Using non-linear analogue of Nyquist diagrams for analysis of the equation describing the hemodynamics in blood vessels near pathologies

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Abstract. This article considers method of describing the behaviour of hemodynamic parameters near vascular pathologies. We study the influence of arterial aneurysms and arteriovenous malformations on the vascular system. The proposed method involves using a generalized model of Van der Pol–Duffing to find out the characteristic behaviour of blood flow parameters. These parameters are blood velocity and pressure in the vessel. The velocity and pressure are obtained during the neurosurgery measurements. It is noted that substituting velocity on the right side of the equation gives good pressure approximation. Thus, the model reproduces clinical data well enough. In regard to the right side of the equation, it means external impact on the system. The harmonic functions with various frequencies and amplitudes are substituted on the right side of the equation to investigate its properties. Besides, variation of the right side parameters provides additional information about pressure. Non-linear analogue of Nyquist diagrams is used to find out how the properties of solution depend on the parameter values. We have analysed 60 cases with aneurysms and 14 cases with arteriovenous malformations. It is shown that the diagrams are divided into classes. Also, the classes are replaced by another one in the definite order with increasing of the right side amplitude.

1. Introduction
The cerebral blood vessel network is a complex system with blood circulating. The walls of a blood vessel are viscoelastic and the outer part of the vessel consists of muscles which react reflexively to the pulse wave. Besides, the vessel is surrounded by the brain substance. Sometimes different pathological defects, for example aneurysms \cite{2} and arteriovenous malformations (AVM), \cite{1} may occur in the cerebral blood vessel network. The AVM is a pathological plexus of the veins and arteries. This leads to violation of blood circulation. Moreover, AVM leads to the direct emission of blood from arterial pool to vein pool. Another pathology is the arterial aneurysm. It is the bulging of artery wall as a result of its extension. The material of the aneurysm wall is different from the material of the health vessel. Intra-vascular surgery is used for the treatment of patients with these pathologies. Embolization which means selective sealing up of blood vessels is applied in case of AVM or intra-vascular setting of the stent in case of aneurysm.
2. Materials and methods
During the neurosurgical operations, the hemodynamic parameters are monitored. ComboMap
device with ComboWire sensor \((d \approx 0.3 \text{ mm}, L > 1 \text{ m})\) is used for this purpose. It is unique
equipment for complex measurement inside of small vessels. The sensor measures simultaneously
the pressure and velocity in the blood vessel. During surgery, series of measurements are made
in different areas of the vasculature. The measurements are made both in arterial and venous
pool. Data collection frequency is about 200 Hz. The obtained data are written into the file
with ADC device [3, 4].

The obtained data namely pressure and velocity are cleaned by using software noise wavelet
filters. This is done by the expending signals in Gabor wavelet of frequency 6. Then the highest
harmonics of wavelet expanding are removed. The signals are recovered from the remaining
coefficients of wavelet decomposition.

The authors use PV-diagrams to present the obtained data. The practice of investigation has
shown the high efficiency of this representation. PV-diagram is a parametric curve in the plane.
The velocity is marked on the horizontal axis, the pressure is marked on the vertical axis, the time
is the parameter along the curve. Also, we use QU-diagrams built on normalized dimensionless
values of pressure and velocity. Important to note that the forms of diagrams constructed
according to data obtained near aneurysms and AVM qualitatively differ (see Figure 1 and
Figure 2).

![Figure 1. QU-diagram in case of aneurysm.](image1)

![Figure 2. QU-diagram in case of AVM.](image2)

Diagrams in the venous and arterial pools differ too. The image point moves the diagram
anticlockwise in arterial part, and clockwise in venous part with time.

To identify the characteristic behaviour of hemodynamic parameters in the surroundings of
vascular pathologies the model of generalized Van der Pol–Duffing equation [6] was suggested.

\[
\varepsilon q''(t) + P_2(q)q' + P_3(q) = ku(t). \quad (1)
\]

The normalized velocity \(u\) is a given value measured during the operation. The normalized
pressure \(q\) is the solution of the equation. In the equation (1) \(P_2(q) = a_1 + a_2q + a_3q^2,\)
\(P_3(q) = b_1q + b_2q^2 + b_3q^3\). The coefficients are constructed based on the experimental data
[5]. Coefficients \(b_i\) respond for the elastic properties of the vessels, \(a_i\) respond for the viscous
friction, \(\varepsilon\) corresponds to the relaxation oscillation character. The various clinical cases are
characterized by different coefficients of the equation. These coefficients are founded by the
methods of inverse problem theory.

The model was confirmed experimentally with large amount of clinical data (about 300). The
pressure values obtained in the experiment coincide well with the pressure values predicted by
the model. Figure 3 shows typical QU-diagrams constructed on experimental data (black) and ones obtained by solving the equation (red).

**Figure 3.** QU-diagrams. a–d: typical for aneurysms, e–f: typical for AVM. Black – experimental data, red — data obtained by solving the equation (1).

3. Results
From the medical point of view it seems important to know the state of the patient vascular bed before operation and monitor changes in this state at time of surgery. In this regard it is necessary not only to know the current response of blood vessels to pulse wave, but also be able to predict their response to the changes in blood flow. For ethical reasons if the effects on
patients are not justified medically, they are considered to be intolerable. Thus, it is impossible to conduct research on real patient aiming to find out the reaction of bloodstream to the changes in blood flow. That is why it seems to be natural to investigate the model of vascular system of that patient.

To accomplish this we analyse the solutions of generalized Van der Pol–Duffing equation built for certain patients. The analysis is carried out by replacing the right side by a harmonic function, which parameters are the amplitude and frequency. We relate the solution behaviour with these two parameters. The analysis of the solution behaviour is important to predict how the system will react to outer force.

The generalized Van der Pol–Duffing equation is non-linear. So the solutions are not harmonic functions and have fairly complex behaviour even in case of harmonic right side. The analysis of main solution characteristics is necessary to find out the key influence patterns of right side amplitude and frequency on the solution. Such characteristics are primarily the solution amplitude and the solution phase change relative to the phase of the right side.

Due to the large amount of built solutions, direct behaviour analysis of the amplitude and phase change is difficult. Therefore, the authors suggested and used the non-linear generalization of the Nyquist diagrams (ND). In linear case ND is the amplitude-phase-frequency characteristic of the system. ND is depicted as a curve in polar coordinates and built for the fixed value of the right side amplitude. The right side frequency is the parameter along the curve. Polar radius is the amplitude and angle is the phase change of the appropriate solution.

But since in the non-linear case the oscillations are not harmonic, the modules of the solution maximum and minimum do not coincide. In this regard two curves in the polar coordinates are suggested to be used as a non-linear analogue of ND. The first curve is for module of the solution maximum and the second is for minimum. On figures in the paper the curve of maximum is red and the curve of minimum is blue. The number on plot corresponds to the right side frequency value. Figure 4 shows typical ND.

![Figure 4. Example of Nyquist Diagram.](image)

**Table 1.** The number of measurements for different patients.

|   | Gu | Ko | Pi | Po | Si | Ch |
|---|----|----|----|----|----|----|
|   | 15 | 15 | 6  | 10 | 14 | 14 |

For the construction of the equation (1) the clinical data of 6 patients were used. It was aneurysms in 5 cases and AVM in 1 case. The measurements were made at various sensor positions in the surroundings of the pathologies for each patient. Table 1 shows the number of measurements for each patient.
Generalized Van der Pol–Duffing equation characterized by its own set of coefficients was obtained for all measurements [3]. Further, we constructed ND for all of the coefficient sets using 4 fixed right side amplitude values. When constructing ND the following set of amplitudes was used: 0.3, 0.5, 0.75, 1. This choice of amplitude is due to the fact that dimensionless values in the equation vary from 0 to 1. In addition, the right side frequency varies from 0.01 Hz to 50 Hz. As a result we have analysed about 300 ND.

![Graphs of ND classes](image)

**Figure 5.** Classes of ND. a – normal case, b – divergent case, c – loop case, d – gap case, e – break case.

4. Discussion
While analysing the obtained ND we revealed that diagrams may be classified. For the time being it is possible to identify the following classes: normal case, divergent case, loop case, gap case, break case. These classes are often found between different patients. Typical ND for these classes are shown on Figure 5. It was observed that diagrams move from class to class in the following order with the increasing of the amplitude.

\[
\text{normal case} \rightarrow \text{divergent case} \rightarrow \text{loop case} \rightarrow \text{gap case} \rightarrow \text{break case}
\]  

(2)

If the right side frequency value changes continuously, the graph of the relevant solution transforms in a continuous manner too.

Next, we consider the solution behaviour corresponding to different classes of ND (Figure 6).
In normal case ND resembles the diagram for linear system. Besides, the solution of the equation (1) with a harmonic right side is close to a harmonic function. In the picture the blue curve denotes the right side of the equation (1), the yellow curve denotes corresponding solution. The plot of solution is built for the fixed frequency value in the point of the greatest distance between the curves of ND.

In the divergent case the difference between solution deviation up and down from the horizontal axis is increasing. As the amplitude grows, the solution differs more from a harmonic function.

In the loop case the typical situation is the occurrence of subharmonics in the decision. These subharmonics appear in the surroundings of the loops on ND.

In the gap case subharmonics are also observed. Moreover, the oscillation breakdown takes place in the gap area.

The break case is characterized by a long transient regime of oscillation establishment.

**Figure 6.** Typical solutions of equation (1) in different cases: a – normal case, b – divergent case, c – loop case, d – gap case, e – break case.

ND runs the chain (2) entirely not for the all sensor positions. There are cases when the ND remains within the first two classes for all the amplitude values from the set.
As the authors suppose, complicated non-linear oscillations may indicate a pathological state of vascular system in the surroundings of the sensor position. Such oscillations are mostly peculiar to the last three classes in the chain (2).

5. Conclusion
The study of generalized Van der Pol–Duffing equations built on the clinical data of real patients is presented in this paper. It is shown that ND constructed on the solutions of these equations are divided into several classes. The diagrams move from one class to another in definite order with the increasing of the right side amplitude. The dependence of the characteristic solution behaviour on the form of ND is found out.

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