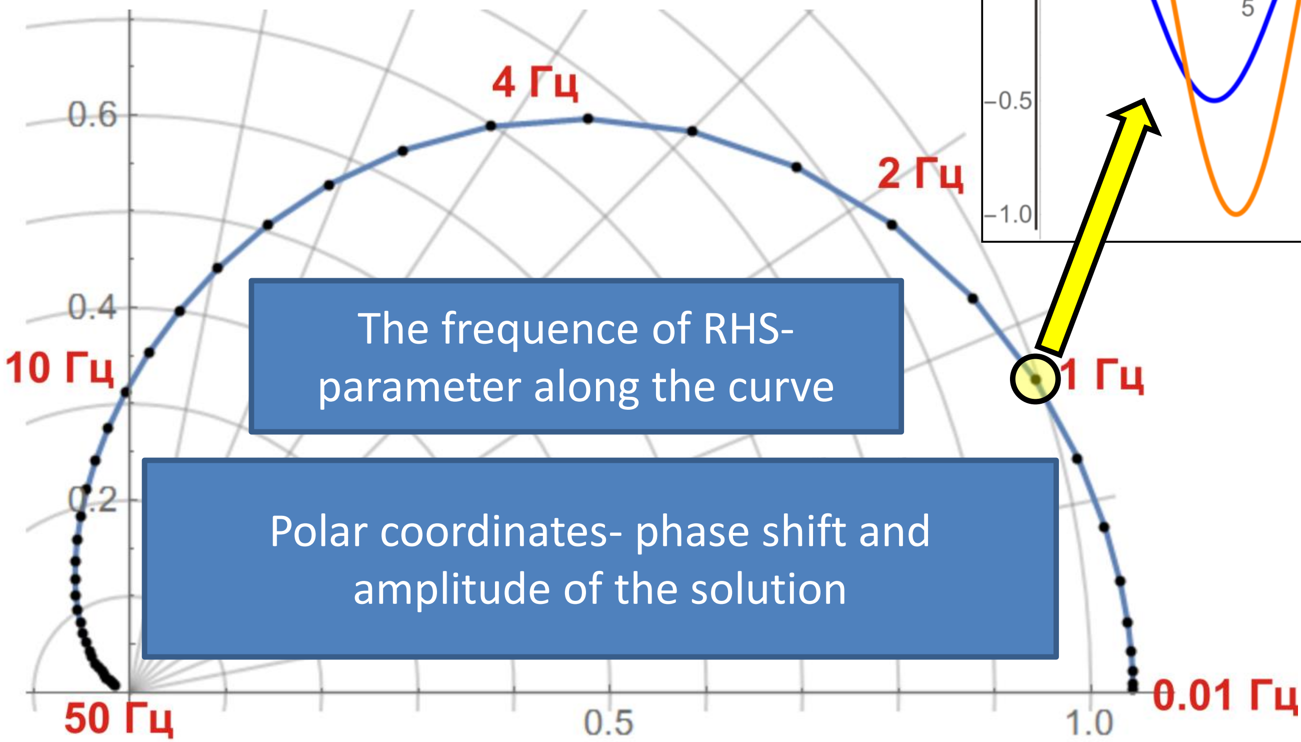
- Nonlinear generalization of Nyquist plot is used for the analysis of the how the amplitude and the frequency of RHS affect on the solution,
- Amplitude *u* is fixed while diagram is plotting. Frequency of RHS – parameter along the curve.
- Polar coordinates – dimensionless phase shift respectively RHS of the equation and the amplitude of the solution.

- For the nonlinear case maximum and minimum of the solution can be distinct. Blue line– absolute value of the minimum of the solution, red one – absolute value of the maximum of the solution.



Amplitude-phase-frequency characteristics

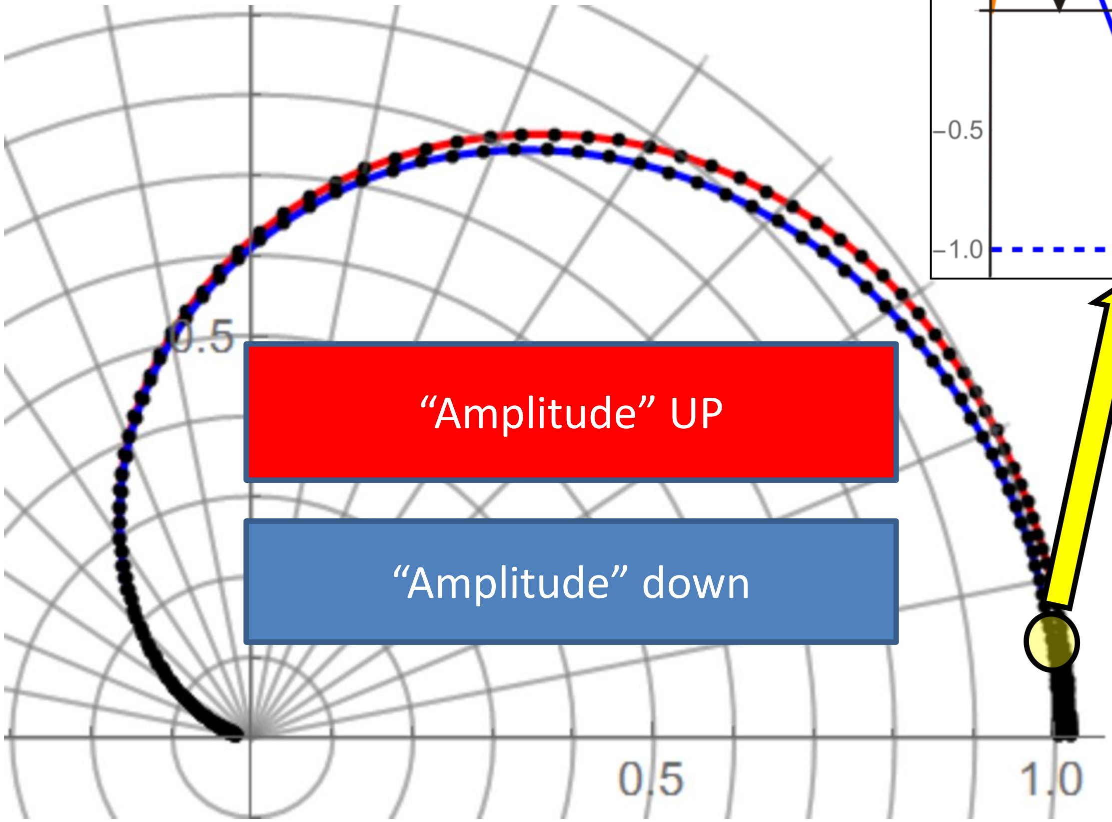


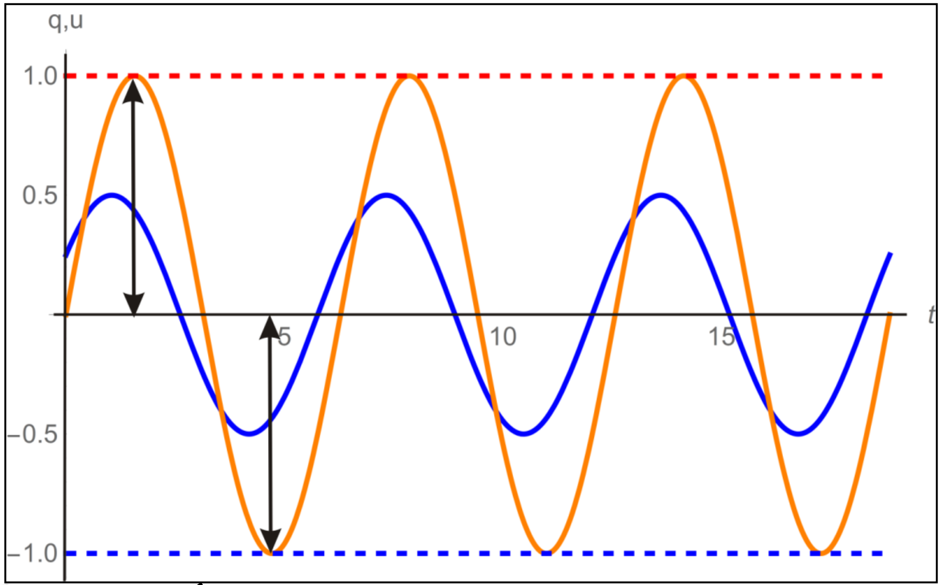


The frequence of RHS-parameter along the curve

Polar coordinates- phase shift and amplitude of the solution

Amplitude-phase-frequency characteristics

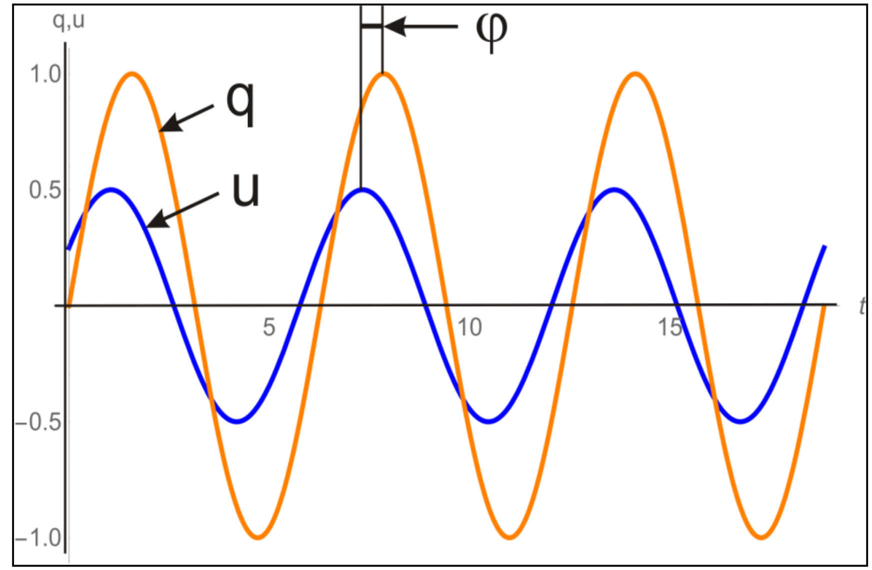


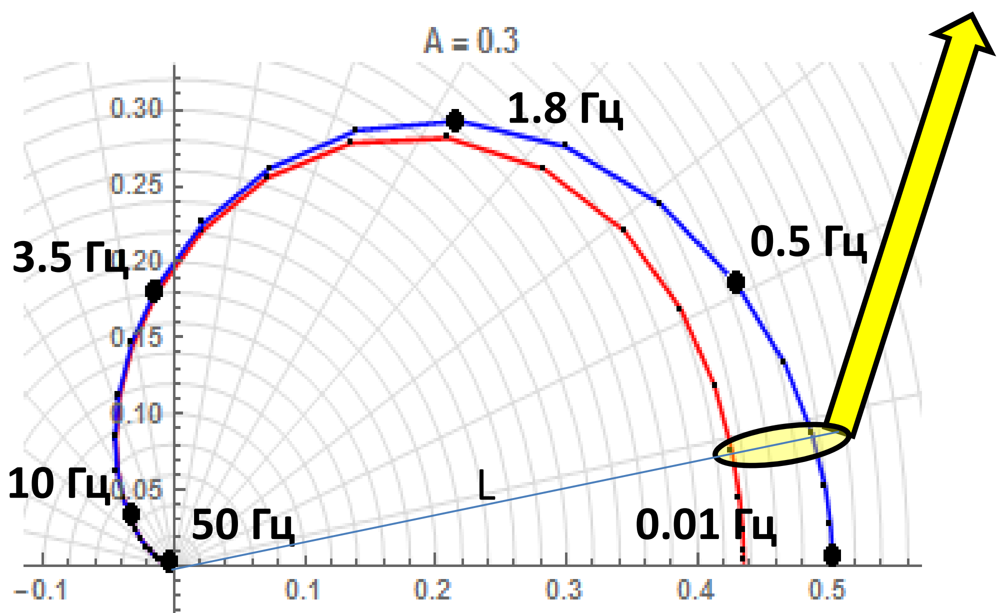


Nyquist plot

For each pair of points L1 and L2 there is a correspondence of a solution and right hand side of equation (1).

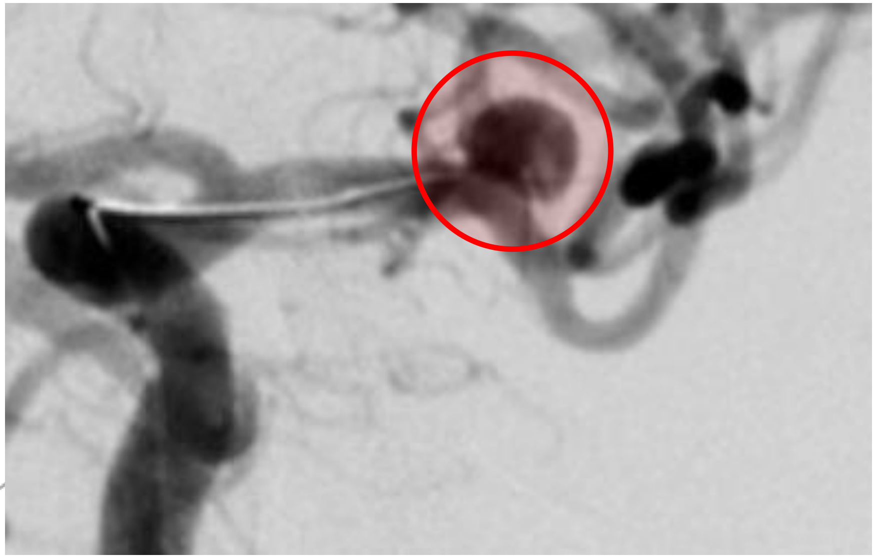
Solution plot (yellow) and right hand side of Eq.(1) plot (blue).

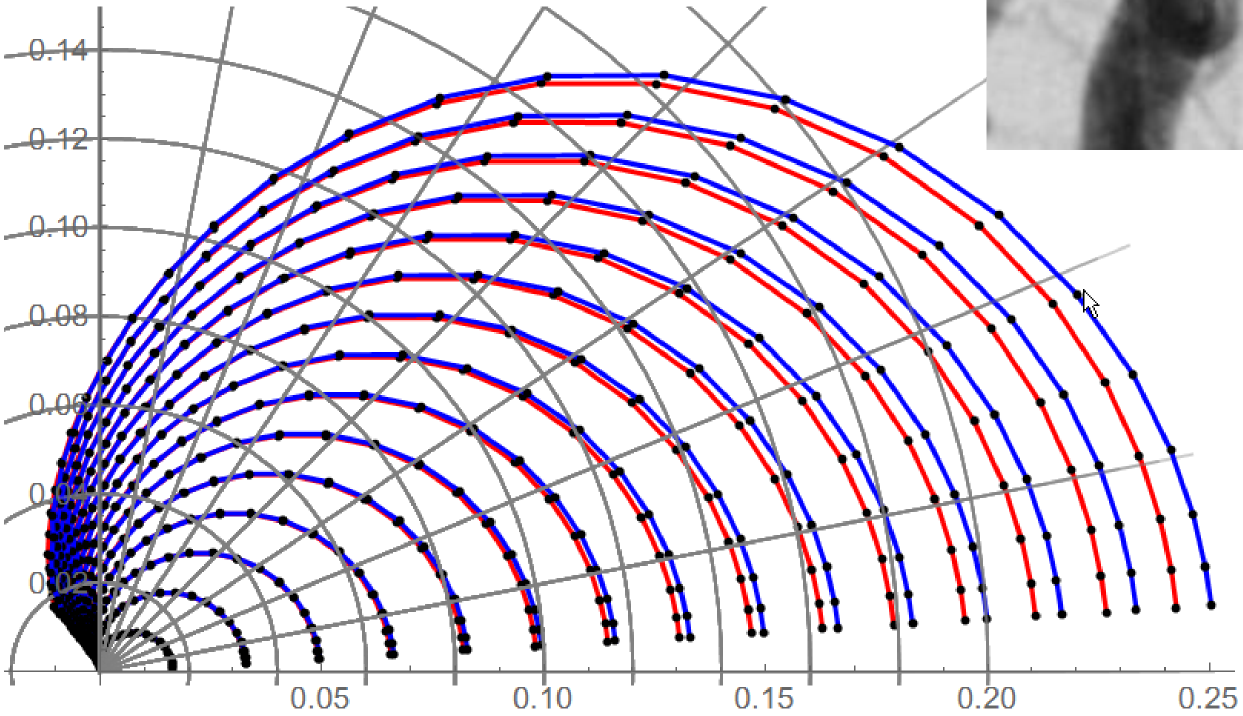




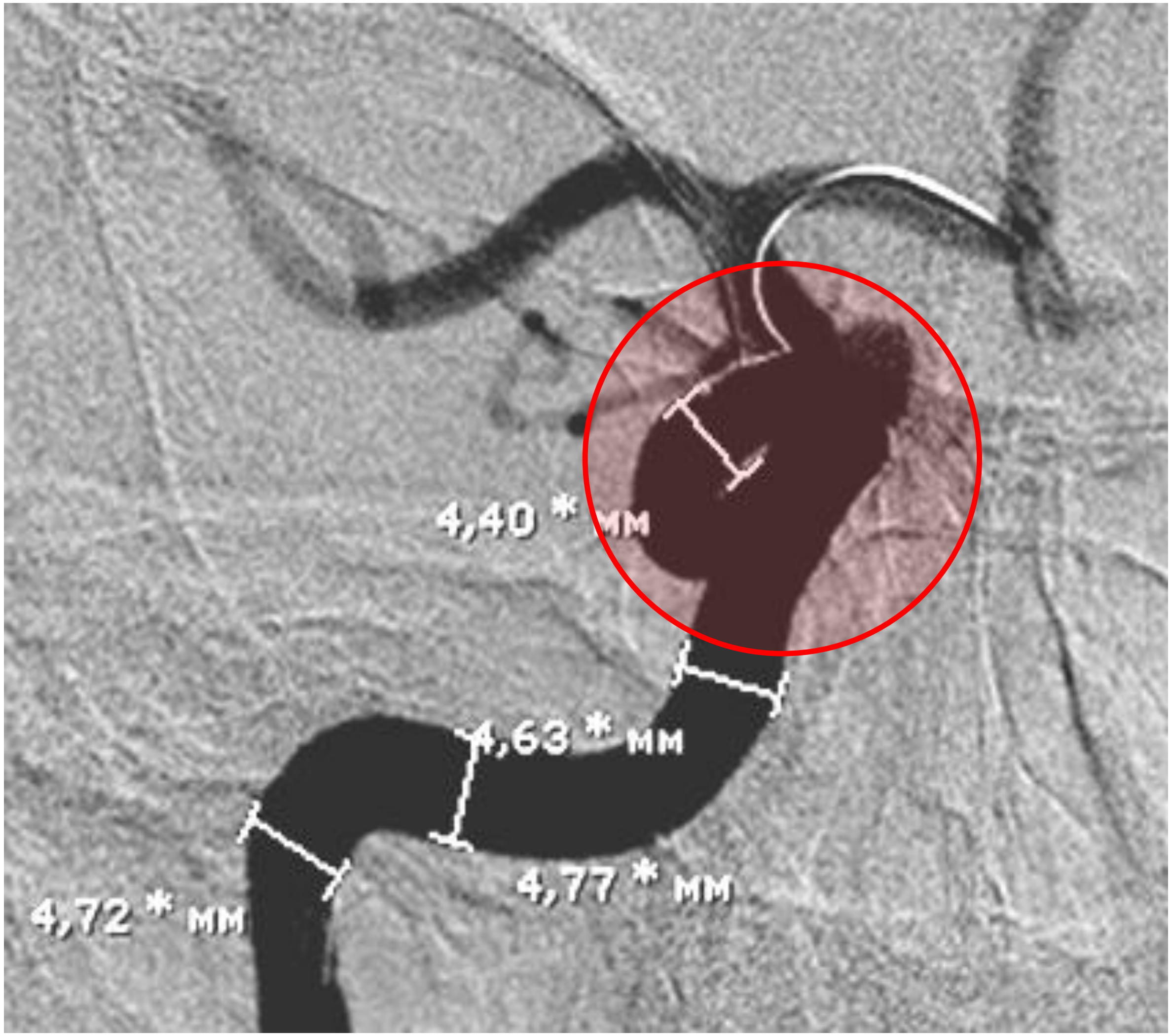
Patient P1 has «almost linear» behavior

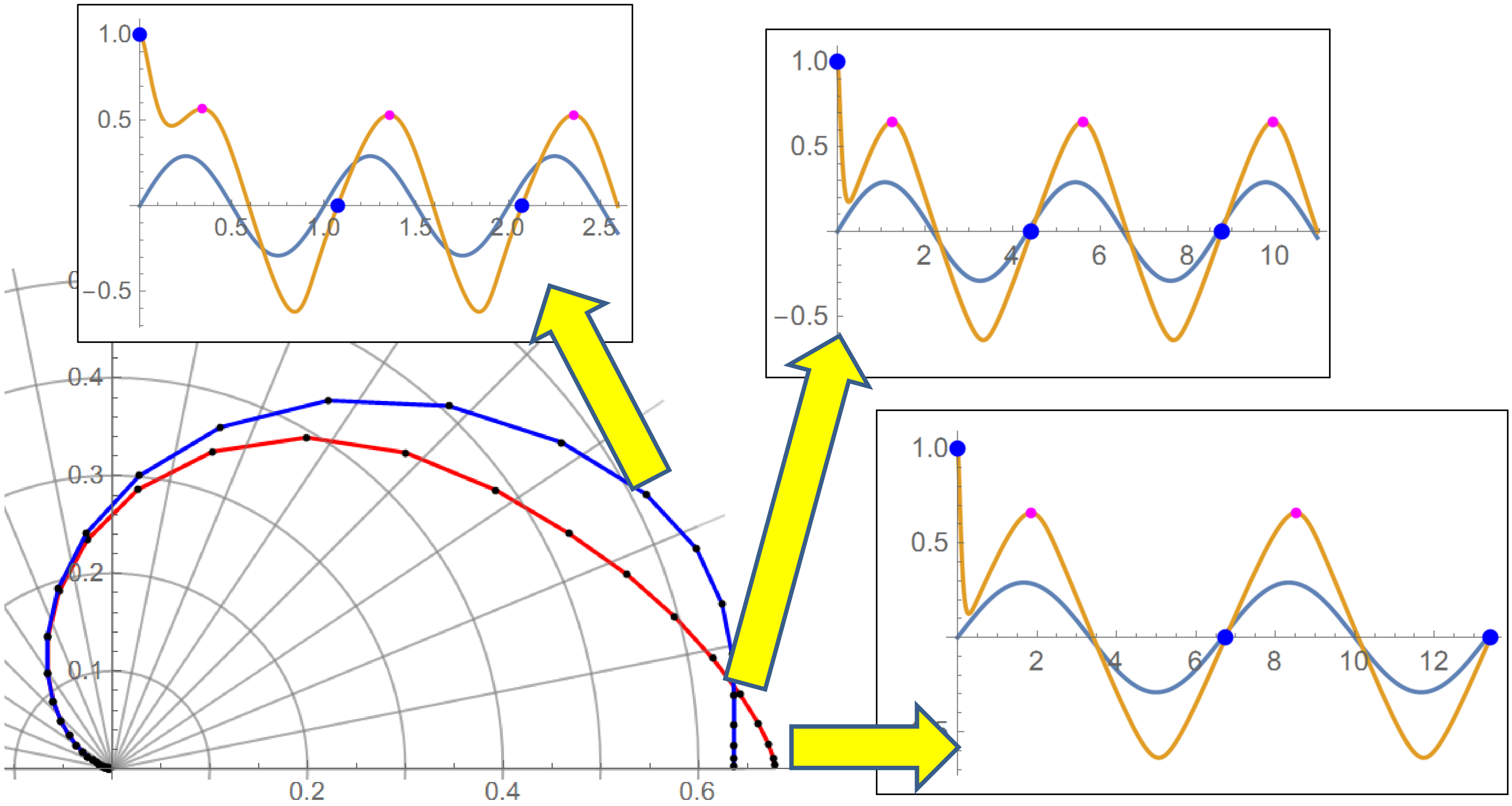
When an aneurysm has a small neck –this aneurysm doesn’t affect substantially on the circulation.



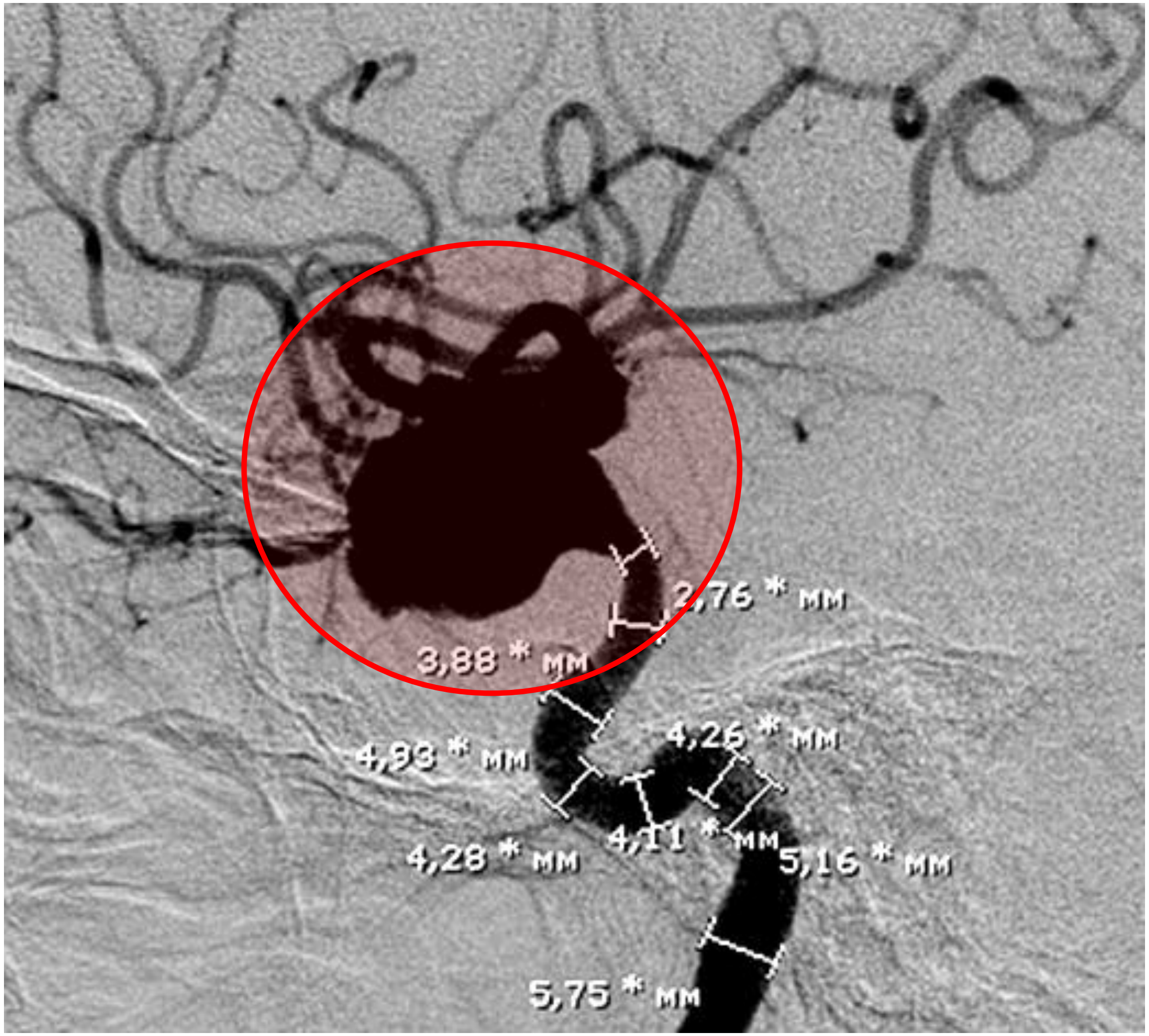


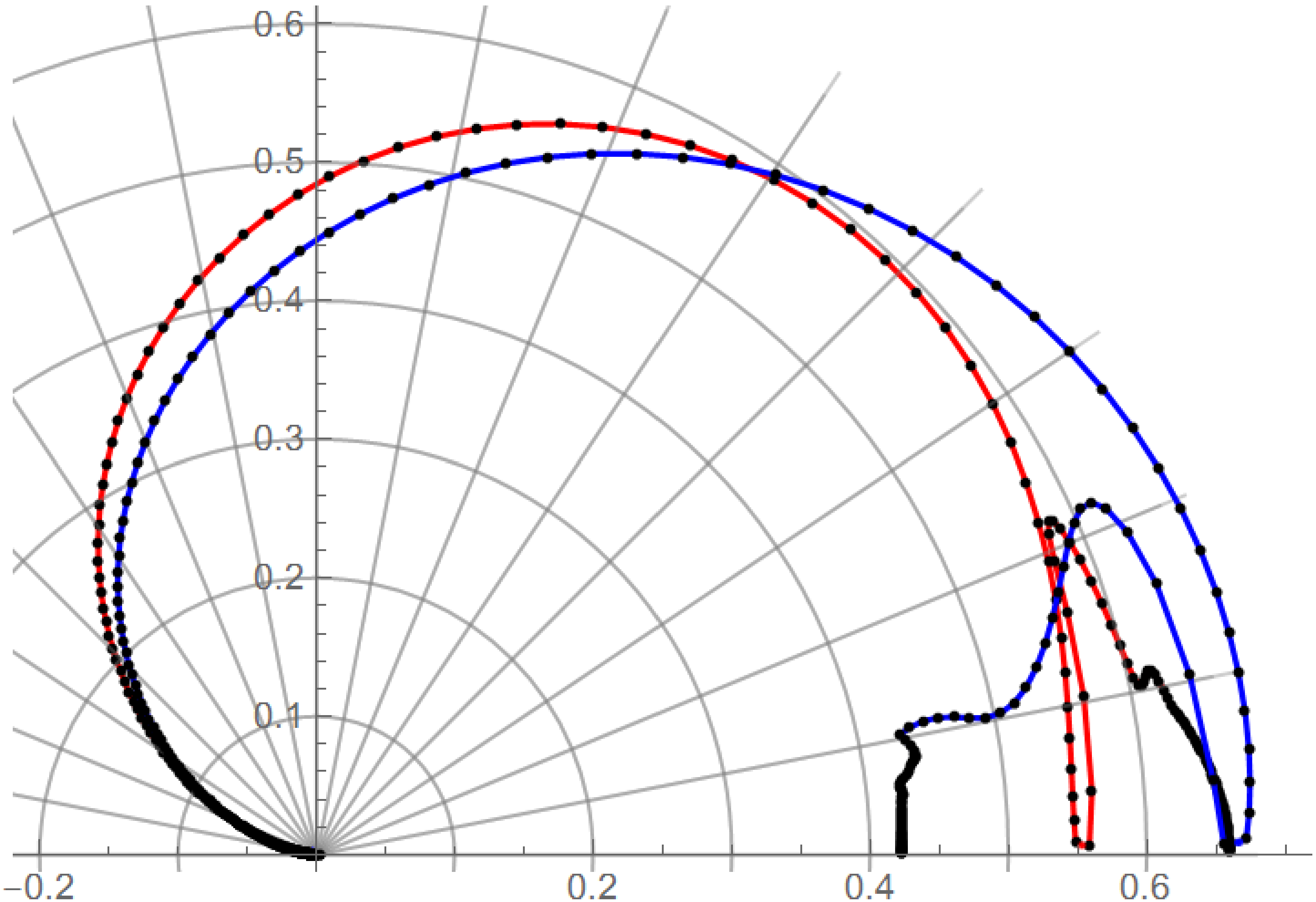
Patient G1 – normal aneurysm of the right internal carotid artery (ICA)



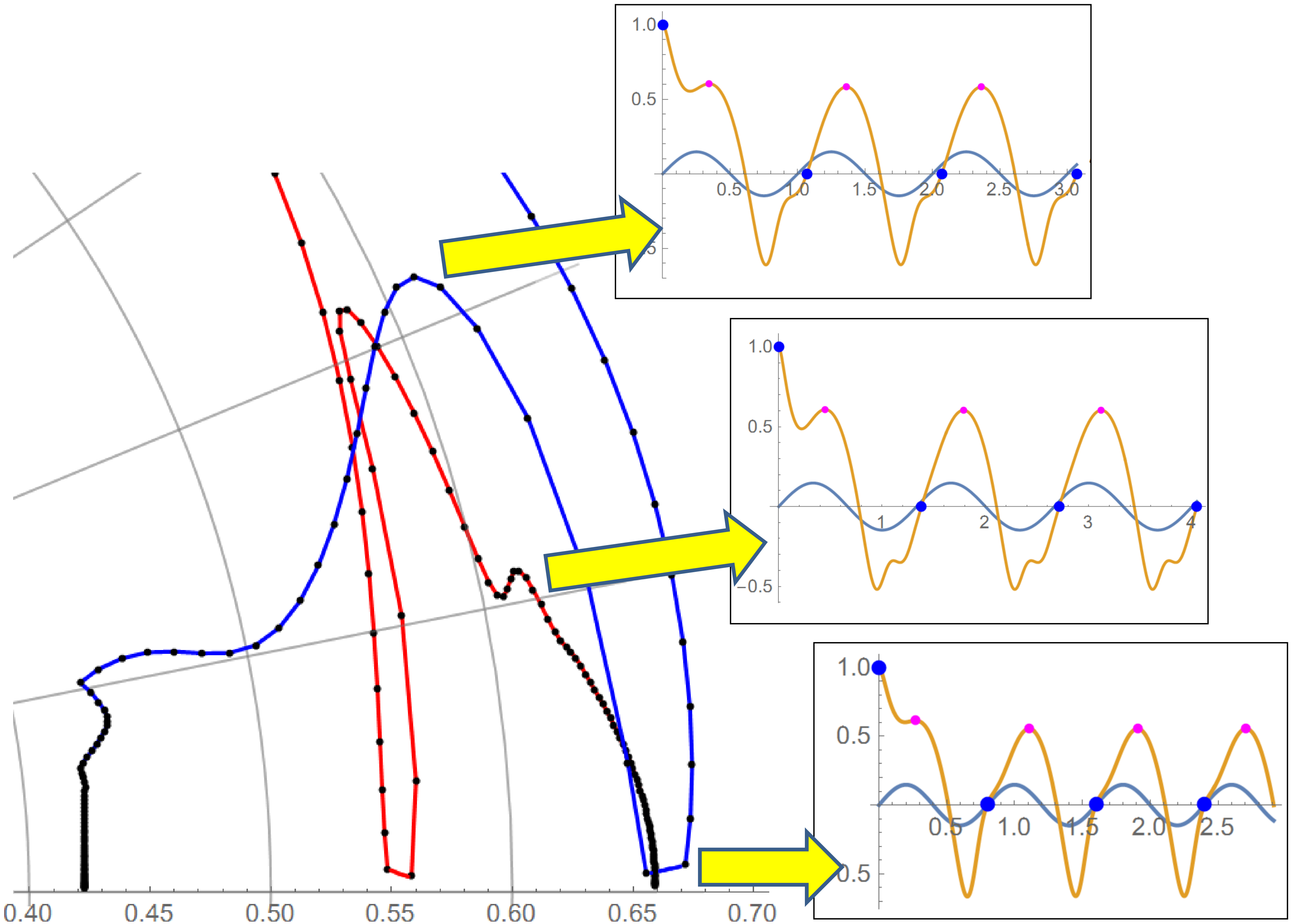

1.0
0.5
−0.5
0.5
1.0
1.5
2.0
2.5
1.0
0.5
−0.5
2
4
6
8
10
1.0
0.5
2
4
6
8
10
12
0.4
0.3
0.2
0.1
0.2
0.4
0.6

Patient K1 – giant aneurysm of the right ICA





0.6
0.5
0.4
0.3
0.2
0.1
−0.2
0.2
0.4
0.6



0.40
0.45
0.50
0.55
0.60
0.65
0.70
1.0
0.5
0.5
1.0
1.5
2.0
2.5
3.0
1.0
0.5
−0.5
1
2
3
4
1.0
0.5
0.5
1.0
1.5
2.0
2.5
0.5

Approach 2. Stationary points.

Let us denote: $p = \varepsilon q' / a_3{}^2 + a_1 q / a_3 + a_2 q^2 / a_3{}^2 + q^3 / 3$

$\theta(t) = \omega t, a_3 \neq 0$

Then the equation (1) could be represented like a system:

$$\begin{cases} p' = (b_1 q + b_2 q^2 + b_3 q^3) - 2\sin(2\pi\theta), \\ \varepsilon q' = a_3{}^2 p - a_1 a_3 q - a_2 a_3 q^2 / 2 - a_3 q^3 / 3, \\ \theta' = \omega. \end{cases} \qquad (2)$$

with relaxation oscillations,

ε - is a small parameter.

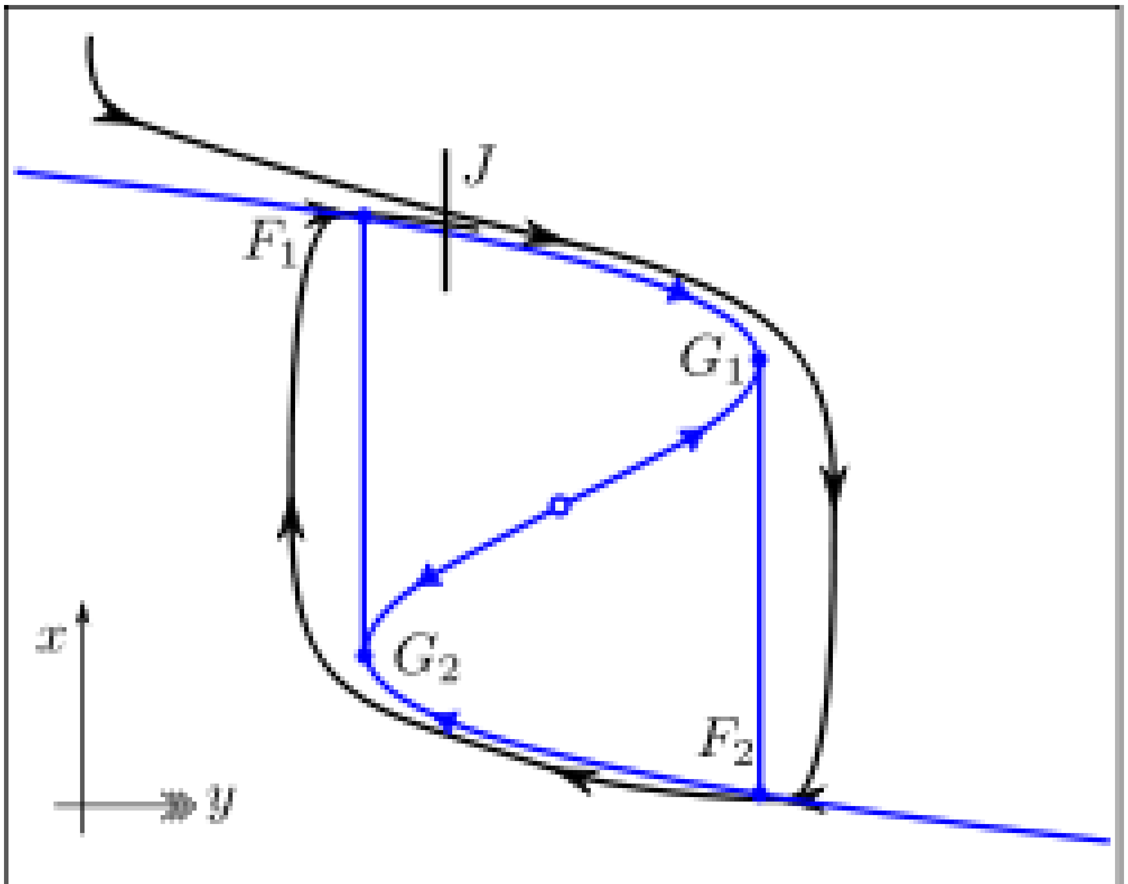
Slow and fast susystems

$$\begin{cases} p' = (b_1 q + b_2 q^2 + b_3 q^3) - 2\sin(2\pi\theta), \\ \varepsilon q' = a_3{}^2 p - a_1 a_3 q - a_2 a_3 q^2 / 2 - a_3 q^3 / 3, \\ \theta' = \omega. \end{cases}$$

Fast subsystem

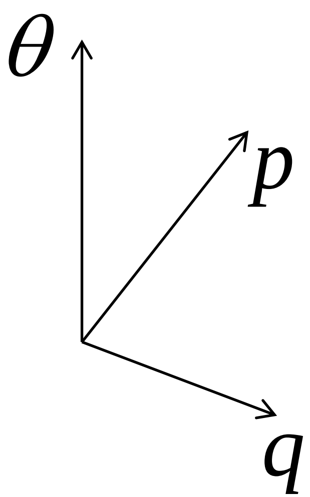
Slow subsystem

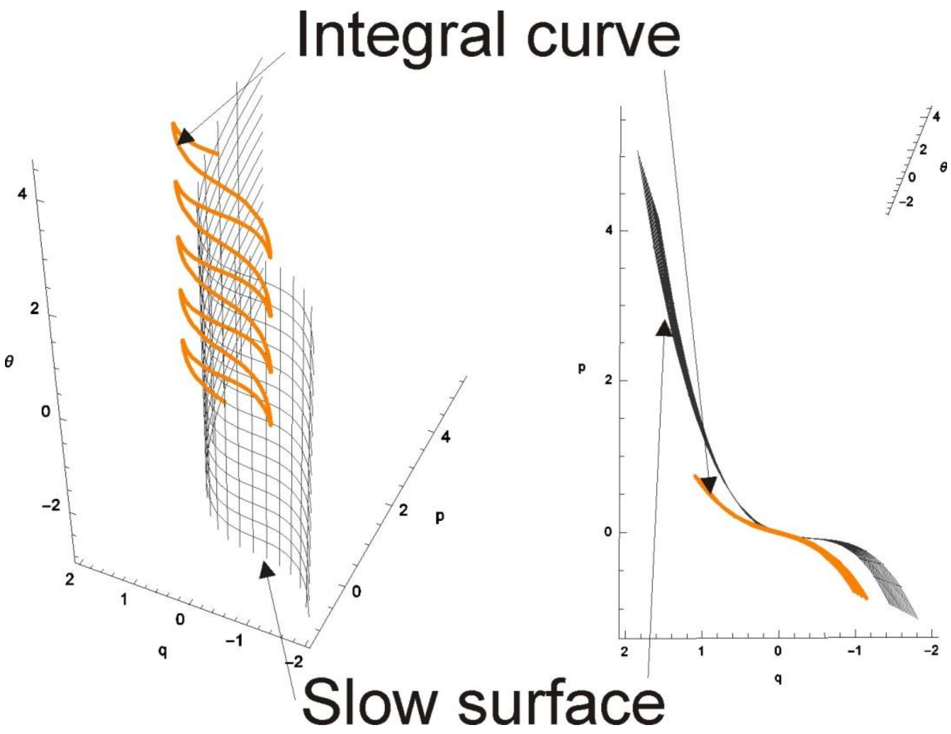
Physical interpretation of slow and fast movements



Slow surface of a system

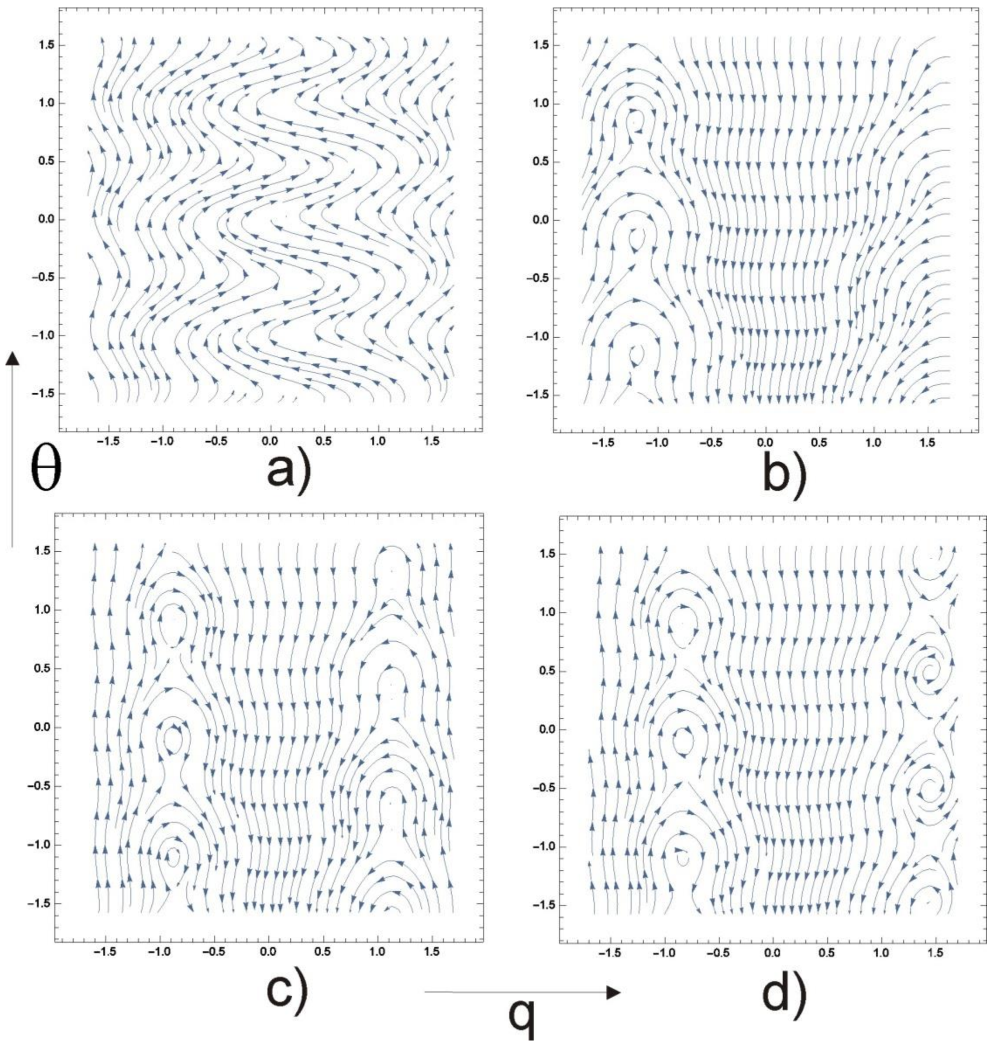
The solution of system (2) is in $\delta(\varepsilon)$- vicinity of slow surface for almost all *t* (Arnold).





Directions field and stationary points(SP)

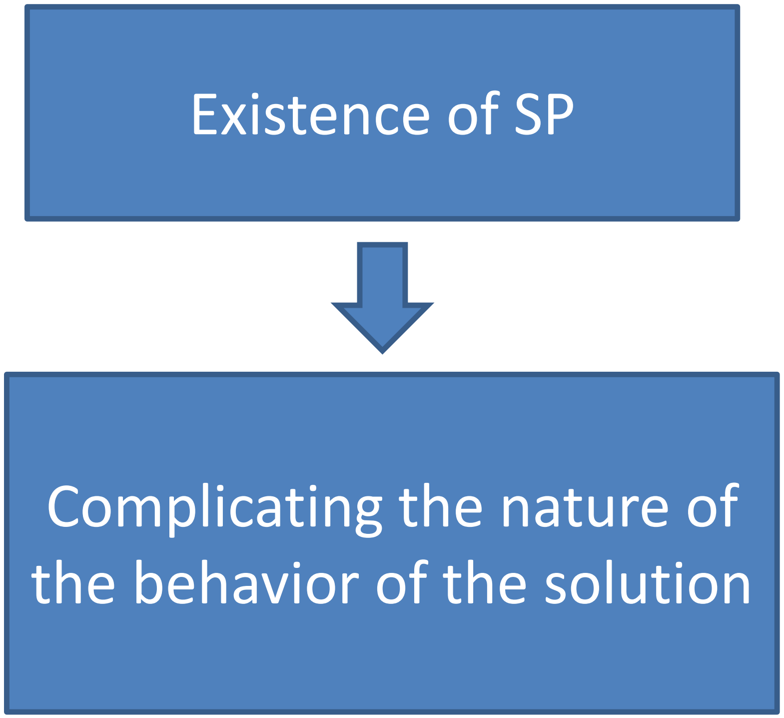
Let us denote ***index*** – a number of different types of SP of system (2)



a) No SP

b) index=2

c,d) index=4



Classification of SP

Classification of hyperbolic SP ahs been performed.

Stationary points $(q_0^{\pm}, \theta^{\pm}{}_n), n = 1,2..$ are defined:

$$q_0^{\pm} = (-a_2/a_3 \pm \sqrt{a_2^2/a_3{}^2 - 4a_1/a_3})/2 \qquad \theta_n^{\pm} = \frac{\arcsin((b_1 q_0^{\pm} + b_2 q_0^{\pm}{}^2 + b_3 q_0^{\pm}{}^3)/k)}{2\pi} - n$$

To classify hyperbolic ones let us denote:

$$\mathrm{C}(q_0^{\pm}) = b_1 + 2b_2 q_0^{\pm} + 3b_3 (q_0^{\pm})^2$$

$$\Gamma = \pm 8\pi(2q_0^{\pm} + {}^{a_2}/_{a_3})\sqrt{k^2 - (b_1 q_0^{\pm} + b_2 \left(q_0^{\pm}\right)^2 + b_3 (q_0^{\pm})^3)^2},$$

$$tr_0 = -C,$$

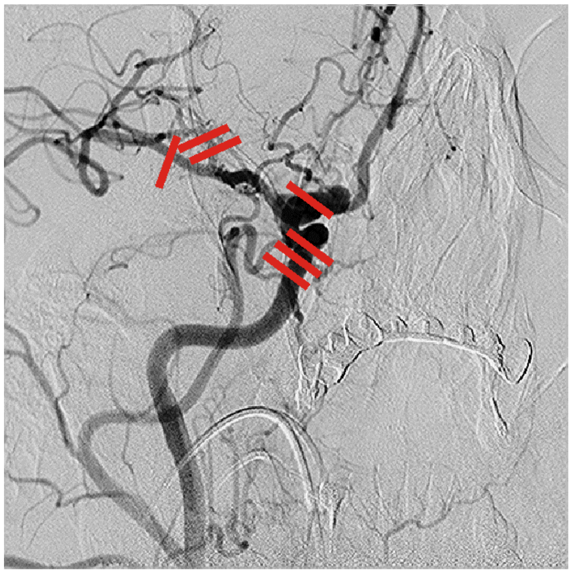
$$\theta_i = {}^1/_2\ (i-1) + l, l \in \mathbb{Z}$$

Classification of SP

Value of C,Γ	Value of tr0	Phase	Type of SP
$C^2 > \Gamma$	$tr_0 > 0$	$\theta \in (\theta_1, \theta_2]$	q_0^+ unstable node q_0^- saddle
$C^2 > \Gamma$	$tr_0 < 0$	$\theta \in (\theta_1, \theta_2]$	q_0^+ Stable node q_0^- saddle
$C^2 > \Gamma$	$tr_0 > 0$	$\theta \in (\theta_3, \theta_4]$	q_0^+ saddle q_0^- unstable node
$C^2 > \Gamma$	$tr_0 < 0$	$\theta \in (\theta_3, \theta_4]$	q_0^+ saddle q_0^- Stable node
$C \neq 0, C^2 < \Gamma$	$tr_0 < 0$	-	Stable focus
$C \neq 0, C^2 < \Gamma$	$tr_0 > 0$	-	Unstable focus

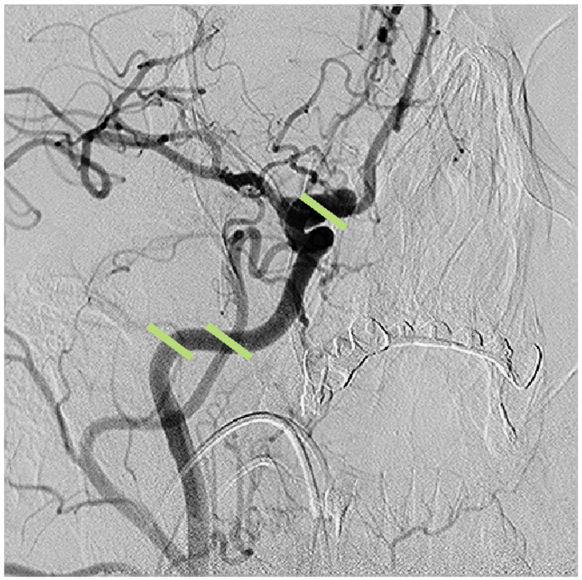
Stationary points and scheme of the treatment (G1)

before the operation

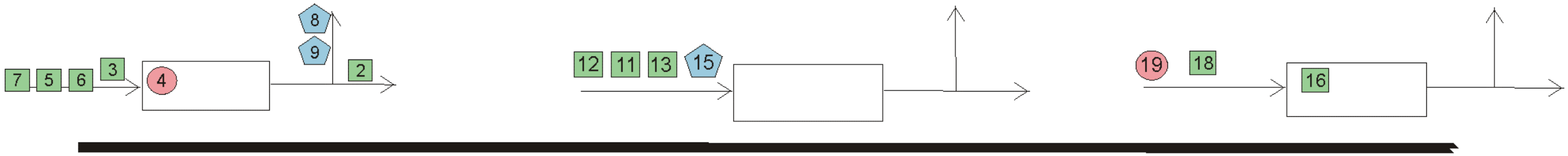


during the operation

after the operation



Scheme of the mesurements and number of the singularuties (*Patient G1.*)



2 -index=0

8 -index=2

19 -index=4

-aneurysm body

blood flow direction

19 "19" is a number of acquisition

Artery test. Statistics of confirmation

Note. Aneurysm position corresponds to system (2), which has **index** $\neq 0$ at this position.

confirmation of the test is 83%.

Patient ID	Gender, Age	Type of CA	Aneurysm location	confirmed
G1	M,42	Normal	ICA	+
K1	F,65	Giant	ICA	+
P1	M,68	Normal	MCA	+
P2	F,65	Giant	ICA	+
R1	F,47	Giant	Bifurcation of BA	+/-
S1	M,40	Normal	Bifurcation of basilar apex	+
T1	F,67	Giant	ICA	-

Damping of the circulation

The governing equation is

$$\varepsilon q'' + (a_1 + a_2 q + a_3 q^2) q' + (b_1 q + b_2 q^2 + b_3 q^3) = ku$$

These agregats represent

$P\quad(q) = a_0 + a_1 q + a_2 q^2,$ -damping

$Q\quad(q) = b_1 q + b_2 q^2 + b_3 q^3$-elastic properties of the system

Let us denote the quantities

$P_1(q)$ -damping before the treatment

$P_2(q)$ -damping after the treatment

Damping alterations before and after the treatment

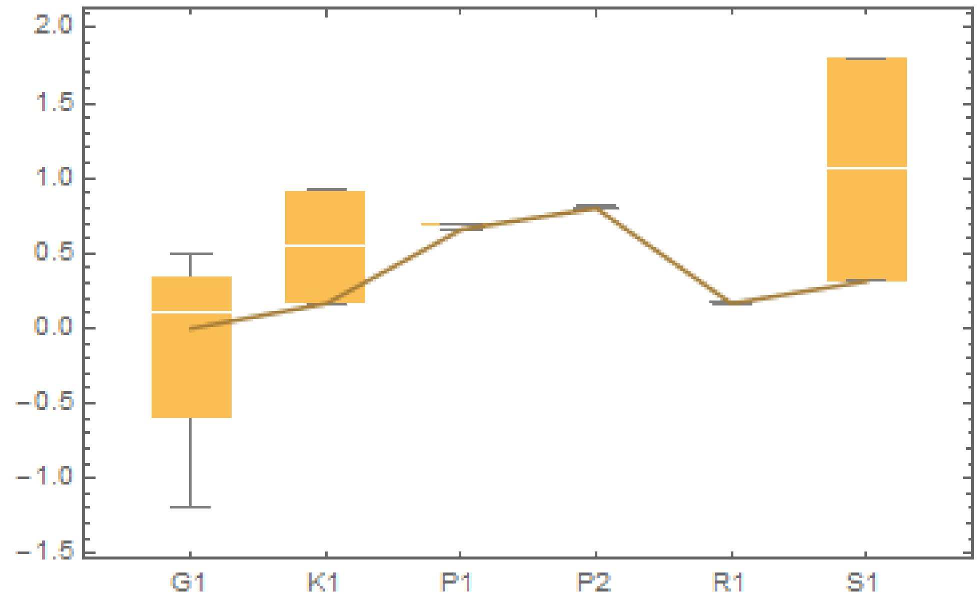
Let us consider the point q_0, where:

$$q_0 : P_1(q_0) - P_2(q_0) = \max\big(P_1(q) - P_2(q)\big)\ for\ all\ q$$

Let us define the alteration of the damping of the system:

$$\Delta = {}^{(P_1 - P_2)}/_{P_1}.$$

We have to norm this subtraction by P_1 value due to the big difference in values of P_1 and P_2 for the different measurements and different patients .



Δ median value is over the zero.
Damping is decreasing!

Conclusion

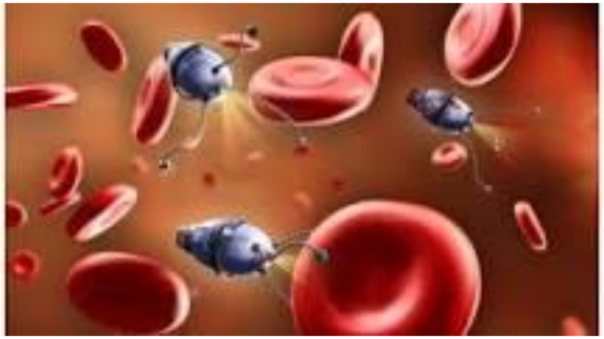
- The criterion to characterize vessel wall properties is obtained.

+ Such criterion is useful to develop a perspective embolization system.

+ Damping analysis could be useful to value the quality of embolization.

- It was illustrated that Nyquist plot could be separate on several cohorts with respect to aneurysm type.

Li et al, Small 2016,
DOI: 10.1002/smll.201601846



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Thank you for your attention!