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# Differential properties of Van der Pol — Duffing mathematical model of cerebrovascular haemodynamics based on clinical measurements

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# Differential properties of Van der Pol – Duffing mathematical model of cerebrovascular haemodynamics based on clinical measurements

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**Abstract.** The present paper discusses the method of identification (diseased/healthy) human cerebral vessels by using of mathematical model. Human cerebral circulation as a single tuned circuit, which consists of blood flow, elastic vessels and elastic brain gel tissue is under consideration. Non linear Van der Pol-Duffing equation is assumed as mathematical model of cerebrovascular circulation. Hypothesis of vascular pathology existence in some position of blood vessel, based on mathematical model properties for this position is formulated. Good reliability of hypothesis is proved statistically for 7 patients with arterial aneurysms.

## 1. Introduction

Human cerebral circulation is a complex haemodynamics system. It consists of elastic vessels, surrounded by elastic brain tissue and the blood in vessels, which is a liquid with complex reology[1]. Cerebrovascular pathologies are not as frequent as heart or aorta pathologies [2, 3], however, they are extremely dangerous because of it's mortality and disability risks. Arterial aneurysms (AA) are rather common for all nationalities and genders and occur in about 2 cases for 10 000 people. They are extremely increasing risk of morbidity for pregnant women in case of rupture [4].

All aneurysms are dangerous because of rupture risk. There are two different approaches in treatment. When such kind of pathology is located in exterior brain vessels– neurosurgeons usually apply microsurgery methods with using clips [5]. Aneurysm of proximal brain vessels is usually treated by using noninvasive methods, for example like in [6].

Present study is about features of Van der Pol-Duffing oscillator mathematical model in applications to cerebrovascular haemodynamics in presence of arterial aneurysm. The whole research is devised on several stages: clinical measurements, data processing, analytical research. The current study deals with analysis of data processed. Clinical data was obtained at Meshalkin institute of circulation pathology, Novosibirsk. This data was obtained during real-time cerebrovascular measurements for neurosurgery operations. The pressure and velocity were measured with ComboWire sensor and ComboMap station (Volcano Corp.)[7, 8]. The data for

7 patients (totally 99 measurements) was collected and processed. All measurements were made in arteries of human brain. By ethical reasons we will use only first letters of patients last names to identify them: G1,K1,P1,P2,T1,R1,S1. Data set of the clinical measurements for one patient consists of pressure and velocity values obtained on the interval from 5 sec till 2 minutes, for different ComboWire sensor positions in blood vessel (minimum 5 sec per each position). The data obtained is processed as in [8].
So the mathematical model which is under consideration is empirical and described by Van der Pol-Duffing nonlinear ordinary differential equation:

$$\varepsilon q^{''} + (a_1 + a_2 q + a_3 q^2)q^{'} + (b_1 q + b_2 q^2 + b_3 q^3) = ku, \tag{1}$$

where $q$–pressure and $u$–velocity in some position in blood vessel with respect to time. Clinical data obtained describes the pressure and velocity values on the same intervals, on which values are seen during the operation. The mathematical model constructed in [9] allows to expand the region of haemodynamics parameters that can be investigated and to try different modes of external force-right hand side of equation (1).

In equation (1) quantity $\varepsilon$ is a small parameter, $q, u$- are dimensionless pressure and velocity in a flow. Comparison of the numerical solution of the equation (1) to the clinical data shows that this equation has good approximation of pressure and velocity values. So we may assume that generally $a_3 \neq 0$. Also point that the region of interest of variables is $\{q \subset [-1, 1], u \subset [-1, 1]\}$, because equation 1 is dimensionless, and upload is assumed as $u = sin(2\pi\omega t)$.

## 2. Mathematical model and methods

By using of several substitutions like in [10] or more modern approach [11] the equation (1) leads us to dynamic system:

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

Here the prime means the differentiation with respect to $t$ and $p = \varepsilon q^{'}/a_3^2 + a_1 q/a_3 + a_2 q^2/a_3^2 + q^3/3$. When value of $\varepsilon$ is small, the system (2) is slow-fast [10, 11, 12]. The right hand side of the second equation of this system defines *slow surface*. It is pure fact [13] that, the solution of equation (1) is in vicinity $\delta(\varepsilon)$ of slow surface $S$ and consists of the combination of the solutions of slow and fast subsystems (view Fig. 1). For system (2) surface $S$ is defined by formula:

$$f(p, q, \theta) \equiv a_3^2 p - a_1 a_3 q - a_2 a_3 q^2/2 - a_3^2 q^3/3 = 0. \tag{3}$$

As seen from Fig. 1 study of slow motions of system (2) is very important. Slow motions for system (2) are motions of integral curves through the surface $S$. As for points of $S$ the equation (3) is done. System 2 over surface $S$ seems like:

$$\begin{aligned} q^{'} &= -(b_1 q + b_2 q^2 + b_3) + k \sin 2\pi\theta, \\ \theta^{'} &= (q^2 + qa_2/a_3 + a_1/a_3)\omega \end{aligned} \tag{4}$$

Here the prime means the differentiation with respect to new modified "time" $t_1 = t(q^2 + qa_2/a3 + a_1/a_3)$. To simplify calculations let us denote new variable $t_1$ just $t$ again.

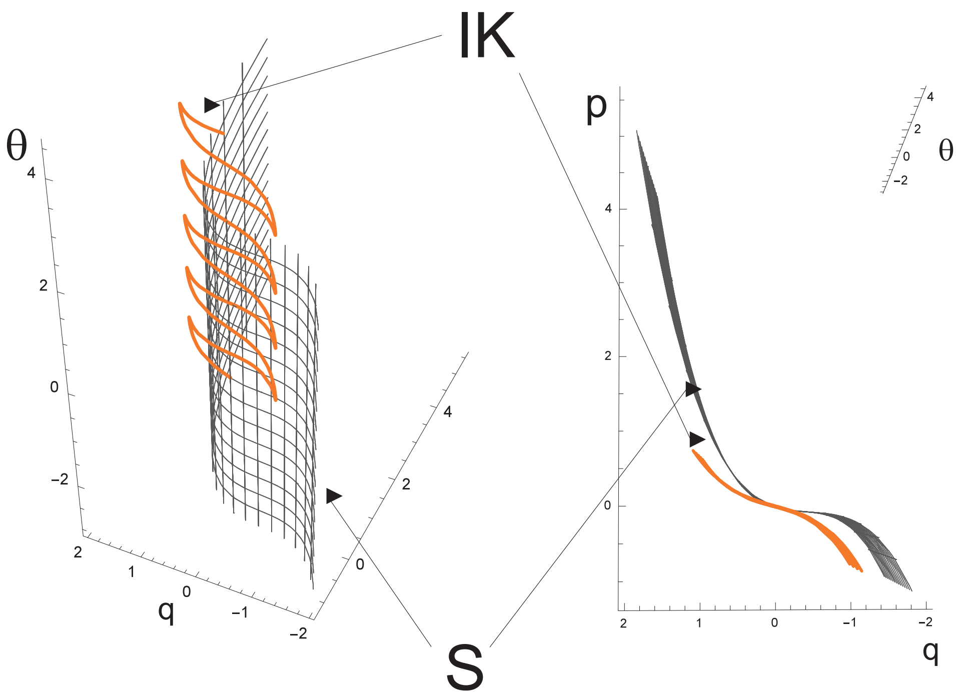


**Figure 1.** Slow surface $S$ and integral curve $IK$ of system (2) where ($k = 1.4422, a1 = 0.095381, a2 = -0.027, a3 = 0.056639, b1 = 1.1068, b2 = 0.1231, b3 = -0.14913$).

To investigate the properties of the solution of system (4) it is important to find the singularities and stationary points of this system. In order to calculate the stationary points it is necessary to solve the system of equations:

$$\begin{gathered} \sin 2\pi\theta = (b_1 q + b_2 q^2 + b_3)/k, \\ q^2 + q a_2/a_3 + a_1/a_3 = 0. \end{gathered} \tag{5}$$

To obtain the singularities it is necessary to calculate eigenvalues of Jacoby-matrix for system (4). Here this Jacoby-matrix is presented:

$$J = \begin{pmatrix} -(b_1 + 2b_2 q + 3b_3 q^2) & -2\pi k \cos 2\pi\theta \\ 2q + a_2/a_3 & 0 \end{pmatrix}. \tag{6}$$

Let us consider eigenvalues of $J$ on the solution of system (5):

$$q_0^{\pm} = (-a_2/a_3 \pm \sqrt{a_2^2/a_3^2 - 4a_1 a_3}), \theta_n^{\pm} = \frac{\arcsin{(b_1 q_0^{\pm} + b_2 q_0^{\pm 2} + b_3 q_0^{\pm 3})/k}}{2\pi} - n, \tag{7}$$

where $n$-whole numbers. It is useful to denote:

$$\sigma = k^2 - (b_1 q_0 + b_2 q_0^2 + b_3 q_0^3)^2, tr_0 = -(b_1 + 2b_2 q_0^{\pm} + 3b_3 \left(q_0^{\pm}\right)^2),$$

$$\Gamma(q,\theta) = s(\theta) 8\pi (2q + a_2/a_3)\sqrt{k^2 - (b_1 q + b_2 q^2 + b_3 q^3)^2}, C_0 = b_1 + 2b_2 q_0^{\pm} + 3b_3 \left(q_0^{\pm}\right)^2, \tag{8}$$

where

$$s(\theta) = 1|\theta \in [\theta_1, \theta_2], s(\theta) = -1|\theta \in [\theta_3, \theta_4], \quad (9)$$

and $\theta_1 = 0 + l, \theta_2 = 1/2 + l, \theta_3 = 1/2 + n, \theta_4 = 1 + n$, and $l, n$-whole numbers. It is of importance that singularities exist only when:

$$\sigma \geq 0. \quad (10)$$

The condition (10) is used for numerical analysis to define the existence of the singularities. Further assumption is very essential:
*Assumption.* It is reasonable to consider only hyperbolic singularities for living systems.
Really, this assumption is very essential because for living system some variability of parameters is necessary. This variability allows the system to be stable under small parameters perturbations.
*Note.* Only hyperbolic singularities of system (4) were found by numerical investigation with varying of $\omega$.

The cases when one or both of eigenvalues of Jacoby-matrix equal to zero or pure imaginary are out of interest for current study for the reasons mentioned above, but anyway they should be considered as critical modes of living system. However, this problem is very complicated and deserves special consideration.
So the classification of all hyperbolic singularities of system (4) was completely obtained (view Table. 1):

**Table 1.** Classification of hyperbolic singularities of system (4)

| Values of $C, \Gamma$ | Value of $tr_0$ | Phase of $\theta$ | Type of singularity at $q_0^{\pm}$ |
|---|---|---|---|
| $C^2 > \Gamma$ | $tr_0 > 0$ | $\theta \in (\theta_1, \theta_2]$ | $q_0^+$-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 |

## 3. Protocol, data development and statistics

In present study the clinical data of 7 patients is under consideration. Generally 99 measurements were performed and 73 packs of coefficients of equation (1) were obtained. Only one patient is discussed in details. For other only final results will be presented in the table.
*Definition.* Let us talk that measurement position has index $n$ if the system (4) has $n$ different singularities.

And now let us present the changing of measurement index for patient $G1$ before treatment, during the operation and after the operation for different positions in blood vessel, containing arterial aneurysm.

Angiogram and measurements scheme are presented (view Fig. 2). The number in box/pentagon/round means the ordinal number of measurement. The boxes correspond to the case, when the index of measurement is equal to zero, pentagons– the case when index is

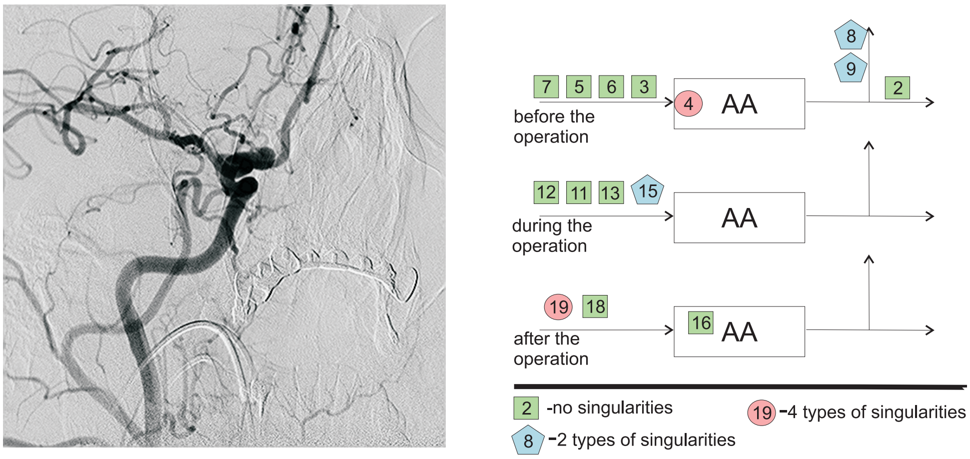


**Figure 2.** Angiogram and scheme of singularities for patient G1.

equal 2, and the circles, for the case when index is 4. The measurement scheme (view Fig. 2 at the right) consists of three parts. The top part corresponds to the measurements before the operation, the center part corresponds to the operation time measurements and the bottom part corresponds to the measurements after the operation (20-40 minutes).

It is seen from Fig. 2 that before the operation the measurement near arterial aneurysm has 2 or 4 types of singularities in terms discussed above.

## 4. Results and discussion

Comparison of the current analysis results to the clinical visualization data allows us to formulate hypothesis.

*Hypothesis(Test).* The presence of arterial aneurysm in blood vessel could be detected by index value of the measurement for this position.

In terms of Van der Pol-Duffing mathematical model it means the existence of singularities.

Some statistics obtained is shown here (view Table. 2) and proofs the Test. In the column "Test" + means that test is proved, −–test is refuted and ±–results obtained do not contradict to the test. It is seen from Fig. 2 that test is proved in $71,5\%$ of cases, and refuted in $14,3\%$ of

**Table 2.** Test statistics

| Ptient id | Gender, Age | Aneurysm type | Aneurysm location | Test |
|---|---|---|---|---|
| $G1$ | $M, 42$ | normal | ICA | + |
| $K1$ | $F, 65$ | giant | ICA | + |
| $P1$ | $M, 68$ | normal | MCA | + |
| $P2$ | $F, 55$ | giant | ICA | + |
| $R1$ | $F, 47$ | giant | bifurcation of BA | ± |
| $S1$ | $M, 40$ | normal | bifurcation of the basilar apex | + |
| $T1$ | $F, 67$ | giant | ICA | - |

cases considered. This statistics shows rather high reliability of the test. For patient $R1$ the test could not be proved or refuted, because there were no measurements near aneurysm obtained before the operation. For the most frequent location of aneurysm considered (ICA-interior carotid artery) the test has reliability 75%. Concerning to the size of aneurysm it is seen that test is proved for all (100%) of normal aneurysms and has reliability only 50% for giant aneurysms.

From physiological point of view this test is reasonable. The living system can not live normally under complicated conditions. The existence of such systems completely depends on their ability of energy saving and optimal energy transformation. The presence of singularities (aneurysms) makes such systems less effective and that is bad from the medical point of view, because the blood vessel with aneurysm can not transport blood from aneurysm to distal parts of the brain circulation system optimally. Hence, the existence of aneurysm coincides with the existence of singularities system (4)based on the clinical measurements taken near the aneurysm.

The results obtained during and after the operations do not show any common behavior of singularities system (4). Further research is necessary to answer the question whether there are any addictions to differential properties of system (4). This difficulty is due firstly to the perturbations– occur during and immediately after the treatment. These perturbations occur because regeneration of a normal blood flow function could lead to substantial restructuring of the cerebral circulation.

## 5. Conclusions

The analysis of the non linear oscillator model, based on clinical data obtained during neurosurgery treatment monitoring was performed. As result of the analysis the test on presence of arterial aneurysm in blood vessel was developed. Good reliability of this test was statistically proven for ICA cerebral aneurysms. The test is proven by the measurements obtained before the operation. The influence of treatment on differential properties of Van der Pol-Duffing model could not be discussed from the data considered.

The test is a challenge for medical and engineering society, which should pay attention to 0-d models of cerebral haemodynamics and use of modern measurement devices for developing of personalized treatment protocols in vascular neurosurgery. Also this test can be used for perspective aneurysm diagnostics (without MRI or CT) and for developing of perspective embolization devices.

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