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«КИЇВСЬКИЙ ПОЛІТЕХНІЧНИЙ ІНСТИТУТ
імені ІГОРЯ СІКОРСЬКОГО»
ФАКУЛЬТЕТ БІОМЕДИЧНОЇ ІНЖЕНЕРІЇ
(повна назва інституту/факультету)

КАФЕДРА БІОМЕДИЧНОЇ ІНЖЕНЕРІЇ
(повна назва кафедри)

«До захисту допущено»
Завідувач кафедри
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(підпис) (ініціали, прізвище)
"___" _____ 2021р.

Дипломна робота
на здобуття ступеня бакалавра

зі спеціальності 163 «Біомедична інженерія»
(код і назва)

на тему: Система статистичного аналізу даних для доказової медицини на платформі LabVIEW

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(full name of the department)

«As a manuscript»
UDC 615.849.19

«Approved for defense»
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" ____ " _____2021

Diploma thesis
for a bachelor's degree

in the specialty 163 « Biomedical engineering »
(code and name)

topic: Statistical data analysis system for evidence-based medicine on the LabVIEW platform

Completed: 4th year student, group BM-73i
(group code)

Ahmed Sani _____
(Full Name) (signature)

Supervisor Assoc. dep. BMI, Ph.D., Assoc. prof. A. Solomin _____
(position, academic degree, academic title, surname and initials) (signature)

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I certify that in this diploma thesis there are no borrowings from the works of other authors without appropriate references.
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FACULTY OF BIOMEDICAL ENGINEERING
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Level of education Level 6 (bachelor), QF-EHEA
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" ____ " _____2021

TASK
For student`s bachelor thesis

Ahmed Sani
(Full Name)

1. topic Statistical data analysis system for evidence-based medicine on the LabVIEW platform
supervisor Ph.D., Assoc. prof. A. Solomin
(last name, first name, patronymic, academic degree, academic title)

approved by the order of the university №257 / 19-si from 11/18/2021

2. The deadline for students to submit a bachelor thesis 04.06.2021

3. The object of study is evidence-based medicine

4. The subject of research is statistical data analysis system

5. List of tasks to be developed: analytical review of existing statistical methods and algorithms for information processing for evidence-based medicine; development of tree-like architecture of software system with decision-making nodes and algorithms of statistical analysis modules; implementation in the NI LabVIEW environment of statistical analysis algorithms with preliminary automatic verification of the relevant criteria for their applicability.

6. Approximate list of graphic material 15 tables, 25 figures

7. Approximate list of publications: publication of an article in a journal "Biomedical Engineering and Technology", the bachelor thesis protection

8. Final deadline 07.06.2021

SCHEDULE

№ з/п	Name of stages of execution diploma thesis	Deadline for stages diploma thesis	Note
1	Analysis of scientific literature	10.11.2020	
2	Development of the content and structure of bachelor thesis	26.02.2021	
3	Development of statistical analysis algorithms on the topic of the diploma	12.03.2021	
4	Development of a tree structure of a software system with decision-making nodes	26.03.2021	
5	Implementation in the NI LabVIEW environment of statistical analysis algorithms with preliminary automatic verification of the relevant criteria for their applicability	24.04.2021	
6	Safety and precautions	24.05.2021	
7	Registration of bachelor thesis	01.06.2021	
8	Getting a review and feedback	04.06.2021	
9	Passing norm control	07.06.2021	
10	The bachelor thesis protection		

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ABSTRACT

The volume of work is 79 pages, the number of illustrations - 30, tables - 17, sources on the list of links - 62.

The problem of creating tools to simplify the correct use of statistical research methods remains relevant, especially in the biomedical field, where experts are not familiar enough with the mathematical methods of statistics

The algorithm is developed and the automated system of statistical analysis for evidence-based medicine is created. Its feature is to provide automatic verification of the criteria for the applicability of each statistical method and decision-making on the selection of the appropriate for a particular situation. The algorithm is implemented in the form of a decision tree in the software environment NI LabVIEW, which provides easy connection to the equipment, versatility and ease of further modification of algorithms.

The object of research is the methodology of evidence-based medicine.

Subject – statistical methods of data analysis in evidence-based medicine.

The aim of the work is to ensure the reliability of the statistical analysis conclusions by creating a software system of statistical processing modules with prior automatic verification of the relevant criteria of their usability.

To achieve this goal, the following research objectives were identified:

- analytical review of existing statistical methods and algorithms for information processing for evidence-based medicine;

- development of tree-like architecture of software system with decision-making nodes and algorithms of statistical analysis modules;

- implementation in the NI LabVIEW environment of statistical analysis algorithms with preliminary automatic verification of the relevant criteria for their applicability.

The use of an automated system to detect statistical relationships and statistically significant results of the influence of factors can reduce the number of

erroneous results in evidence-based medicine, especially with widespread access to such a system.

Key words: evidence-based medicine, statistical analysis, NI LabVIEW, usability criteria, decision tree, research automation.

РЕФЕРАТ

Обсяг дипломної роботи складає 79 сторінок, кількість ілюстрацій – 30, таблиць – 17, джерел за переліком посилань – 62.

Проблема створення інструментальних засобів для спрощення коректного використання статистичних методів досліджень залишається актуальною, особливо в біомедичній галузі, де фахівці не надто володіють математичним апаратом.

В роботі розроблено алгоритм і створено автоматизовану систему статистичного аналізу для доказової медицини. Її особливістю є забезпечення автоматичної перевірки критеріїв вживаності кожного статистичного методу та прийняття рішень щодо обирання відповідного до конкретної ситуації. Алгоритм реалізовано у вигляді дерева рішень в програмному середовищі NI LabVIEW, що забезпечує легке підключення до апаратури, універсальність та простоту подальшої модифікації алгоритмів роботи.

Об’єктом дослідження є засоби доказової медицини.

Предметом – статистичні методи аналізу даних в доказовій медицині.

Метою роботи є забезпечення достовірності висновків статистичного аналізу інформації шляхом створення програмної системи модулів статистичної обробки з попередньою автоматичною перевіркою відповідних критеріїв їх вживаності.

Для досягнення поставленої мети, були визначені наступні завдання дослідження:

- аналітичний огляд існуючих статистичних методів і алгоритмів обробки інформації для доказової медицини;

- розробка деревоподібної архітектури програмної системи з вузлами прийняття рішень та алгоритмів модулів статистичного аналізу;

- реалізація в середовищі NI LabVIEW розроблених алгоритмів статистичного аналізу з попередньою автоматичною перевіркою відповідних критеріїв щодо можливості їх застосування.

Використання автоматизованої системи для виявлення статистичних зв’язків та статистично достовірних результатів впливу факторів може зменшити кількість помилкових результатів в доказовій медицині, особливо при широкому доступі до такої системи.

Ключові слова: доказова медицина, статистичний аналіз, NI LabVIEW, критерії вживаності, дерево рішень, автоматизація досліджень.

CONTENTS

LIST OF SYMBOLS, UNITS, ABBREVIATIONS AND TERMS

NI LabVIEW	–	National Instrument Laboratory Virtual Instrument Engineering Workbench
MS	–	Microsoft
U- test	–	Wilcoxon - Mann – Whitney test
F-test	–	Fisher test
t-test	–	Student's test
ANOVA	–	Analysis of variance

INTRODUCTION

Relevance: One of the main methods of obtaining scientifically reliable data in the biomedical sector are evidence-based medicine. It is based on statistical methods of information analysis [1 – 52]. But, according to some studies [53-56], a lot of conclusions made by this method are erroneous. This is due to the complexity of statistical analysis mathematical apparatus, primarily the criteria and limits of possible use of statistical tools, and the insufficient level of their mastery of biomedical specialists.

There are a number of computer software packages that facilitate the use of statistical methods of information processing, but the problem remains, because for correct use of specific tools from these packages, professionals still need to know quite deeply and check the necessary conditions.

It should be emphasized that the consequences of erroneous conclusions in evidence-based medicine may be quite dangerous because they relate to human health. Reducing the likelihood of errors is very important.

Purpose: ensure the reliability of the statistical analysis conclusions by creating a software system of statistical processing modules with prior automatic verification of the relevant criteria of their usability.

The object of research is the methodology of evidence-based medicine.

The subject of research is statistical methods of data analysis in evidence-based medicine.

Based on the purpose for this work, the following tasks were set:

1. Analytical review of existing statistical methods and algorithms for information processing for evidence-based medicine;

2. Development of tree-like architecture of software system with decision-making nodes and algorithms of statistical analysis modules;

3. Implementation in the NI LabVIEW environment of statistical analysis algorithms with preliminary automatic verification of the relevant criteria for their applicability.

Research methods. NI LabVIEW was chosen as the software development environment, which is currently an informal standard in the field of biomedical instrumentation and biomedical research and is easily integrated into most modern software and hardware systems [57–59]. The computer software system was built in the form of a tree, where nodes automatically check conditions and criteria for specific statistical methods, branching to next nodes of the algorithm, and the final node of chain draws statistical conclusions.

The use of an automated system to detect statistical relationships and statistically significant results of the influence of factors can reduce the number of erroneous results in evidence-based medicine, especially with widespread access to such a system.

SECTION 1
ANALYTICAL REVIEW OF STATISTICAL METHODS FOR EVIDENCE-BASED MEDICINE

1.1 The concept of evidence-based medicine

Evidence-based medicine, according to the most popular definition, is the conscious, clear use of the best available evidence to make decisions about care for specific patients. This definition is not complete because the subject misses an important aspect of evidence-based medicine – the use of mathematical methods. It was therefore formulated a different definition: "Evidence-based medicine – a strengthening of traditional skills in medical diagnosis, treatment, prevention and other areas through systematic formulation and application on mathematical probability and risk assessments".

One of the main means of obtaining scientifically reliable data in evidence-based medicine is statistical methods of information analysis. At the current stage of development of medicine, statistical analysis is an integral part of almost any study and only with its help it is possible to supplement the evidence base. The most significant results of research are made on the basis of the comprehensive and carefully carried out statistical analysis in which rather difficult algorithms are used. According to some studies [53–56], a lot of conclusions made by these methods are erroneous. This is due to the complexity of statistical analysis mathematical apparatus, primarily the criteria and limits of possible use of statistical tools, and the insufficient level of their mastery of biomedical specialists.

There are many software tools that provide this analysis. This is, for example, in the simplest case, MS Excel or a more functional package STATISTICA (StatSoft). These tools meet the needs of the scientific and technical field, where specialists know the basics of mathematics, but are often a source of errors in biomedicine, which is due to the unjustified use of statistical analysis without checking the criteria of their applicability. It should be

emphasized that the consequences of erroneous conclusions in evidence-based medicine can be quite dangerous.

The Table 1.1 lists the traditional means of statistical data processing, the circumstances that accompany such studies, the criteria to be met, and the methods of drawing appropriate conclusions.

Typical statistical studies involve the detection of the influence of a factor on the experimental group. Moreover, depending on the situation, the effect can be investigated using control and experimental groups, or on the basis of one group before and after the action of this factor. The influencing factor may be numerical or non-numerical, the statistical distribution of the measured value may be Gaussian or not, the variance of the samples may be the same or not.

The table shows how many factors a researcher must consider to make a statistically significant conclusion. This requires a fairly deep knowledge of mathematical principles, which is not always present in medical professionals.

Therefore, despite the existence of a number of computer software packages that facilitate the use of statistical methods of information processing, the problem remains, because for the correct use of specific tools from these packages, professionals still need to know and check the necessary conditions.

1.2 The variants of applied problems of statistical analysis

In Table 1.1 the variants of applied problems of statistical analysis in various conditions and the corresponding methods are presented in a visual form.

The leftmost column is the formulation of the problem in the application area.

The next column – formulation of this problem in the terminology of statiscal literature.

Column "Additional Terms" allows to refine the choice of method depending on the characteristics of problem and data.

The last column – a list of methods that are appropriate to certain set of conditions.

Table 1.1 – Traditional means of statistical data processing

<table>
<tr><th>Formulation of the problem in the applied setting</th><th>Formulation of the problem in a statistically statement</th><th colspan="2">Additional terms</th><th>Applied method</th></tr>
<tr><td rowspan="4">Comparison of control and experimental samples</td><td rowspan="4">Testing the hypothesis of equality of means (distribution centers) two independent samples</td><td rowspan="2">Normal law distribution</td><td>Dispersions of the samples are equal</td><td>Student's t-test for equal variances</td></tr>
<tr><td>Dispersions of the samples unequal</td><td>Student's t-test for unequal variances</td></tr>
<tr><td rowspan="2">Law distribution different from normal, or data is measured in discrete scale</td><td>Dispersions of the samples are equal</td><td>Mann - Whitney (U- test of Wilcoxon - Mann - Whitney)</td></tr>
<tr><td>Without the assumption about dispersions</td><td>Wilcoxon two-samples median test</td></tr>
<tr><td rowspan="2">Comparison of samples before and after experiment</td><td rowspan="2">Testing the hypothesis of equality of means in two dependent samples</td><td colspan="2">Normal distribution law</td><td>Student's t-test for dependent samples</td></tr>
<tr><td colspan="2">The distribution law is different from the normal or data are measured in a discrete scale</td><td>Wilcoxon signed rank test</td></tr>
</table>

Continuation of table 1.1

Comparison of indicator dispersion in two samples	Testing the hypothesis of equality of variances (belonging of variances to the same general population)	Normal distribution law	**F-test (Fisher)**
		The distribution law is different from the normal or data are measured in a discrete scale	**Siegel - Tukey, Moses**
Testing the hypothesis about the presence of correlation between the variables	Correlation analysis	Normal distribution law	**Pearson's correlation**
		The distribution law is different from the normal or data are measured in a discrete scale	**Spearman's correlation**
Testing the hypothesis about the presence of the influence of a factor on a statistic	Analysis of variance (ANOVA)		**ANOVA, F-test (Fisher)**

Consider the variants of applied problems of statistical analysis in Table 1.1.

• Comparison of indicators of control and experimental samples. There are two independent samples in which the average values of some parameters need to be compared. For example, the two groups of patients, which are treated by various methods.

Formulation of the problem in a statistically statement – testing the hypothesis of equality of means (distribution centers) two independent samples.

For this task, there may be four options for additional conditions:

1) The data in the samples are distributed according to the normal law and dispersions of the samples are equal. In this case, it is necessary to apply Student's t-test for equal variances.
2) The data in the samples are distributed according to the normal law but dispersions of the samples unequal. In this case, it is necessary to apply Student's t-test for unequal variances.

3) Law distribution of data different from normal, or data is measured in discrete scale and dispersions of the samples are equal. In this case, it is necessary to apply Mann – Whitney method (U- test of Wilcoxon - Mann - Whitney).

4) Law distribution of data different from normal, or data is measured in discrete scale and there is no information about the equality of variances. In this case, it is necessary to apply Wilcoxon two-samples median test.

• Comparison of sample indicators before and after the experiment. In this case, we are dealing with the so-called linked samples. In the literature, you can also find the expression "samples that are naturally divided into pairs". For example, the value of a certain indicator in the same group of patients before and after treatment.

Formulation of the problem in a statistically statement – testing the hypothesis of equality of means in two dependent samples.

For this task, there may be two options for additional conditions:

1) The data in the samples are distributed according to the normal law. In this case, it is necessary to apply Student's t-test for dependent samples.

2) Law distribution of data different from normal, or data is measured in discrete scale. In this case, it is necessary to apply Wilcoxon signed rank test.

• Comparison of dispersion of the indicator in two samples. In some biological experiments, it is not the average value of the indicator that is important, but its dispersion. For example, for the subsequent selection of new varieties, it is necessary to select such a type of influence on seeds so that the dispersion of traits is greatest. Or, it is necessary to choose a drug (treatment method) in which the dispersion of a controlled symptom after application will be minimal.

Formulation of the problem in a statistically statement – testing the hypothesis of equality of variances (belonging of variances to the same general population).

For this task, there may be two options for additional conditions:

1) The data in the samples are distributed according to the normal law. In this case, it is necessary to apply F-test (Fisher).

2) Law distribution of data different from normal, or data is measured in discrete scale. In this case, it is necessary to apply method Siegel-Tukey, Moses.

• Testing the hypothesis about the presence of correlation between the variables, that is checking the presence of a linear relationship between the values of one random variable and the mean values of another.

Formulation of the problem in a statistically statement – correlation analysis.

For this task, there may be two options for additional conditions:

1) The data in the samples are distributed according to the normal law. In this case, it is necessary to apply Pearson's correlation testing.

2) Law distribution of data different from normal, or data is measured in discrete scale. In this case, it is necessary to apply Spearman's correlation testing.

• Checking the presence of the influence of some factor (usually of a non-numerical nature) on a random variable of a numerical nature. For example, does the diet of feeding livestock affect their weight gain.

Formulation of the problem in a statistically statement – analysis of variance (ANOVA).

The point is to compare the variance in samples due to random causes with the variance due to the influence of some factor. If they differ significantly, then the factor has a statistically significant effect on the studied value.

For this task must be use F-test (Fisher).

1.3 Traditional means of statistical data processing

Normal distribution law

This law is widely used in probability theory and mathematical statistics. The standard normal distribution is the distribution with zero mathematical expectation and unit variance. Almost all parametric statistics are based on the normal distribution law. This is due to the fact that most of the distributions used to test statistical hypotheses (Fisher, Student, etc.) are only transformations of the normal distribution law [60–62]. The widespread application of the normal distribution law accordingly needs to be explained. The origin of the normal distribution law

$$p(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-x^2/(2\sigma^2)}$$

is attributed to the limit theorems on the sums of independent random variables. If instead of a random variable we consider a random vector with independent coordinates x_i

$$x = \{x_1, \dots, x_n\}$$

and the distribution density ρ(x) independent of the direction x, these assumptions are sufficient to guarantee the normal distribution of all x_i. Coordinate independence means

$$p(x) = p_i(x_i) \dots p_n(x_n),$$

and the independence of ρ(x) from the direction x is the constancy of the distribution ρ(x), as well as its logarithm

$$\ln p(x) = \ln p_i(x) + \cdots + ln\, p_n(x)$$

on spheres $x_1^2+\ldots+x_n^2$= const. In other words, these functions have the same level surfaces, which in turn is possible only when their normals (gradients) are collinear (equally or oppositely directed).

The average absolute deviation is found by the formula:

$$\Delta_{abs} = \frac{\sum_{i=1}^{N} |X_i - \bar{X}|}{N} \qquad (1.1)$$

Also, in order to check the normality of the distribution, it is enough to check the following conditions [60–62]:

$$\left|\frac{\Delta_{abs}}{S} - 0.7979\right| < \frac{0.4}{\sqrt{N}} \qquad (1.2)$$

Correlation

Correlation is a characteristic of the closeness (strength) of the relationship between variables, expressed in a single number. This characteristic is called the correlation coefficient, usually denoted by the letter r. The correlation coefficient can take values from -1 to +1. The correlation coefficient sign indicates the direction of communication (forward or reverse), and the absolute value indicates the closeness of the relationship. The coefficient is equal to -1, determines a strong relationship, the same as in case 1. In the absence of a relationship, the correlation coefficient is zero.

Figure 1.1 shows examples of dependencies and their corresponding values of r.

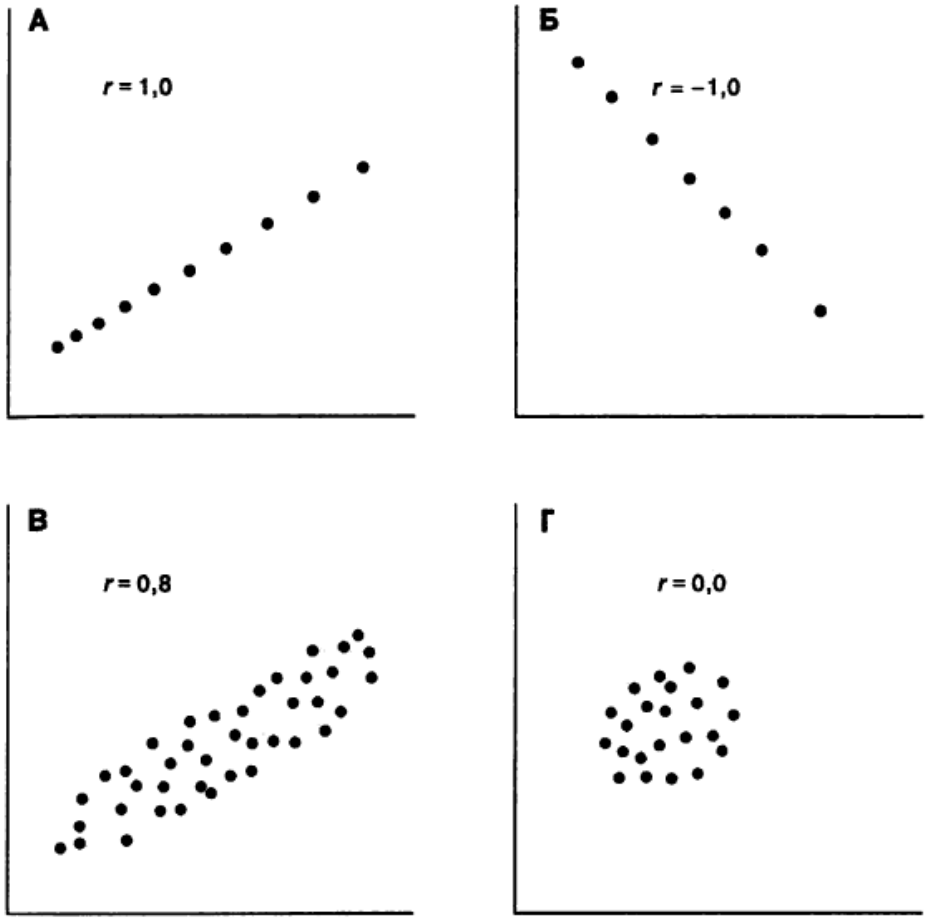

Fig.1.1 – Types of correlation

Rank correlation

Rank correlation is analogous to pairwise correlation for those cases when the values of the relationship, between which you want to check, are not presented in the scale of relations, but in any other. This situation most often arises when we are dealing with subjective assessments of objective phenomena that cannot be measured, i.e. with expert assessments. In addition, rank correlation is also used in cases, where the distribution law of the studied variables is not Gaussian (normal).

Correlation coefficients are called rank, because before calculating the values of the variables are converted into ranks. To do this, the available values of the variables are placed in a ranked series. Then each value is assigned a rank from 1 to N, where N is the number of analyzed objects. In that case, if several elements have the same rank, then each of them is assigned an average of the values occupied by them.

Remark:

• All observations should be statistically independent.

• All values of observations are taken from one two-dimensional population, ie X and Y must be equally distributed. There are several different ways to find the values of rank correlation coefficients. One of the most commonly used is Spearman's correlation coefficient (p, sometimes denoted as r).

Spearman's rank correlation coefficient

The Spearman coefficient is based on the formula

$$p(A,B) = 1 - \frac{6\sum_{i=1}^{N}(R_{1i} - R_{2i})^2}{n^3 - n}$$

where R_{1i} та $R_{2i}$are the ranks of the i-th object for each of the compared variables.

This coefficient is a complete analogue of the pairwise correlation coefficient after conversion, that can be represented as

$$p(A,B) = 1 - \frac{\sum_{i=1}^{N}(R_{1i} - \frac{n+1}{2})(R_{2i} - \frac{n+1}{2})}{\frac{1}{12}(n^3 - n)}$$

To test the significance of Spearman's rank correlation coefficient at n> 9, we can use the Student's t test. Validation for the general case is performed using special tables.

Test of statistical hypotheses

For the practical application of the methods of probability theory and mathematical statistics, knowledge of the law of probability distribution is extremely important. In fact, the studied random variable for the scientist is represented only by the law of distribution of probabilities of realization of its values. Attempting to apply observational analysis methods developed for specific probability distribution laws in conditions where the real distribution differs from the hypothetical one is the most common error in practice, leading to incorrect conclusions and, ultimately, to significant material loss and time. That is why any processing of the results of observations should begin with the answer to the main question: what is the probability distribution of a number of random variables under study? In practice, this problem is usually formulated as follows. The hypothesis is put forward - "the observed distribution of random variables is described by some specific law (normal, exponential)".

The task of the primary study is to accept or reject the hypothesis.

Statistical is the hypothesis about the type of unknown distribution, or about the parameters of unknown distributions. For example, hypotheses will be statistical:

1) The general population is distributed according to the law of normal distribution;

2) The variances of the two normal sets are equal to each other.

The first hypothesis assumes the type of unknown distribution, and the second – the parameters of two known distributions.

Together with the proposed hypothesis it is required to consider its contradictory hypothesis. if the hypothesis is rejected, then the opposite hypothesis is accepted. Therefore, it is important to be able to distinguish them.

The null hypothesis is called the advanced hypothesis H0.

An alternative hypothesis is called H1, which contradicts H0.

For example, if the null hypothesis is that the mathematical expectation α of the normal distribution is 15, then the alternative hypothesis may state that, $\alpha \neq 15$. In short, it is written as follows: H0: $\alpha = 15$; H1: $\alpha \neq 15$.

The hypothesis may be correct or incorrect, so it is necessary to test it. Because the test is performed by statistical methods, it is called statistical. As a result of statistical verification in two cases the wrong decision can be made, ie mistakes of two kinds can be admitted.

The first kind of error is that the correct hypothesis will be rejected.

The second kind of error is that the wrong hypothesis will be accepted.

The probability of making a mistake of the first kind is usually denoted as α; it is called the level of significance. Most often, the level of significance is taken equal to 0.05 or 0.01. If, for example, the accepted level of significance is 0.05, it means that in five cases out of a hundred we risk making mistakes of the first kind, i.e. rejecting the correct hypothesis.

To test the null hypothesis, a specially selected random variable is used. This variable is denoted by U or Z, if it is distributed normally; F, if distributed according to Fisher's law; T – according to Student's law, $\chi 2$ – according to the law "chi square". In the general case, this variable is denoted by K. A random variable K is called the statistical criterion, which serves to test the null hypothesis. For example, if the hypothesis of equality of variances of two normal general populations is tested, then the criterion K is taken as the ratio of corrected sample variances:

$$F = \frac{s_1^2}{s_2^2}$$

This value is random because, in different studies of variance, will take different, previously unknown values. To test the hypothesis using the sample data, specific values of the parameters in the criterion are calculated, and thus their observed value is obtained.

After selecting a certain criterion, the set of all its possible values is divided into two non-intersecting subsets: one of them has the value of the criterion in which the null hypothesis is rejected, and the other – in which it is accepted. The critical area is called the set of values of the criterion at which the null hypothesis is rejected. The area of acceptance of the hypothesis is called the set of values of the criterion under which the hypothesis is accepted. The basic principle of testing statistical hypotheses can be formulated as follows: if the value of the criterion belongs to the critical area – the hypothesis is rejected, if the value of the criterion belongs to the area of acceptance of the hypothesis – the hypothesis is accepted. Since the criterion K is a one-dimensional random variable, all its possible values belong to a certain interval. Therefore, the critical region and the area of acceptance of the hypothesis are also intervals and as a consequence there are points that separate them. Critical points (boundaries) k_{cr} are points that devides the critical area from the area of acceptance of the hypothesis.

Comparison of two variances

In practice, the problem of comparing two variances arises when you want to compare the accuracy of instruments, tools, measurement methods themselves. Obviously, it is better to use the device or method that will provide the least possible scattering of measurement results, i.e. the lowest variance.

Let the general sets X and Y be distributed normally. From independent samples n_1 and n_2 of these sets corrected sample variances s_X^2 and s_Y^2 were found. It is necessary, at a given level of significance α, to test the null hypothesis, which is that the general variances of the aggregates under consideration are equal to each other:

$$H_0 : D(X) = D(Y)$$

Considering, that the corrected variances are unbiased estimates of the general variances

$$M[s_X^2] = D(X), \qquad M[s_Y^2] = D(Y)$$

the null hypothesis can be written as follows.

$$H_o: M[s_X^2] = M[s_Y^2]$$

Comparison of two average normal general populations, whose variances are unknown and identical.

Let the general sets X and Y be normally distributed, and their variances are unknown. For example, it is not possible to obtain good estimates of general variances from small samples. For this reason, the method of comparing averages cannot be applied.

However, if we additionally assume that the unknown general variances are equal to each other, then we can build a criterion (Student's) for comparison of averages. If there is no reason to believe that the variances are the same, then before comparing the averages, you need to use Fisher's test to pre-test the hypothesis of equality of general variances.

Assuming that the general variances are the same, the null hypothesis should be tested, i.e. the sample averages found in the independent small samples of volumes n and m should be significantly or not significantly different. As a criterion for testing the null hypothesis take a random variable

$$T = \frac{\vec{X} - \vec{Y}}{\sqrt{(n-1)S_x^2 + (m-1)S_y^2}} \sqrt{\frac{nm(n+m-2)}{n+m}}$$

It is proved that the value of T when confirming the null hypothesis has t-Student's distribution with k = n+m-2 degrees of freedom.

Hypothesis about the significance of the sample correlation coefficient

Let the two-dimensional general population (X, Y) be normally distributed. From this set, a sample of volume n was selected and a sampling correlation coefficient r_s was found, which will be nonzero. Since the sample was chosen randomly, it is not yet possible to conclude that the correlation coefficient of the general population r_r is also nonzero.

It is necessary, at a given level of significance α, to test the null hypothesis H0 : r_r= 0 about the equality of zero of the general correlation coefficient, with the competing hypothesis H1 : $r_r \neq 0$.

If the null hypothesis is rejected, it will mean that the sample correlation coefficient is significantly different from zero, and X and Y are correlated, i.e. related by a linear relationship.

If the null hypothesis is accepted, then the sample correlation coefficient is insignificant, and X and Y are not correlated, i.e. not related by a linear relationship.

As a criterion for testing the null hypothesis take a random variable

$$T = r_s \frac{\sqrt{n-2}}{\sqrt{1-r_s^2}}$$

The value of T, if the null hypothesis is valid, has a Student's distribution with $k = n - 2$ degrees of freedom.

Test the hypothesis of the normal distribution of the general population

If the distribution law is not known, but all grounds to assume that it has a certain type (type A), then test the null hypothesis: the general population is distributed according to law A.

Testing the hypothesis of compliance with a law of unknown distribution is carried out in the same way as testing the hypothesis of distribution parameters, i.e. using a specially selected random variable – the criterion of consistency.

The criterion of consistency is the criterion for testing the hypothesis of the proposed law of unknown distribution. There are several consistency criteria: χ2 ("chi square"), Pearson, Kolmogorov, Smirnov and others.

Perform comparisons of empirical (observed) and theoretical (found in the proposed normal distribution) frequencies. Usually empirical and theoretical frequencies differ.

It is possible that the difference in frequencies is random (insignificant) and is due to the small number of observations or the way they are grouped, or other reasons. Perhaps the difference in frequencies is not accidental (significant) and then the null hypothesis must be rejected.

Pearson's criterion answers this question. However, like any other criterion, it does not prove the truth of the hypothesis, but only establishes at the accepted level of significance, its consistency or inconsistency with the observational data.

Suppose that a certain empirical distribution is obtained in the sample of volume n. Suppose that under the assumption of a normal distribution of the general population, the theoretical frequencies n_i are calculated. At the significance level α, you need to test the null hypothesis: the general population is normally distributed. As a criterion for testing the hypothesis, we take a random variable

$$\chi^2 = \sum \frac{(n_i - n_i')^2}{n_i'}$$

This value is random, because in different experiments it takes different previously unknown values. Obviously, the less the empirical and theoretical frequencies differ, the smaller the value of the criterion and, as a consequence, it to some extent characterizes the closeness of the empirical and theoretical distributions. If you square the differences in frequencies, the possibility of mutual repayment of positive and negative differences is eliminated.

It is proved that for $n \to \infty$ the distribution law of a random variable, regardless of the distribution law of the general population, goes to the distribution law $\chi 2$ with k degrees of freedom. Therefore, the random variable is

denoted by $\chi 2$, and the criterion itself is called the criterion of agreement "chi square".

The number of degrees of freedom is found from the equality $k = s - 1 - r$, where s is the number of groups (partial intervals) of the sample; r is the number of distribution parameters proposed, which are estimated from the sample.

Comparison with unknown unequal variances

The problem of comparing the averages of two normally distributed sets with unknown and unequal (according to sample estimates) variances is known as the Behrens – Fisher problem, named after the authors who first formulated it. There is no exact solution to this problem so far. In practice, various approximations are usually used, one of which is a paired t-test for comparing averages.

The criterion value is calculated by the following formula

$$t = \frac{(X_1 - X_2)}{\sqrt{\frac{S_1^2}{N_1} + \frac{S_2^2}{N_2}}}$$

where N_1, and N_2 - the size of the first and second samples; S_1^2 and S_2^2– empirical variances.

Paired t-test for comparing averages

Suppose there are two samples of random variables of the same volume *n*, the values of which are arranged in the order of their observation. It is necessary to test the hypothesis of equality of averages in these samples. In such a formulation, a two-sample problem can be formulated as a single-sample problem if we consider the difference $y_i = x_{n1} - x_{n2}$ of the observed pairs as a random variable.

The statistics of the criterion are similar to the usual Student's statistics

$$t = \frac{\vec{\bar{y}}}{s_y}\sqrt{n},$$

where $\vec{y} = \frac{1}{n}\sum_{i=1}^{n} y_i$; $s_y^2 = \frac{1}{n-1}\sum_{i=1}^{n}(y_i - \vec{y})^2$

Testing the null hypothesis is completely similar to the usual Student's test.

Comparison of two variances. Fisher's criterion

For two samples of normally distributed random variables $x_1 \ldots x_n$ $y_1 \ldots y_m$ it is necessary to test the hypothesis of equality of variances σ_1^2 and σ_2^2, based on their sample estimates s_1^2 and s_2^2.

Fisher's criterion statistics are written as $F = (s_1^2) / (s_2^2)$.

If the null hypothesis H0 : $\sigma_1^2 = \sigma_2^2$ is valid, the criterion statistics has a Fisher distribution with $k_1 = n-1$ and $k_2 = m-1$ degrees of rim, where n and m are the volume of samples to be compared.

Nonparametric criteria for statistical homogeneity

In cases where assumptions about the hypothetical probability distribution law do not seem convincing, other methods should be used to compare random variables and test hypotheses about their significance.

Any distribution can be described by a position parameter characterizing the grouping center of some random variables and a scale parameter characterizing the degree of scattering of random variables relative to the grouping center (for example, in the case of a normal distribution they are mean μ and standard deviation σ, respectively). When the distribution law is unknown, hypotheses about position and scale parameters are tested using special offset and scale criteria.

If $f_1(x)$ and $f_2(x)$ are unknown probability densities, then the displacement hypothesis is written as: H0: $f_1(x) = f_2(x)$ against the alternative

H1: $f_1(x) = f_2(x - \Delta)$, or H0: Δ = 0 against the alternative H1: Δ ≠ 0, where Δ is the shift determined by the difference of the distribution position parameters.

Hypotheses about the difference in variances are formed as hypotheses about scale parameters. For example, if $f_1(x) = \frac{1}{\tau} f\left(\frac{x-\mu}{\tau}\right)$ and $f_2(x) = f(x - \mu)$, then the hypothesis about the scale parameter is written as H0: τ = 1 against the alternative H1: τ ≠ 1.

The advantage of non-parametric (free from distribution) methods of testing statistical hypotheses is their calculated simplicity. However, the power of statistical criteria based on them is inferior to similar parametric criteria (eg, Student's, Fisher's, etc.).

Rank criteria for displacement

Rank criteria are based on a sequence of ranks of sample values of random variables. In this case, we do not consider the sample values themselves, but their ranks, which are determined by the ordinal number of the sample element in the general order, in ascending order. For example, in an ordered sample $x_1 \le x_2 \le \cdots \le x_n$, the sample value x_i is replaced by the rank $R = i$.

Mann–Whitney–Wilcoxon test

Let $x_1 \ldots x_n$ and $y_1 \ldots y_m$ be ordered in ascending order of the sample. To test the bias hypothesis, Mann and Whitney proposed a ranking criterion based on statistics.

$$U = \sum_{i=1}^{n} \sum_{j=1}^{m} h_{ij}, \qquad \text{where } h_{ij} = \begin{cases} 1, x_i < y_j; \\ 0, x_i > y_j; \end{cases}$$

Here U is the exact number of pairs of values x_i and y_j for which $x_i < y_j$

If $U_1(\alpha) \le U \le U_2(\alpha)$, the displacement hypothesis is rejected.

The Mann-Whitney U-statistic is related to Wilkson's statistics, which are determined by the sum of the ranks of the elements of one sample in the general ordered sequence of elements of the joint sample of volume $(n + m)$:

$$R = mn + \frac{n(n+1)}{2} - U.$$

When n, m> 20 apply the approximation

$$W = \frac{R - \frac{n(n+m+1)}{2}}{\sqrt{\frac{nm(n+m+1)}{12}}}$$

The statistic W is approximated by the normal distribution, and the bias hypothesis is rejected with confidence α if $|W| > u_{\frac{1+\alpha}{2}}$.

If there are matching values in the two samples being compared, it is recommended that they be assigned average ranks (arithmetic mean for each series of consecutive ranks). Thus in a denominator of statistics use value

$$\left\{\frac{nm(n+m+1)}{12}\left[1 - \frac{\sum_{i=1}^{k} t_i\,(t_i^2 - 1)}{(m+n)(m+n-1)(m+n+1)}\right]\right\}^{1/2}$$

where *k* is the total number of groups of matching quantities; t_i - the number of matching values in the *i*-th group.

Conclusions to the section 1

Statistical method of information analysis is one of the main means of obtaining scientifically reliable data in evidence-based medicine is. But there are difficulties associated with the insufficient level of mathematical training of medical specialists. This is due to the complexity of statistical analysis mathematical apparatus, primarily the criteria and limits of possible use of statistical tools.

The list of methods of statistical analysis, that researcher should know, demonstrates the complexity of mathematical tools and is the basis for formulating the tasks of the thesis.

SECTION 2
TREE-LIKE ARCHITECTURE OF SOFTWARE SYSTEM

2.1 The proposed algorithm for solving the problem

The Table 1.1 and the following material shows how many factors a researcher must consider to make a statistically significant conclusion. This requires a fairly deep knowledge of mathematical principles, which is not always present in medical professionals.

Therefore, despite the existence of a number of computer software packages that facilitate the use of statistical methods of information processing, the problem remains, because for the correct use of specific tools from these packages, professionals still need to know and check the necessary conditions.

The aim of the work was to create a software system that implements the most commonly used tools of statistical analysis, but at the same time provides verification of the necessary criteria and the limits of their use in automatic mode. Thus, the user is not required to know the appropriate mathematical apparatus, the system will automatically select the optimal statistical methods and draw conclusions according to specific conditions, significantly reducing the likelihood of errors.

To solve this problem, it is proposed to construct a tree-like structure of subroutines representing specific statistical methods, and in the nodes of this tree there are decision-making tools – branches based on the analysis of the conditions of their applicability (Figure 2.1).

The input of the system is two arrays of values, which are two samples of random variables. The result of the system operation will be an assertion about a statistically significant difference in the mean values of random variables in these samples or the absence of such a difference. For example, this may be evidence of the effect of a drug on the patient's blood pressure. Moreover, the samples can be either two groups of patients (experimental – under the influence of the drug

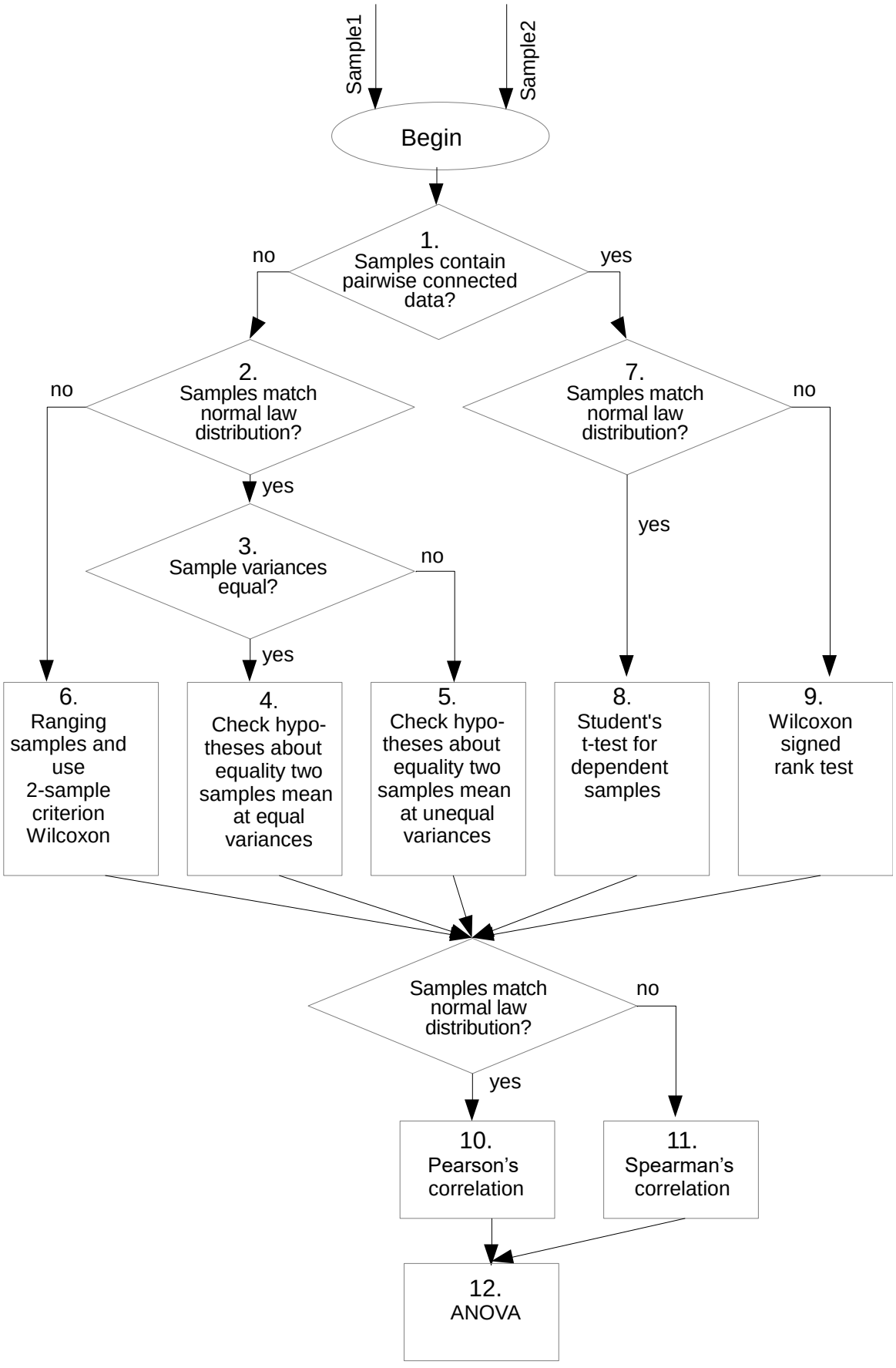

Figure 2.1– Tree-like structure of subroutines representing specific statistical methods

and control – without it), or one group (before and after exposure to the drug). The second case is called linked samples or samples, which are naturally divided into pairs, and the statistical criteria in this case are also different [60–62]. The applied statistical methods also differ for the cases of the normal distribution law of random variables and the distribution law other than normal; for samples with the same and different variances. In the case of a distribution law other than normal, a special statistical method is used, when the values of not the random variable itself are analyzed, but its ranks.

Such a variety of possible situations and the statistical methods and criteria used in this case required the creation of a software system in the form of a tree structure with nodes for making decisions on the ways of further program execution.

In each node of such a structure, the user receives information about the results of checking the parameters of the applicability conditions of specific methods with appropriate branching recommendations. In parallel, along the route, information is available about the equality or difference of variances, about the variety of the distribution law, etc.

The aforementioned decision tree, algorithm and program code can be conditionally divided into 12 main modules, which semi-automatically switch during program operation based on the corresponding decisions in the tree nodes.

The sequence of execution of system modules is as follows (Figure 2.1):

- in module 1 branching occurs into module 2 or module 7, depending on whether the samples presented in the arrays are independent or interconnected; it is implied that either influence of the factor is studied on the experimental and control group, or on one group – before and after influence of the factor;

- in module 2 the normality of the law of data distribution in arrays is checked; if both samples are distributed according to the normal law, then transition occurs to module 3, otherwise – to module 6;

- the module 3 checks uniformity of variances of the input samples by Fisher's test; depending on the result, it is further proposed to branch to module 4

(testing the hypothesis of equality of mean values of two samples by Student's t-test for equal variances) or to module 5 (testing the hypothesis of equality of average values of two samples by Student's t-test for different variances);

- in module 6 the test of hypothesis about the equality of average values of two samples with a distribution law other than normal is implemented by ranking the data and applying the two-sample Wilcoxon test;

- in module 7 the form of distribution law of both input arrays is checked (for the case of connected samples) – is the distribution normal or not. Depending on the result, it is proposed to move to module 8 (testing the hypothesis of equality of mean values of two related samples by Student's t-test) or to module 9 (application of non-parametric sign criterion);

- in module 10, the existence of a parametric correlation between input arrays is checked, if the distribution law is normal, and the Pearson’s correlation coefficient is calculated;

- in module 11, the existence of a rank correlation between input arrays is checked if the distribution law is different from normal, and the Spearman’s rank correlation coefficient is calculated;

- in module 12 the one-factor analysis of variance (ANOVA) of input arrays is implemented in order to detect the influence of the factor, that is to identify a statistically significant difference between average values of the samples by means of analysis of variance.

It should be noted that at each node of the tree structure, the conditions for applicability of statistical methods are checked before transition to the corresponding module occurs. And in each module, the statistical accuracy of the conclusion is checked.

For example, in correlation analysis, not only the correlation coefficient is calculated, but also the statistical accuracy of such a correlation is determined.

2.2 Software development environment

NI LabVIEW was chosen as the software development environment, which is currently an informal standard in the field of biomedical instrumentation and biomedical research and is easily integrated into most modern software and hardware systems [57– 59].

NI LabVIEW (National Instrument Laboratory Virtual Instrument Engineering Workbench) is very convenient for applications that are created and used not by programmers but by engineering professionals, including biomedical engineers. Instead of text programming languages with complex syntactic rules, the graphic language G is used here, which has a more familiar to engineers type of block diagrams.

Additional advantages of the workbench are the presence of a large number of built-in functions and routines, a wealth of developed and visual elements for building interfaces, the ability to interact with other environments.

The convenience of combining with hardware for entering information provides opportunities to create automated workstations for statistical processing, and ease of programming – the ability to improve, configure and adapt the software system to specific situations.

Conclusions to the section 2

It is proposed software system that implements the most commonly used tools of statistical analysis, but at the same time provides verification of the necessary criteria and the limits of their use in automatic mode. Thus, the user is not required to know the appropriate mathematical apparatus, the system will automatically select the optimal statistical methods and draw conclusions according to specific conditions, significantly reducing the likelihood of errors.

The advantages of using the software environment NI LabVIEW are substantiated. A logical diagram of the system operation algorithm has been built with a demonstration of the execution sequence. It is shown how the reliability of statistical inferences is provided in an automatic mode by sequentially checking the conditions of applicability of each method in the tree structure of the algorithm.

SECTION 3
MATERIALS AND METHODS

3.1 System interface and principles of using the system

The appearance of the system interface is shown in Figure 3.1.

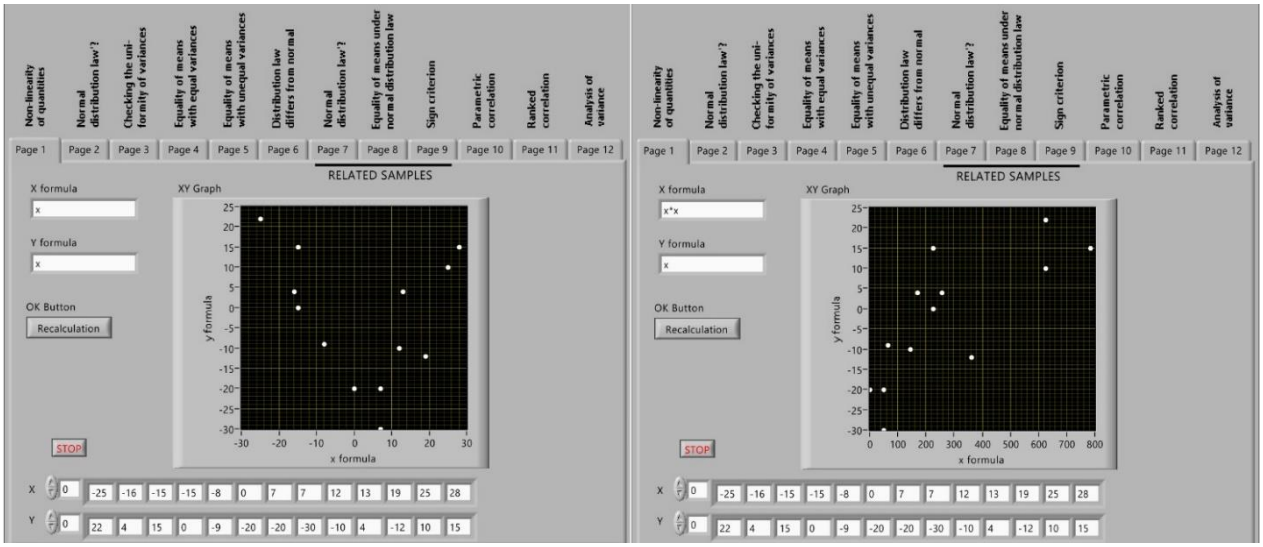

Figure 3.1– View of the software system interface with direct display of input data sets and with the results of the previous functional transformation

Here at the top there are 12 pages of the interface (bookmarks), which correspond to execution of the above modules and are sequentially opened during execution of the algorithm. At the bottom – the input data arrays, given for illustration and settings, and in real circumstances can be entered automatically from various devices or software.

Two options for displaying input data on the left and right screens demonstrate a specially designed ability of the system to analyze either the input data arrays directly, or the results of their preliminary conversion by almost any function that can be simply entered in the interface window. In the example shown in Figure 3.1 on the first screen you can see signs that between the input data arrays there is a relationship similar to quadratic law, so on the second screen instead of the data of one of the arrays enter their squares, then see the trend of linearity of such data connection law. It is possible to select functions of

preliminary transformation of input data either on a kind of curves on the screen, or proceeding from physical essence of the investigated phenomena.

The result of each module is either a branch demonstration with an explanation of reasons for a particular transition, or a statistical conclusion of an algorithm. Thus, after selecting the functions of homomorphic transformation in the first module, a branching take place due to the choice of the option regarding the independence of samples or their connection. Next, the normality of the distribution law of both samples is checked, then the equality of variances; each combination of features uses its own statistical tool. Checks in the modules are performed automatically using the appropriate statistical criteria.

The first tab (Figure 3.2) contains a window for entering data arrays, a formula window for each axis (for the ability to visualize not only linear dependencies), a window for visualizing data arrays, a button to recalculate and a button "Stop" to end the program.

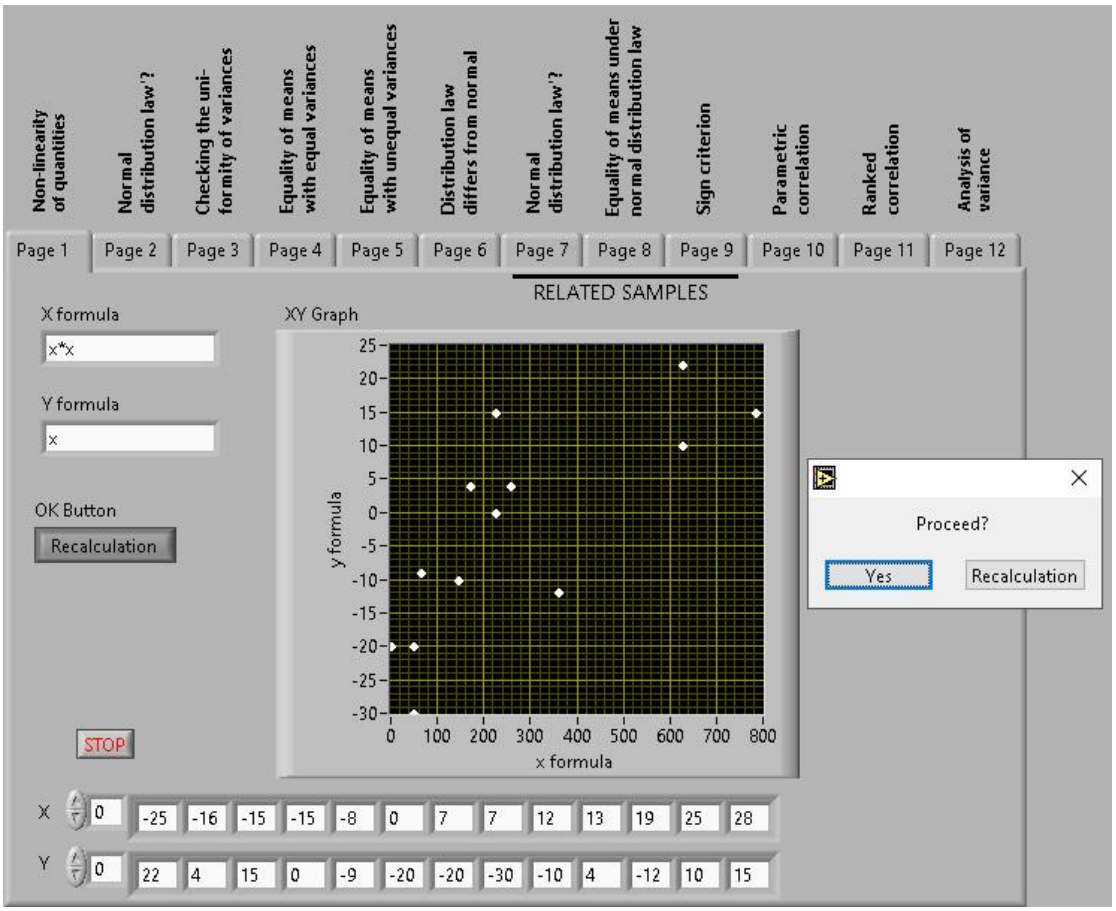

Figure 3.2 – The first tab of the interface

Further a dialog window appears, in which you need to specify whether the samples are related (linked samples) (Figure 3.3).

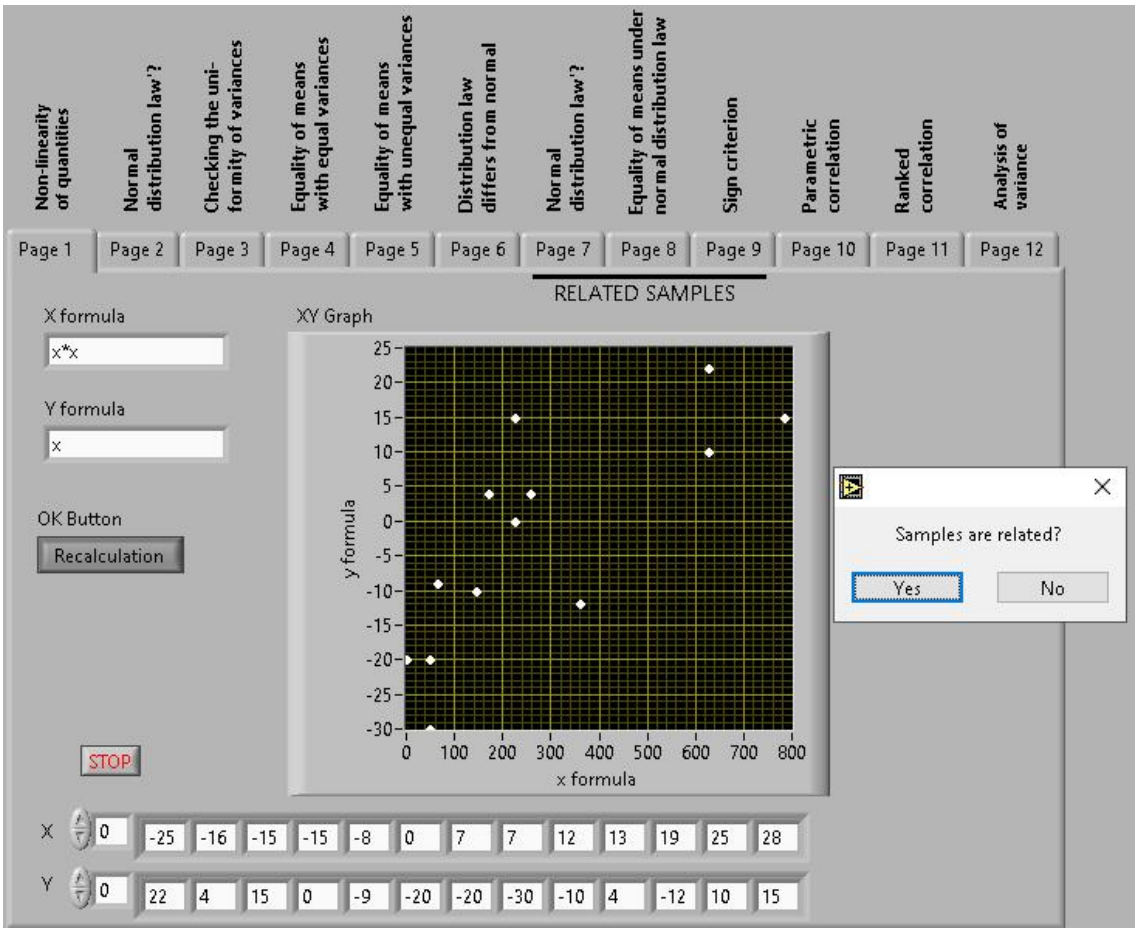

Figure 3.3 – Window for select whether the samples are related

The second tab (Figure 3.4) shows the results of the normality check for unrelated samples (for related samples implemented in another tab module). Separate windows with conclusions for the first and second arrays. Additionally, a dialog box appears with a message about the results of the general inspection and a further recommendation to which pages it is suggested to switch for further operation of the program, it is tab 3 or tab 6, depending on the previous conclusion.

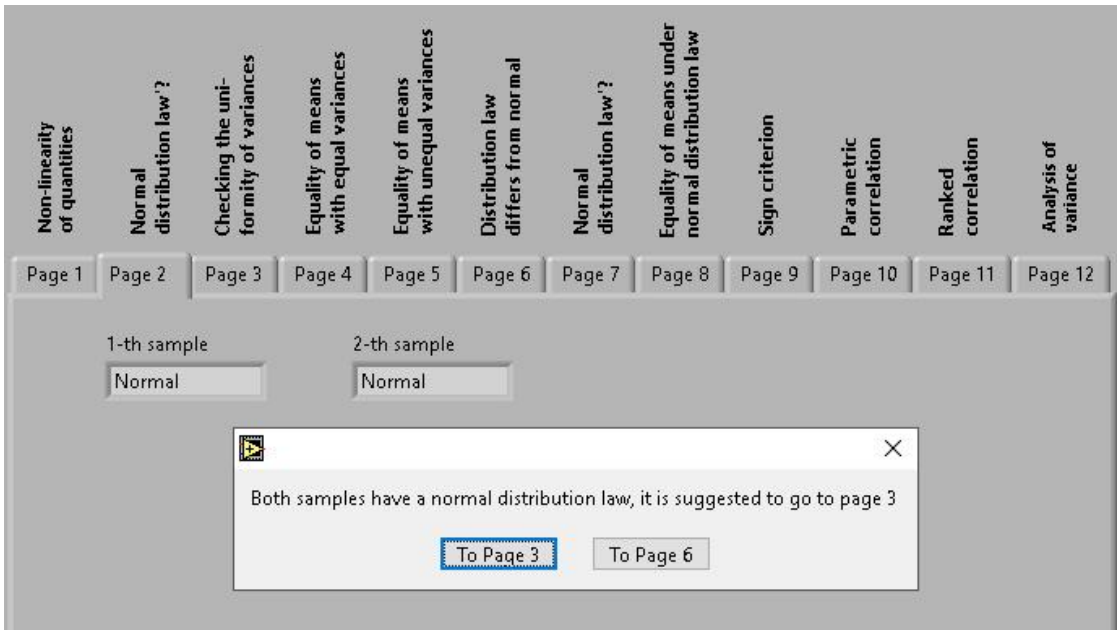

Figure 3.4 – The second tab of the interface

The third tab (Figure 3.5) shows the results of the check for equality of variances. A dialog box appears with the result for variances and a suggestion to switch to tab 5.

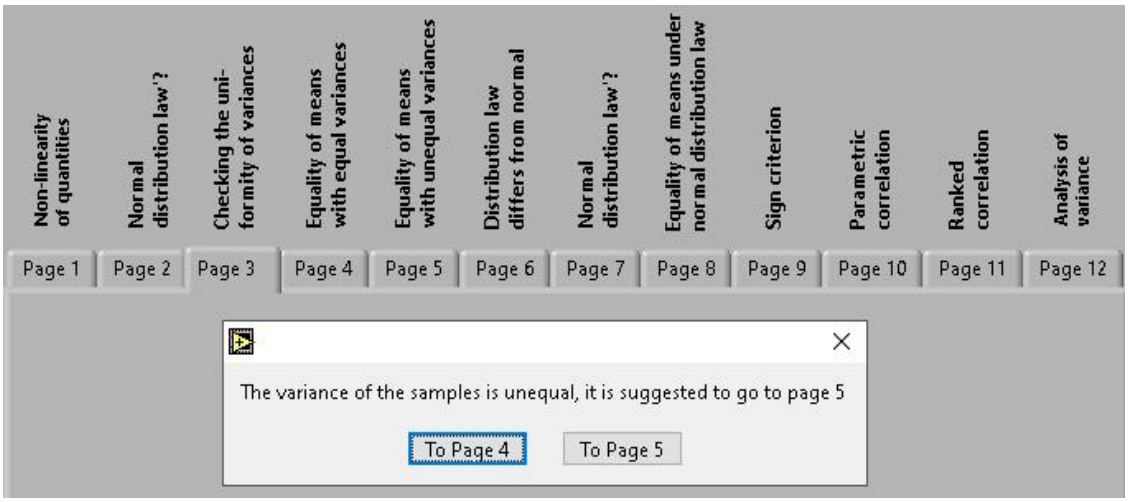

Figure 3.5 – The third interface tab

The fifth tab (Figure 3.6) displays the conclusions of the analysis of hypotheses about the equality of the averages and proposes to continue the analysis by considering the correlation of random variables or return to the first tab to analyze the next problem. The fourth tab is for the same, but with equal variances.

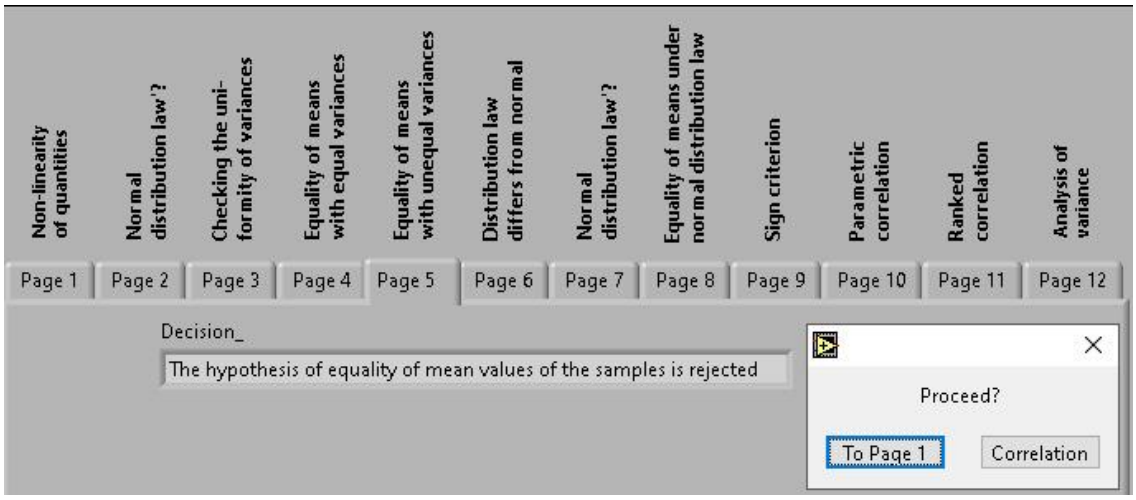

Figure 3.6 – The fifth interface tab

The sixth tab checks if the distribution in the sample is different from normal. In the window box hypothesis of equality of the average values of the samples is accepted or rejected.

The seventh tab checks the normality of the distribution for related samples. A separate window appears with conclusions for the first and second arrays (as well as in the second tab).

The eighth tab tests the hypothesis of the equality of the averages at the equal variances for the related samples.

The ninth module draws a conclusion on acceptance or rejection of the hypothesis on equality of the average values of the samples, based on the criterion of signs.

The tenth module is designed for parametric correlation. The values of the correlation coefficient, the confidence interval and the conclusions of the hypothesis of no correlation are drawn (Figure 3.7).

When the algorithm is finished, a dialog box appears for returning to the first module or Analysis of variance.

The eleventh module displays information about rank correlation: correlation value and confidence intervals for input arrays.

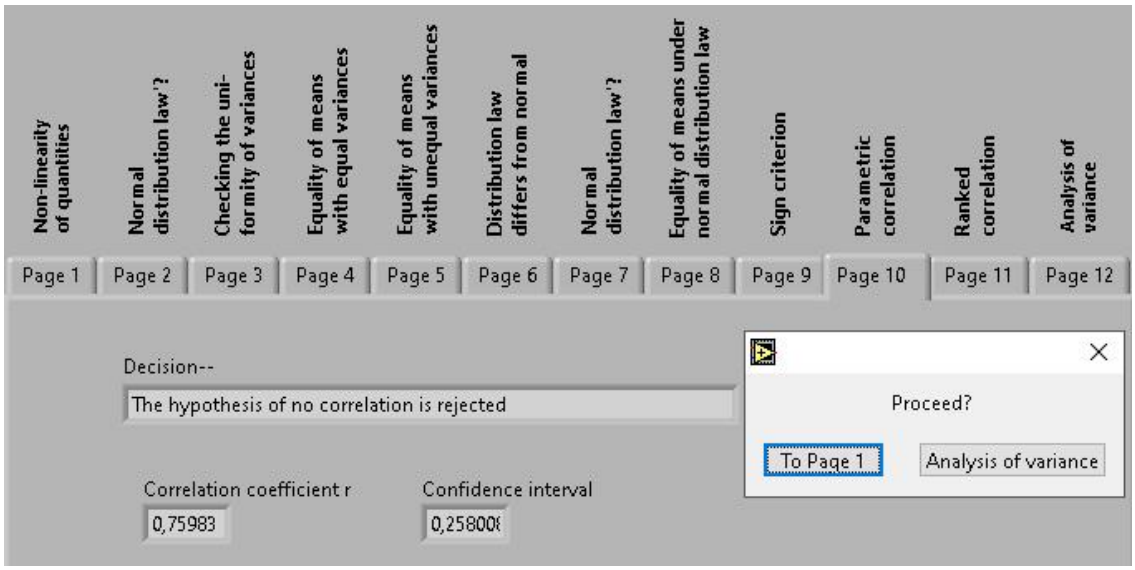

Figure 3.7 – The tenth interface tab, abour correlation

An example of display in the interface of one of the statistical conclusions (analysis of variance) is shown in Figure 3.8.

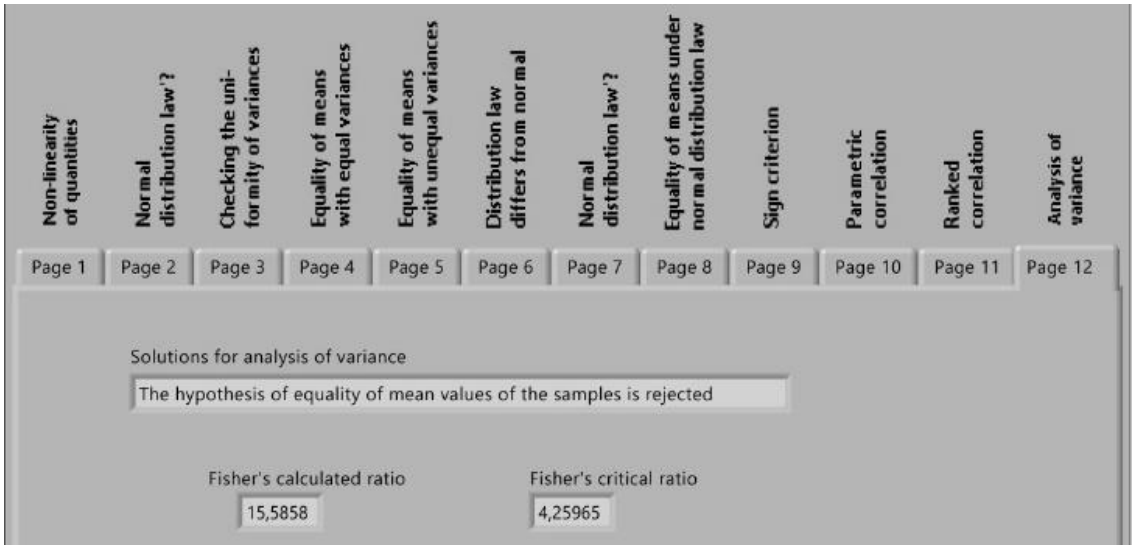

Figure 3.8 – The 12-th interface tab, statistical conclusion of analysis of variance

Here in the text line it is stated that “The hypothesis of equality of mean values of the samples is rejected”, and in the numerical indicators the values of Fisher's calculated ratio and Fisher's critical ratio are given, on which basis this statistical conclusion is made.

3.2 Implementation of algorithm modules

The program has a tree structure. Block diagram of the program is shown in Figure 2.1.

The program has 12 separate modules, and some of them have additional sub-modules to simplify working with the main program code.

The first module reads the input data, visualizes the samples using built-in routines, launches a dialog box to determine whether the samples are linked with the subsequent transition to page two or seven, respectively (Figure 3.9).

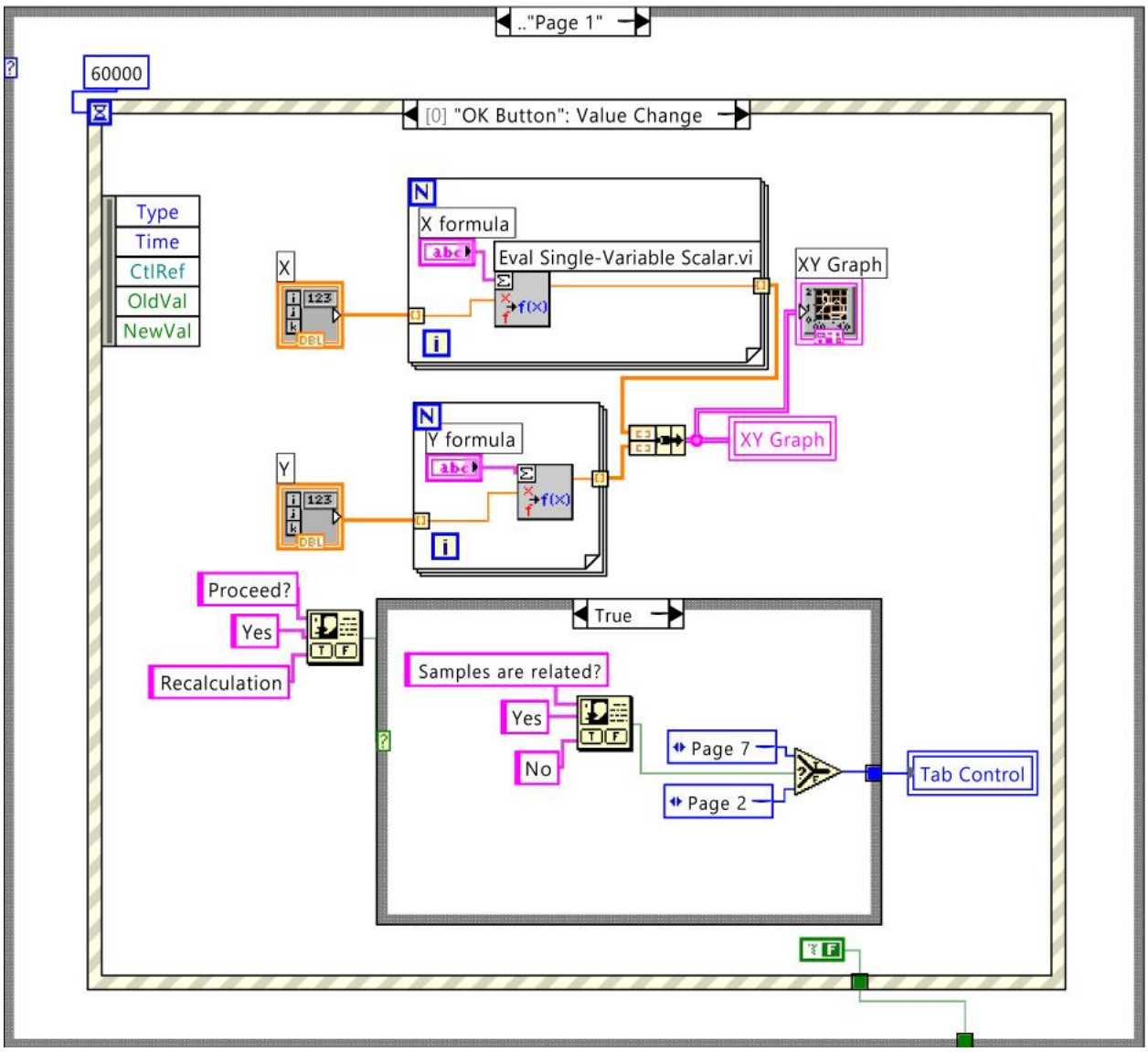

Figure 3.9 – Block diagram of the first module

The second module checks the type of distribution of the two input arrays – is the distribution normal or different from it (Figure 3.10). The module also additionally uses the developed sub-device “norm distr” (Fig. 3.11). The conditions and formulas described in section 1, formulas 1.1 and 1.2 are used.

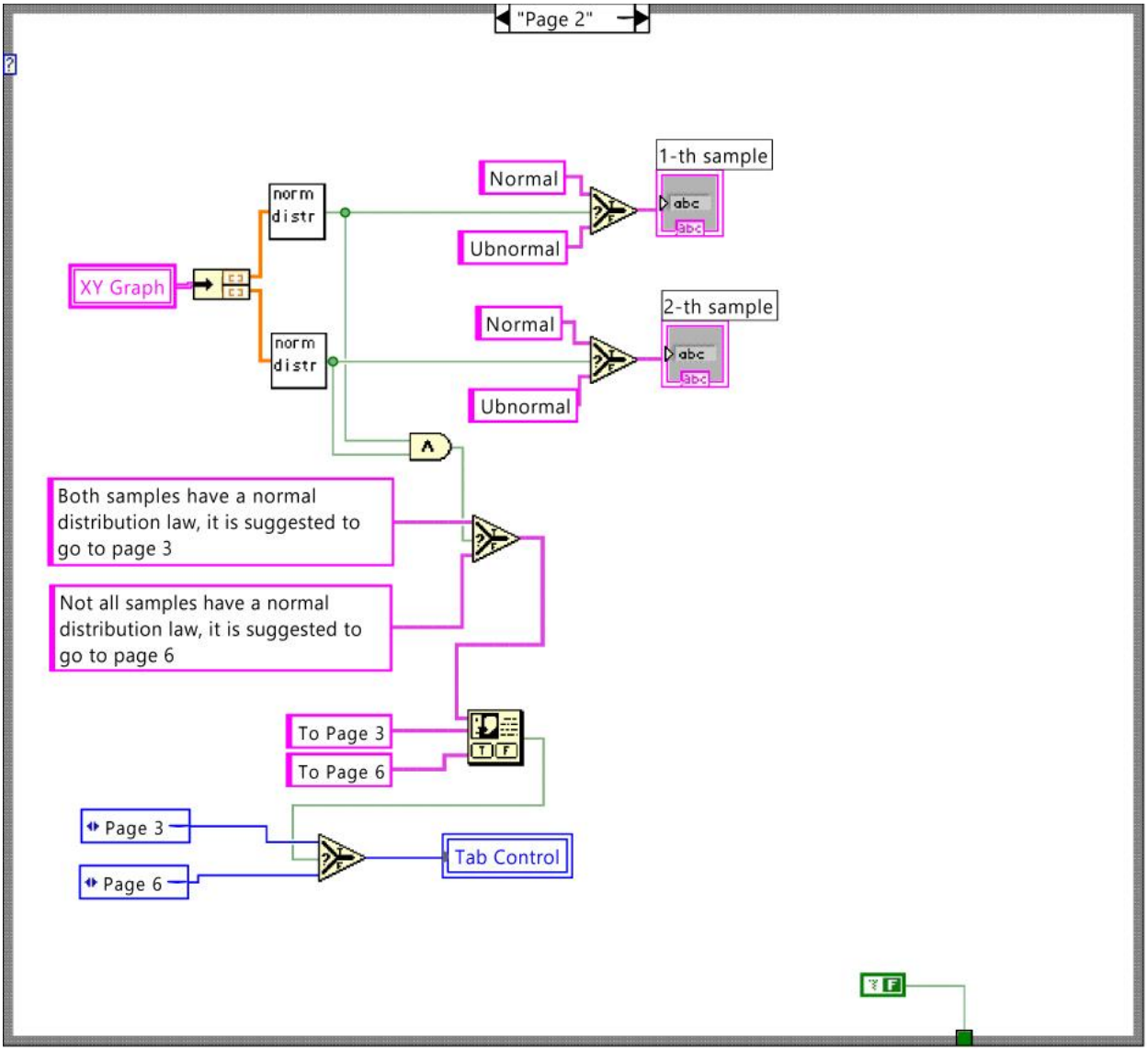

Figure 3.10 – Block diagram of the second module

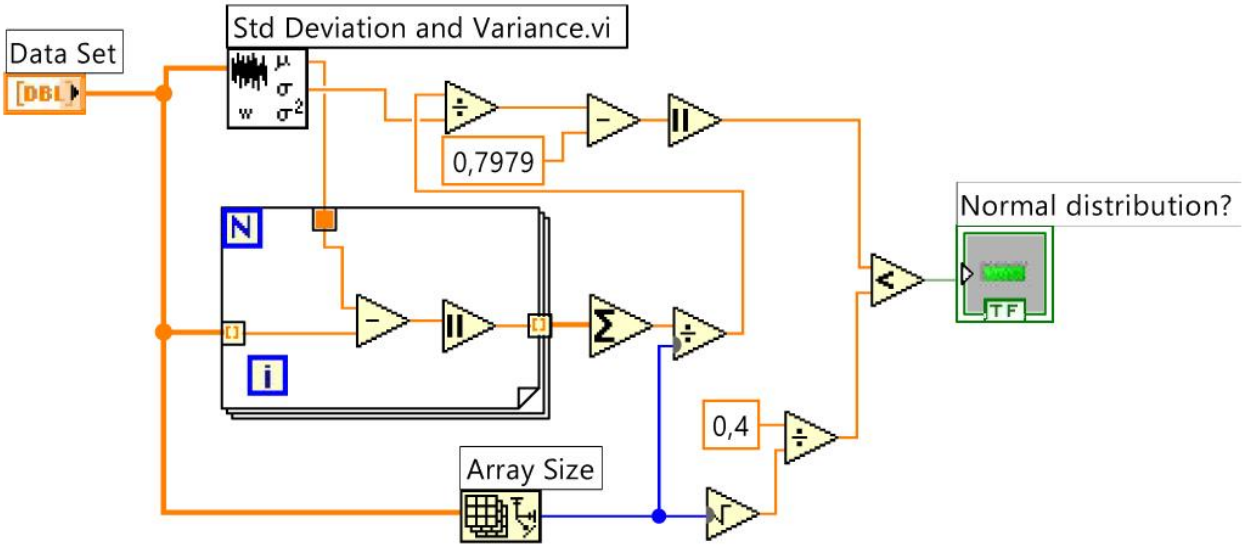

Figure 3.11 – Block diagram of the subdevice "norm distr"

The third module implements the verification of the uniformity of the variances of the input samples (Figure 3.13). The developed “Fisher” sub-device is used (Figure 3.12). Depending on the result of the test, it is suggested to switch to the fourth or fifth tab.

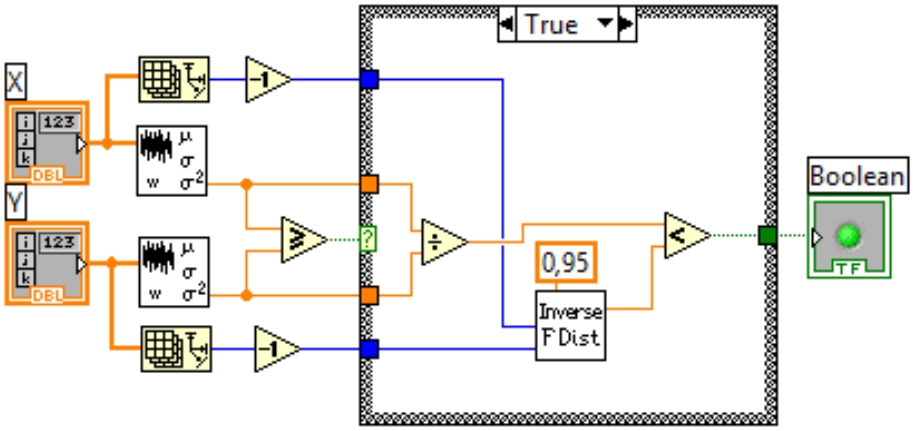

Figure 3.12 – Block diagram for the sub-device "Fisher"

The sub-device is created in accordance with the formulas of section 1.3 “Comparison of two variances. Fisher's criterion”. The structure of the Case is used to always have a ratio of greater dispersion to less, the degree of freedom of the elements is reduced by one position the number of elements of the array.

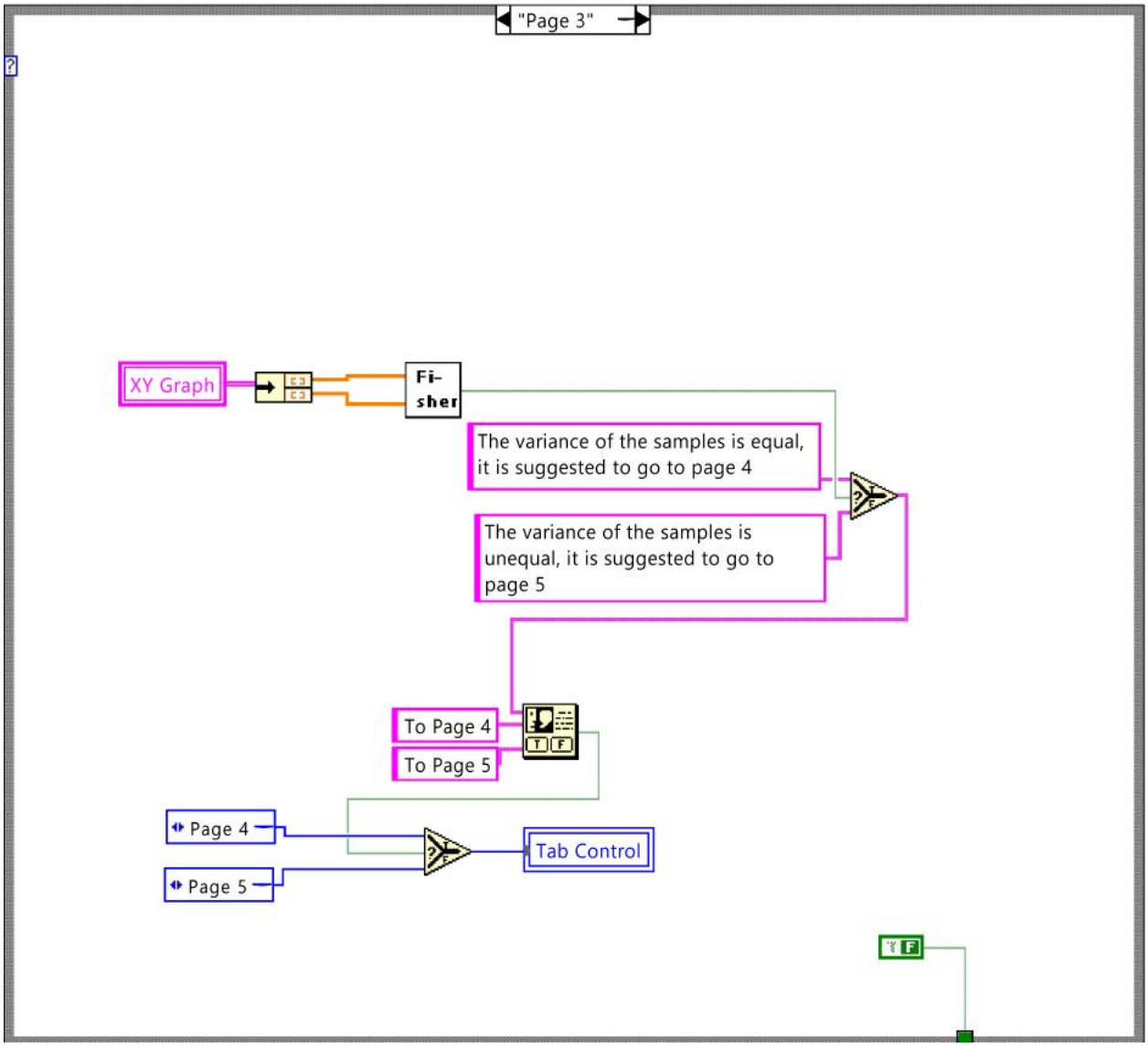

Figure 3.13 – Block diagram of the third module

The fourth module tests the hypothesis of equality of the average values of two samples with equal variances (Figure 3.14).

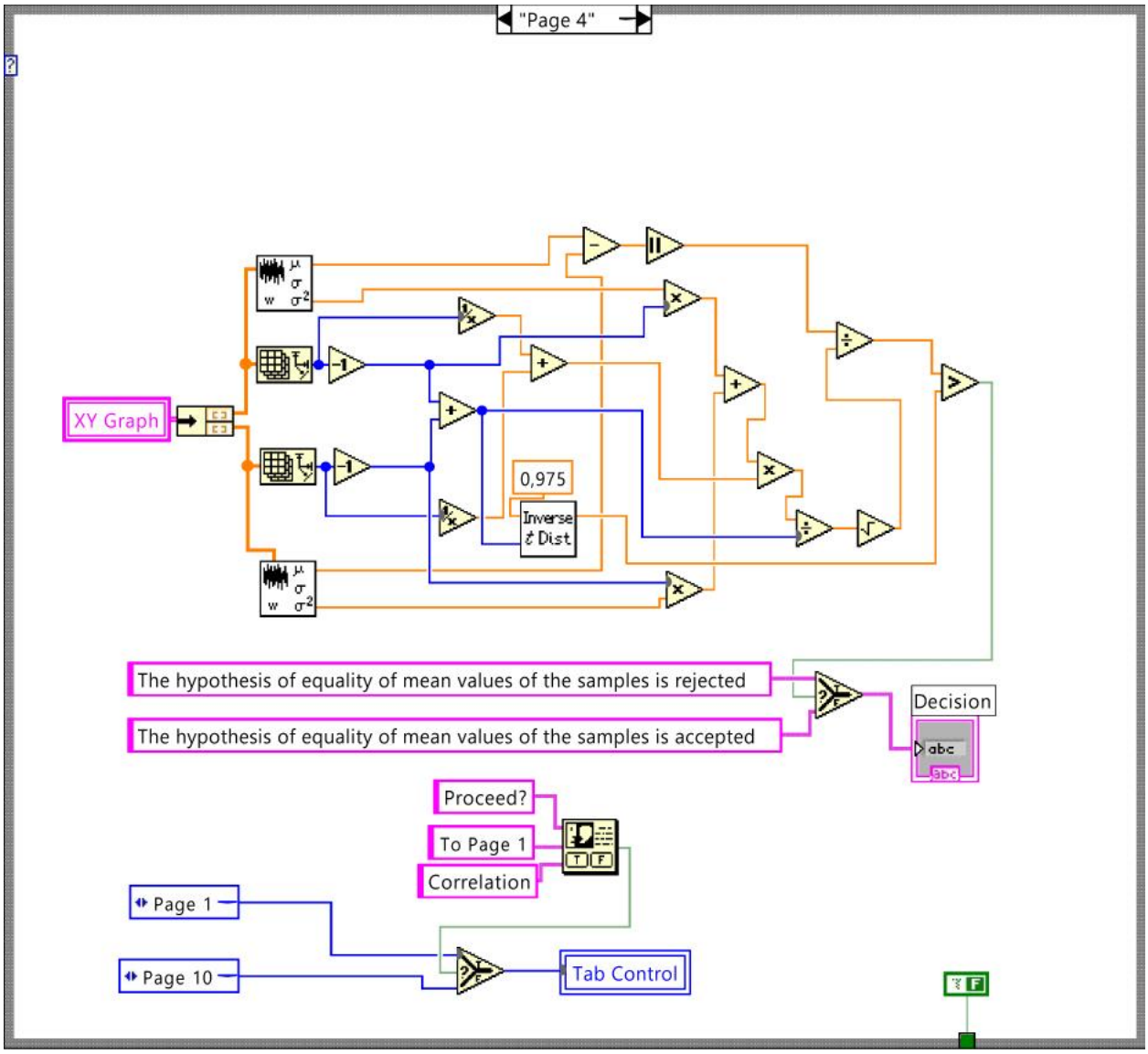

Figure 3.14 – Block diagram of the fourth module

At the end of the program, the ability to go to the first page or to the correlation analysis tab is implemented.

The fifth module (Figure 3.15) tests the hypothesis of equality of the mean values of two samples with different variances and open a dialog box for further work.

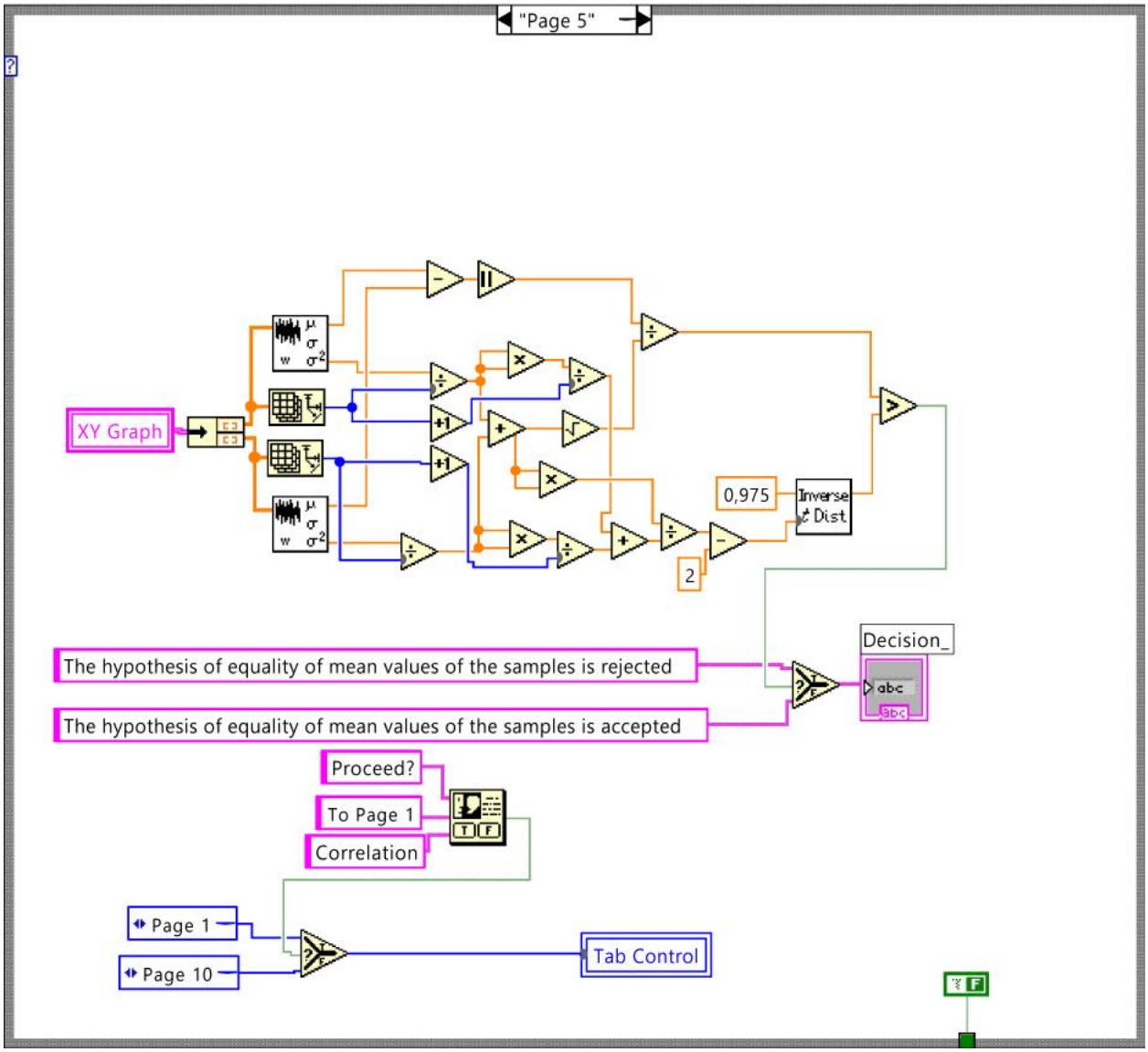

Figure 3.15 – Block diagram of the fifth module

In the sixth module (Figure 3.16) a check is performed for the equality of the average values of the two samples with an abnormal distribution due to the ranking and use of the two-sample Wilcoxon test. Two additional sub-devices "W" (Figure 3.17) and "Rank 2 arr" (Figure 3.18) are built into the module.

In the substructure "Rank 2 arr" (Figure 3.18) the algorithm of ranking of two arrays is executed. First, look for "bundles", i.e. check each cluster with each in the 1st line. Then count how many times each value occurs; for each case of similarity of values we sum in one shift register number of coincidences, and in the second – the sum of indices from the second line of a cluster, then we divide value of the second shift register by value of the first, thus we calculate average ranks of

" bundles ", i.e. average value of those ranks, which they would have if they were different in meaning. The calculated values of the ranks are written in the second line of the cluster. We move the third line of the cluster (where the order of the input array is preserved) to the first place, because the clusters are sorted by the first line. We sort the array of clusters in the order of the input array, and then select the second line, which contains the calculated data in the desired order.

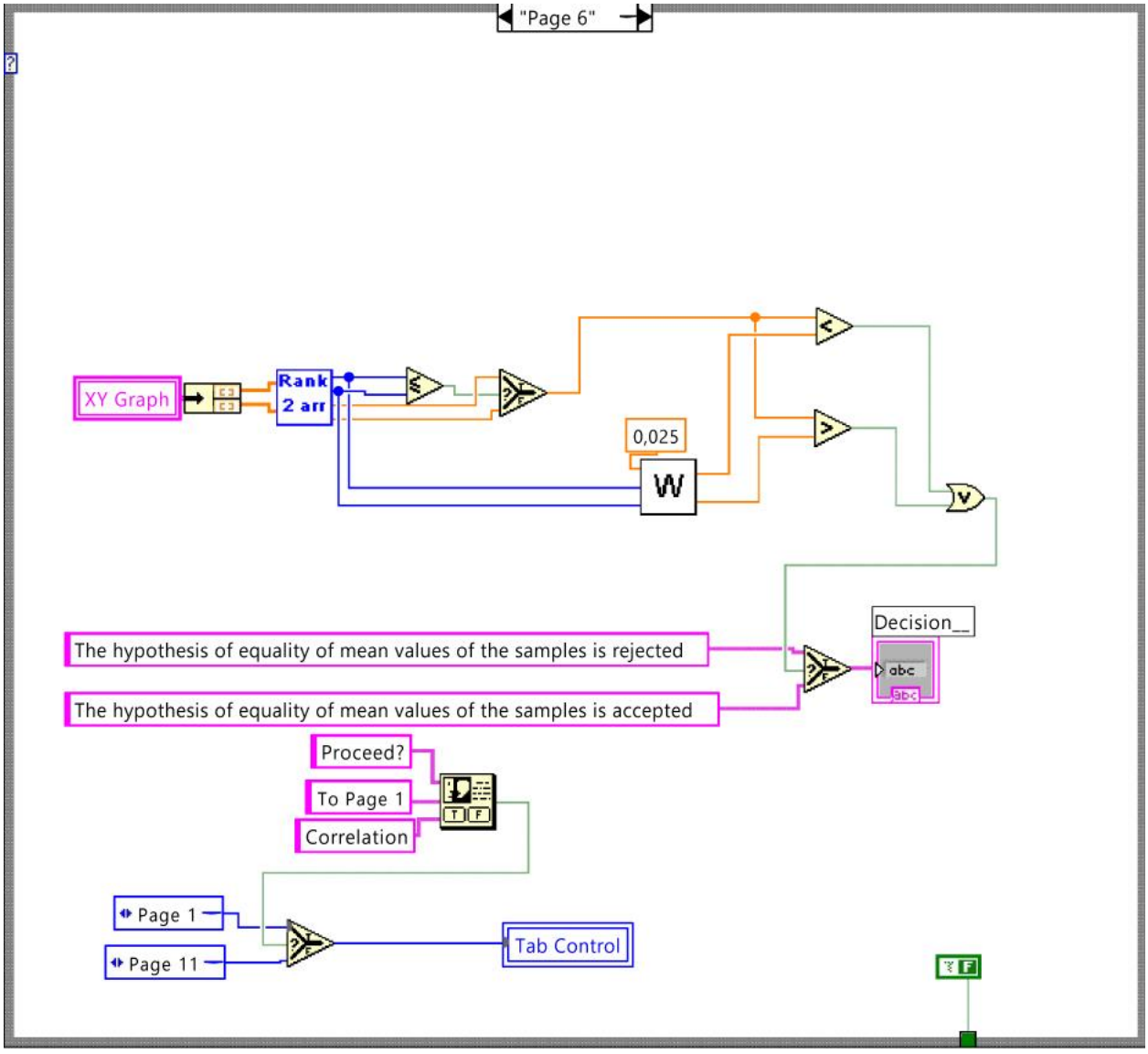

Figure 3.16 – Block diagram of the sixth module

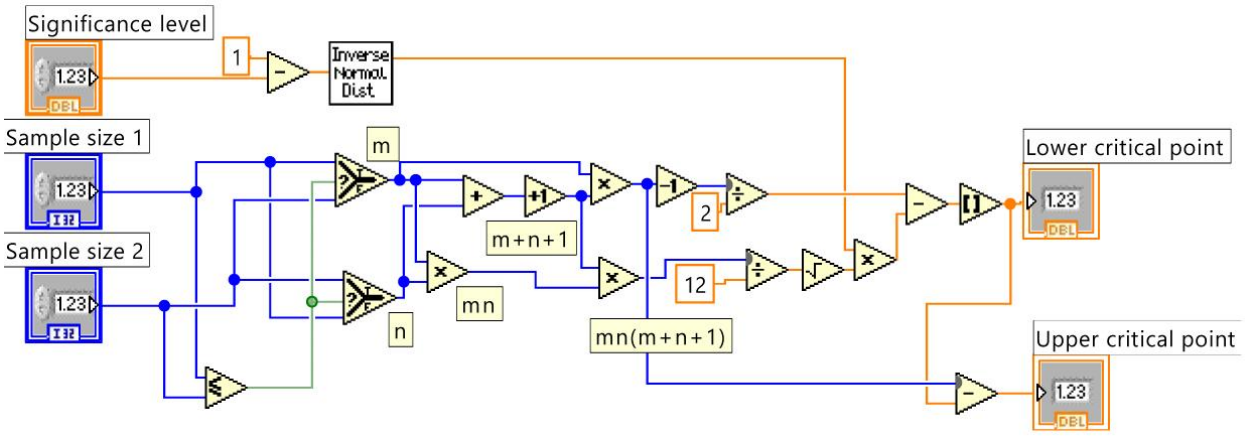

Figure 3.17 – Block diagram for the sub-device "W"

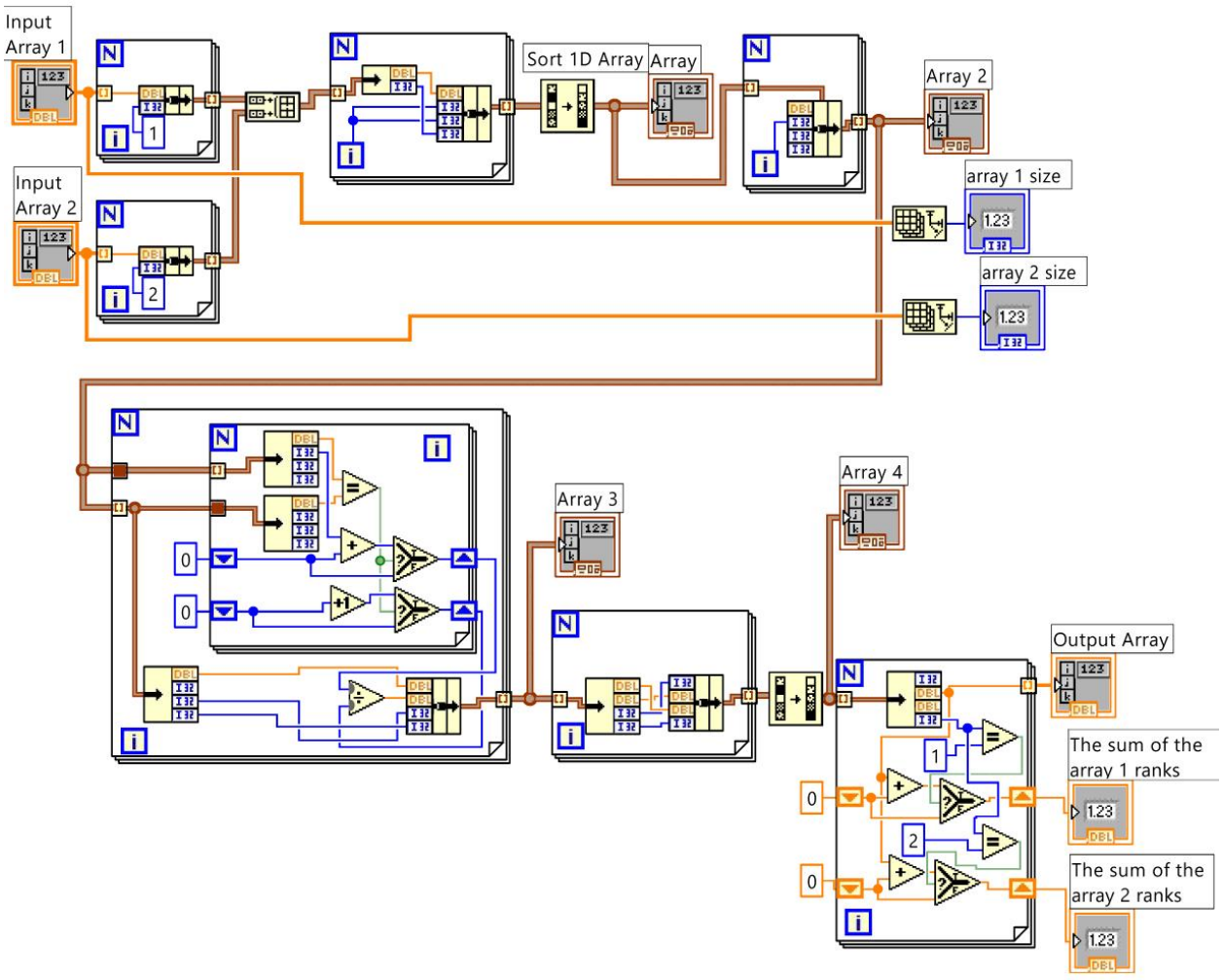

Figure 3.18 – Block diagram for the sub-device "Rank 2 arr"

In the seventh module (Figure 3.19) the normality check for connected input data arrays is performed. It also, like the fourth module, uses the sub-device "normdistr" to check the normality of the distribution, but after hanging on the page, depending on the result, the transition to the eighth, if both samples have a normal distribution, or to the ninth page, if one of the sample has abnormal distribution.

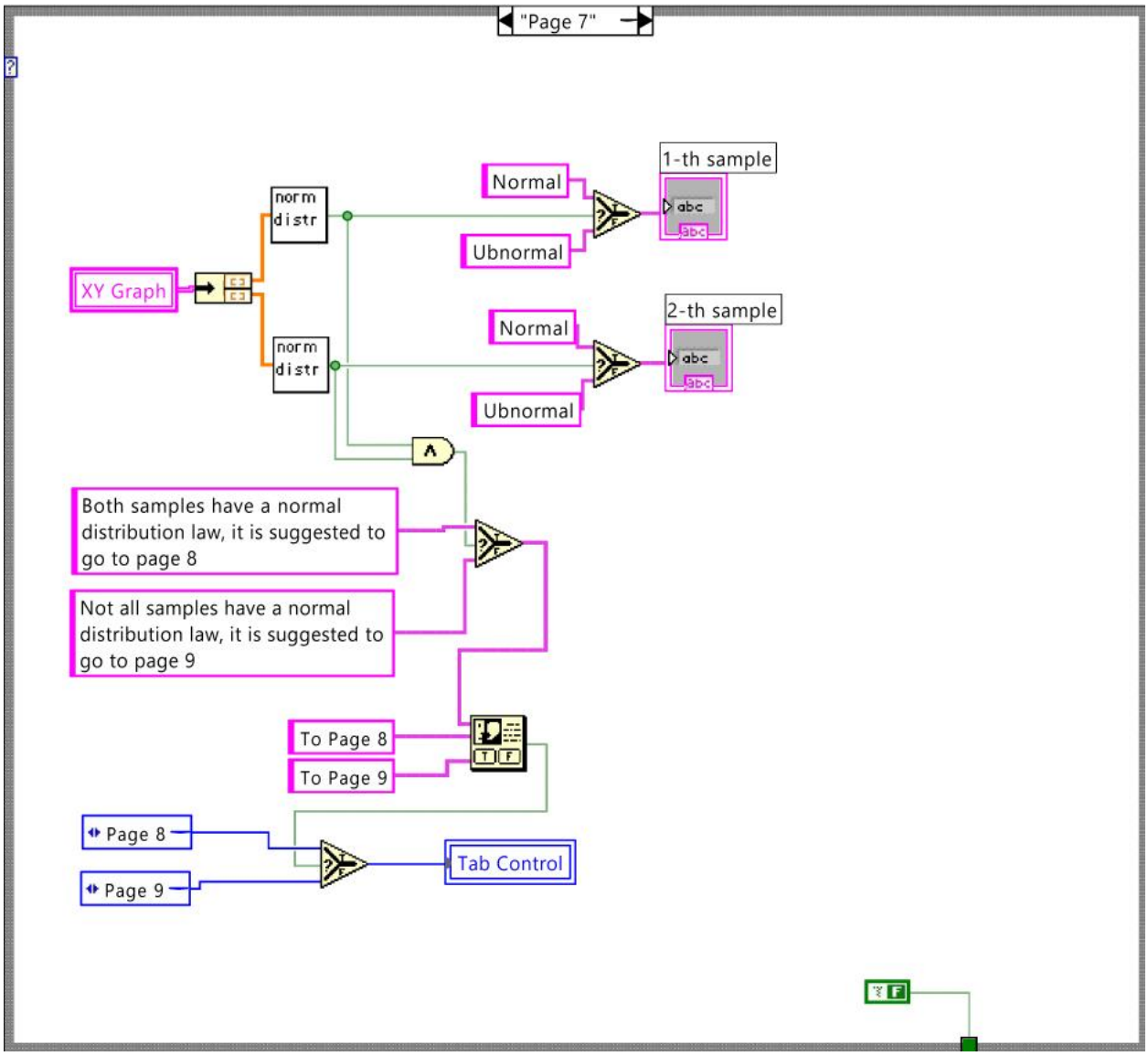

Figure 3.19 – Block diagram of the seventh module

In the eighth module (Figure 3.20) the hypotheses about the equality of the averages in the case of related samples with the normal distribution law are tested.

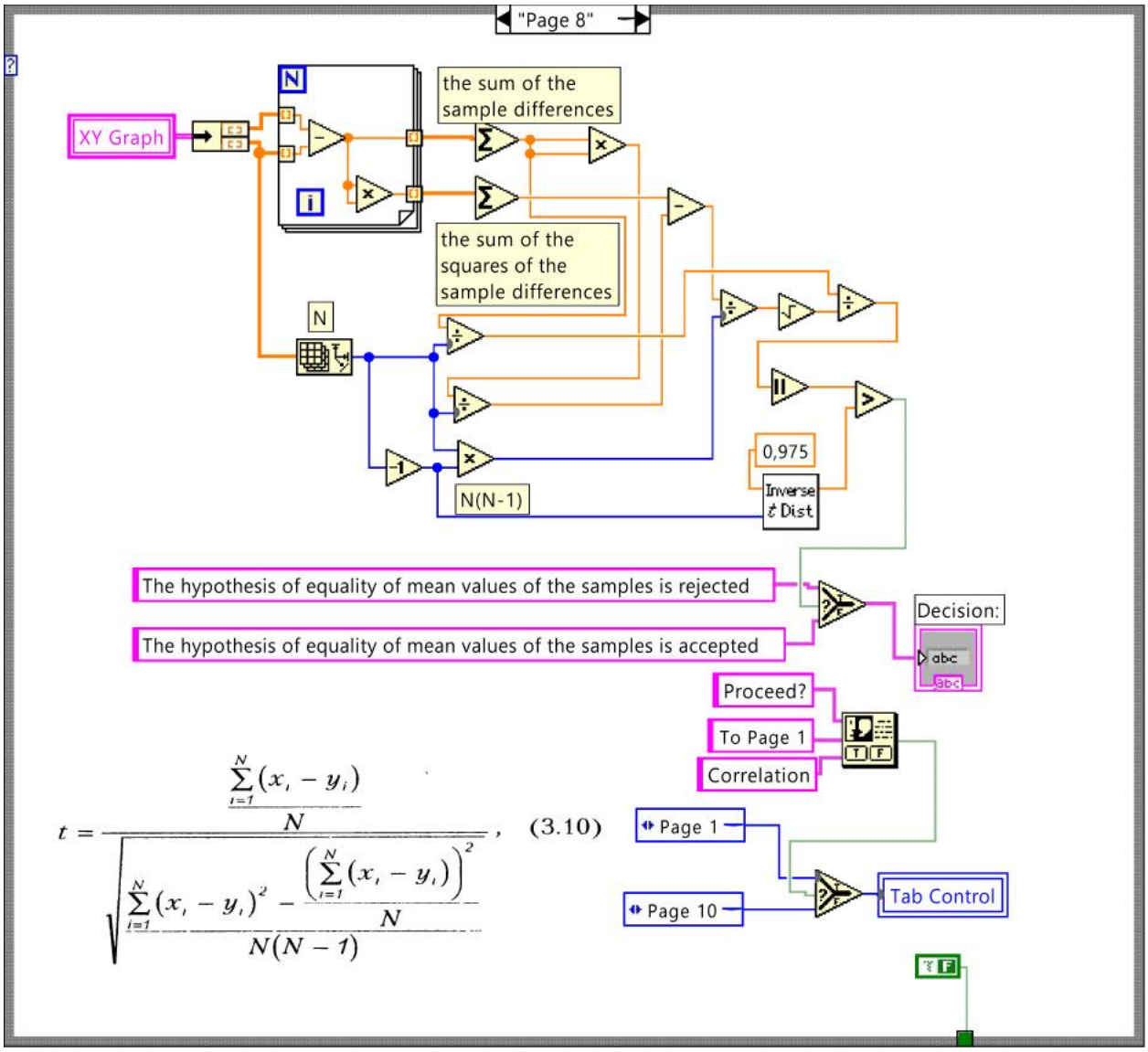

Figure 3.20 – Block diagram of the eighth module

In the ninth module (Figure 3.22) the hypotheses about the equality of the averages in the case of related samples with the law of distribution different from the normal one are tested. This tab also uses the «Bin» subroutine (Figure 3.21).

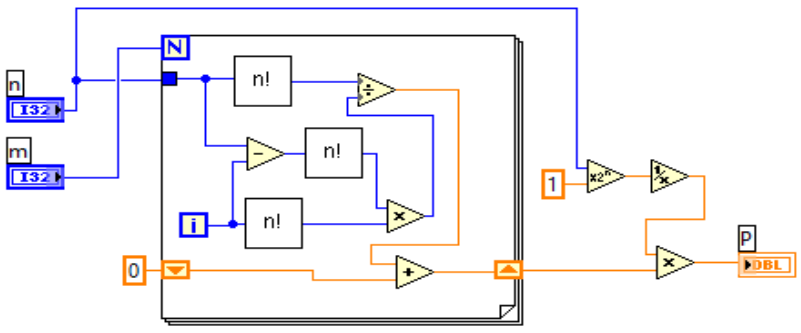

Figure 3.21 – Block diagram for the sub-device "Bin"

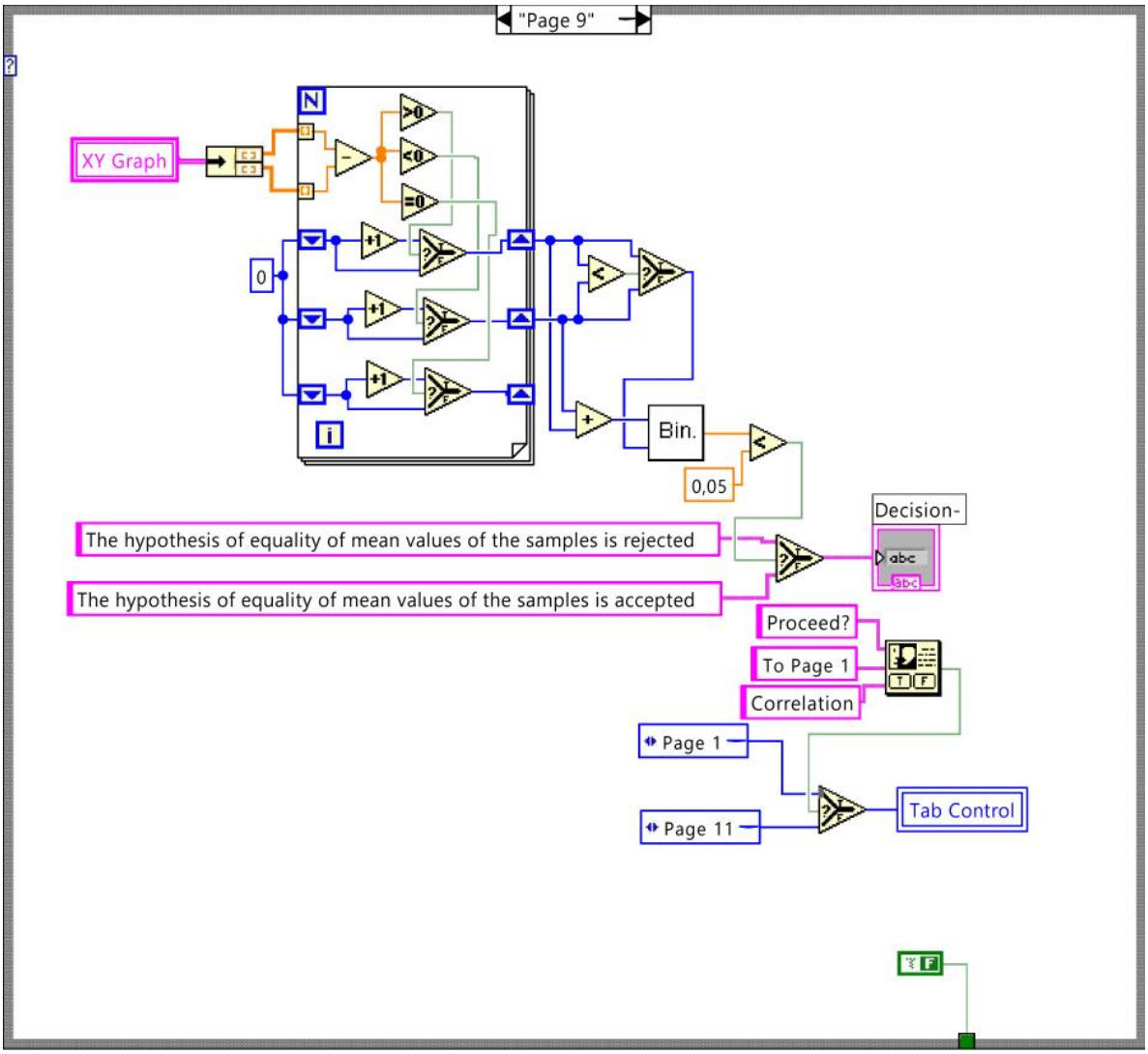

Figure 3.22 – Block diagram of the ninth module

The sub-device “Bin” implements the criteria of signs described in section 1.3. The tail area of the binomial distribution is calculated; the developed device calculates the integral binomial distribution.

Block diagrams of modules that perform correlation analysis for two situations – the normal law of sample distribution and the law other than normal, are located in tenth and eleventh modules and are shown, respectively, on Figure 3.23 and Figure 3.24. The modules additionally use the sub-devices "Correlation" (Figure 3.25) to calculate the Pearson correlation coefficient of two arrays and "Rang for Spirmen" (Figure 3.26), which performs the ranking of input data sets.

In the module of Figure 3.23 the detection of parametric correlation is realized and the Pearson correlation coefficient is calculated by the formula

$$r_{xy} = \frac{\sum_{i=1}^{N}(X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum_{i=1}^{N}(X_i - \bar{X})^2 \sum_{i=1}^{N}(Y_i - \bar{Y})^2}}$$

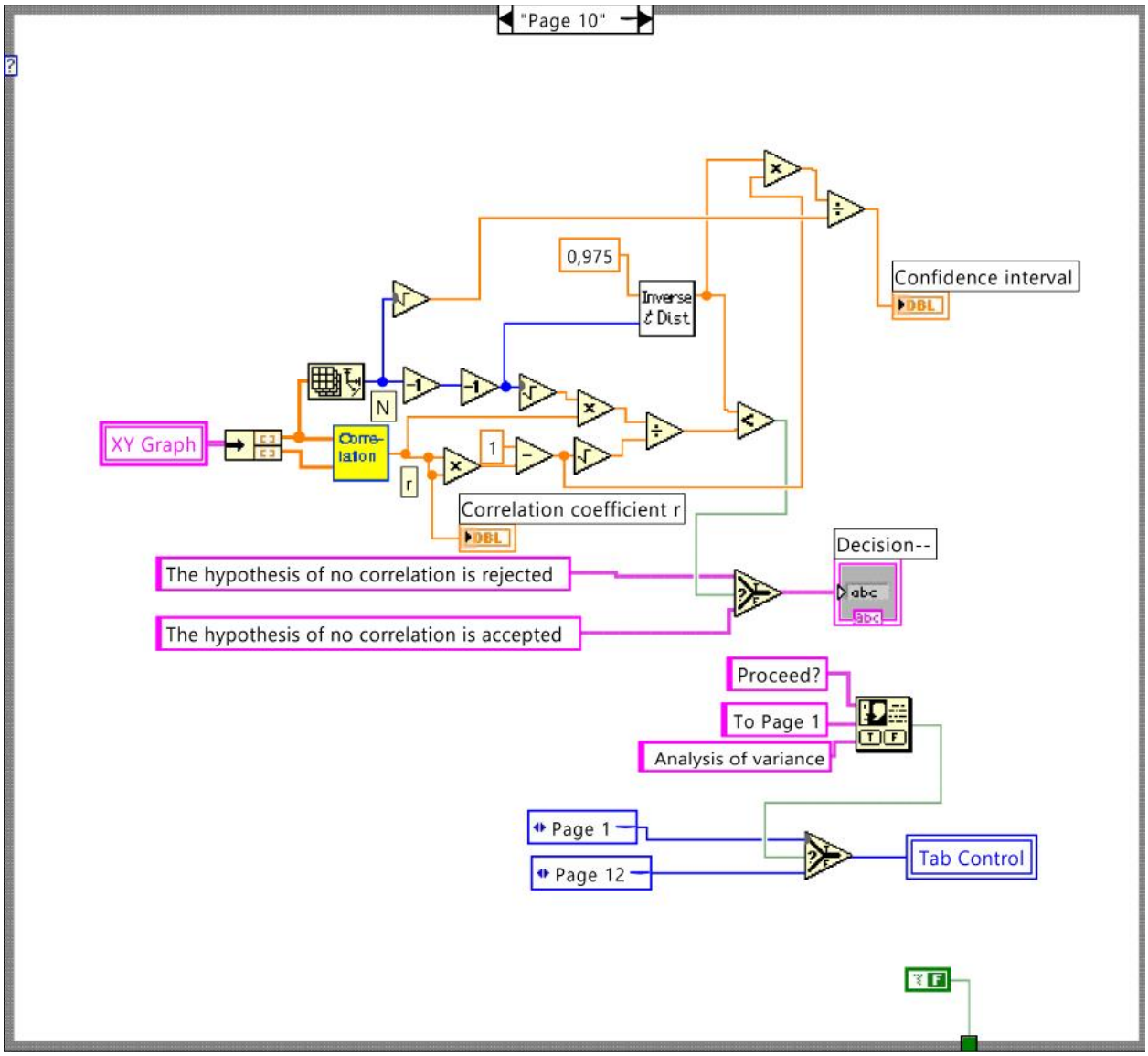

Figure 3.23 – Block diagram of the tenth module

But then the statistical accuracy of the result is checked, i.e. the hypothesis of equality of the correlation coefficient to zero is tested. The interface displays conclusion about the presence or absence of a correlation, the value of correlation coefficient and the half-width of confidence interval for it.

In the module of Figure 3.24 the detection of rank correlation is realized and the Spearman rank correlation coefficient is calculated by the formula

$$\rho(A,B) = 1 - \frac{6\sum_{i=1}^{n}(R_{1i} - R_{2,})^2}{n^3 - n},$$

where R_{1i} and R_{2j} are the ranks of respective objects of two samples.

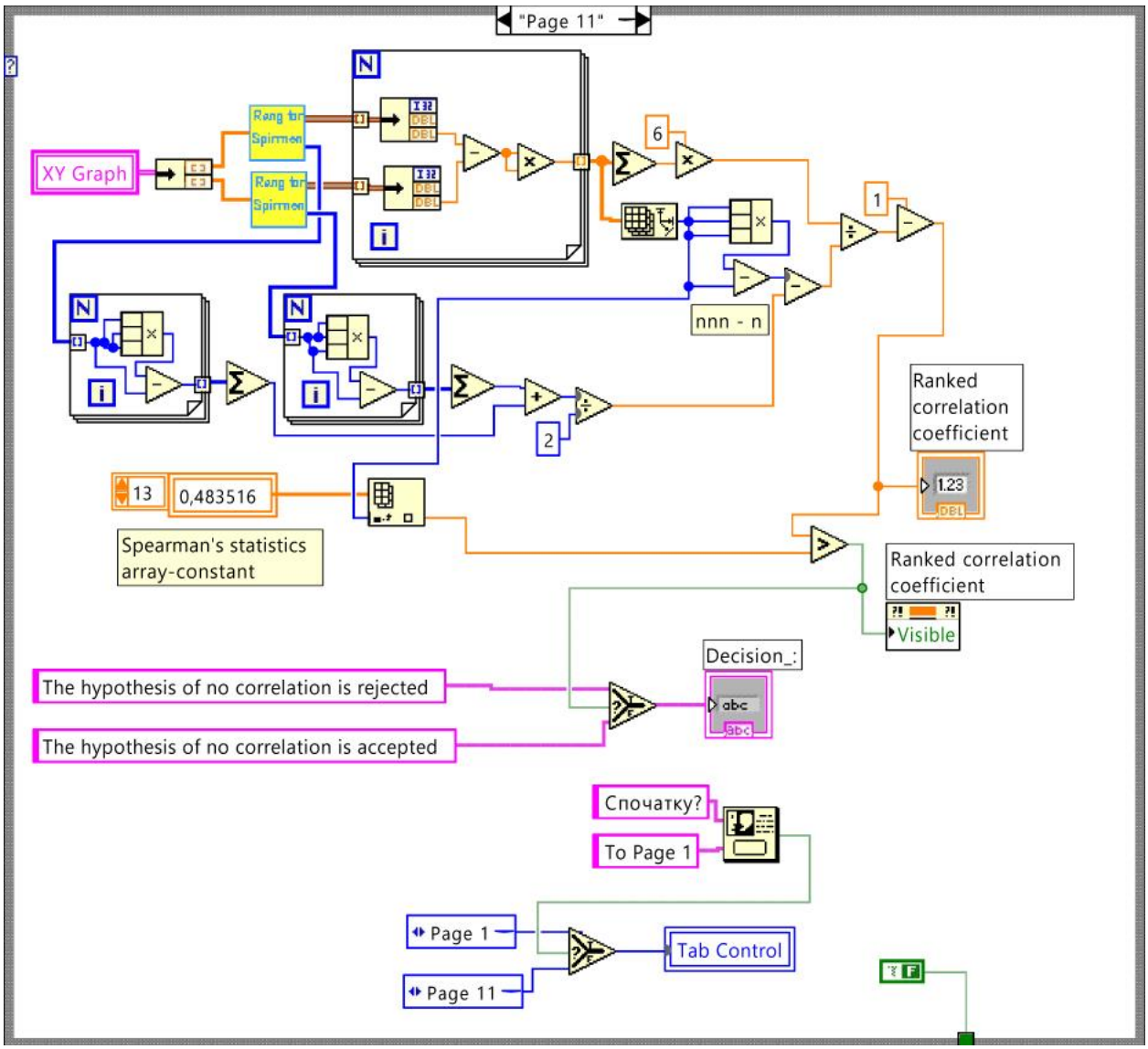

Figure 3.24 – Block diagram of the eleventh module

After calculations, the significance of result is checked according to special tables of Spearman's statistics.

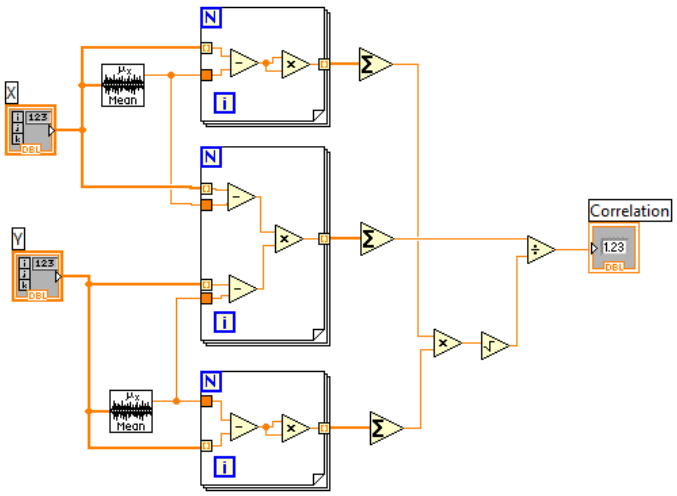

Figure 3.25 – Block diagram for the sub-device "Correlation"

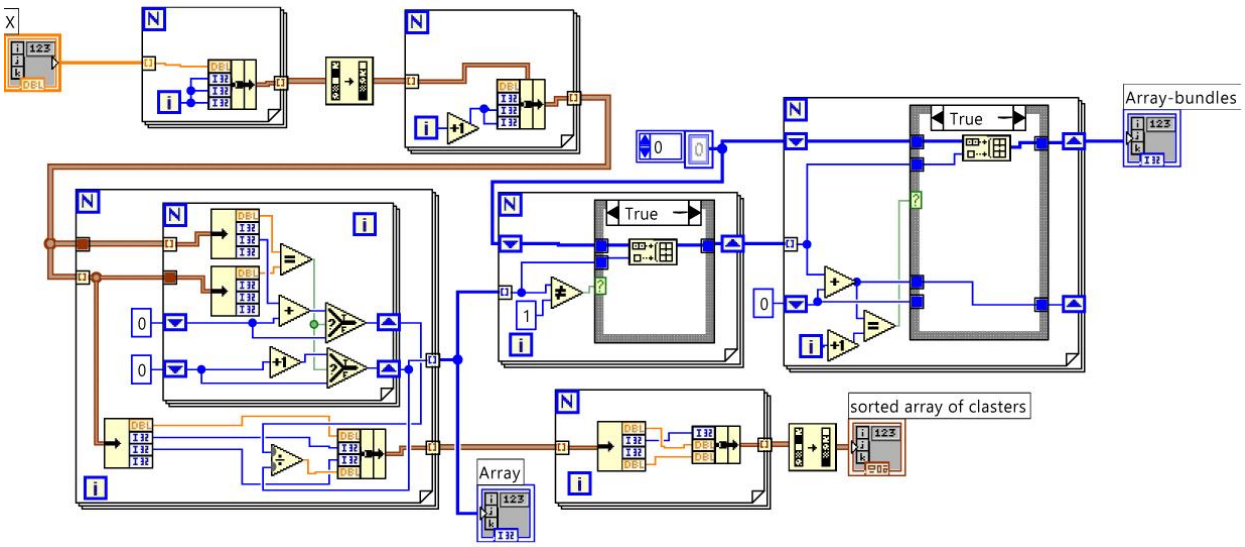

Figure 3.26 – Block diagram for the sub-device "Rang for Spirmen"

Block diagram module, that implements the analysis of variance and located in twelfth module, is shown in Figure 3.27.

The module calculates actual Fisher ratio MSa / MSe – the ratio of variance, which is explained by the influence of factor (intergroup), and unexplained variance (intragroup), and compares with the critical value of Fisher for the appropriate number of degrees of freedom and a given level of significance. The calculated indicators are displayed on the front panel, and based on the result of the comparison, a statistical conclusion is made about the acceptance or rejection of

the hypothesis about equality of the arrays average values. This output is also displayed on the interface panel.

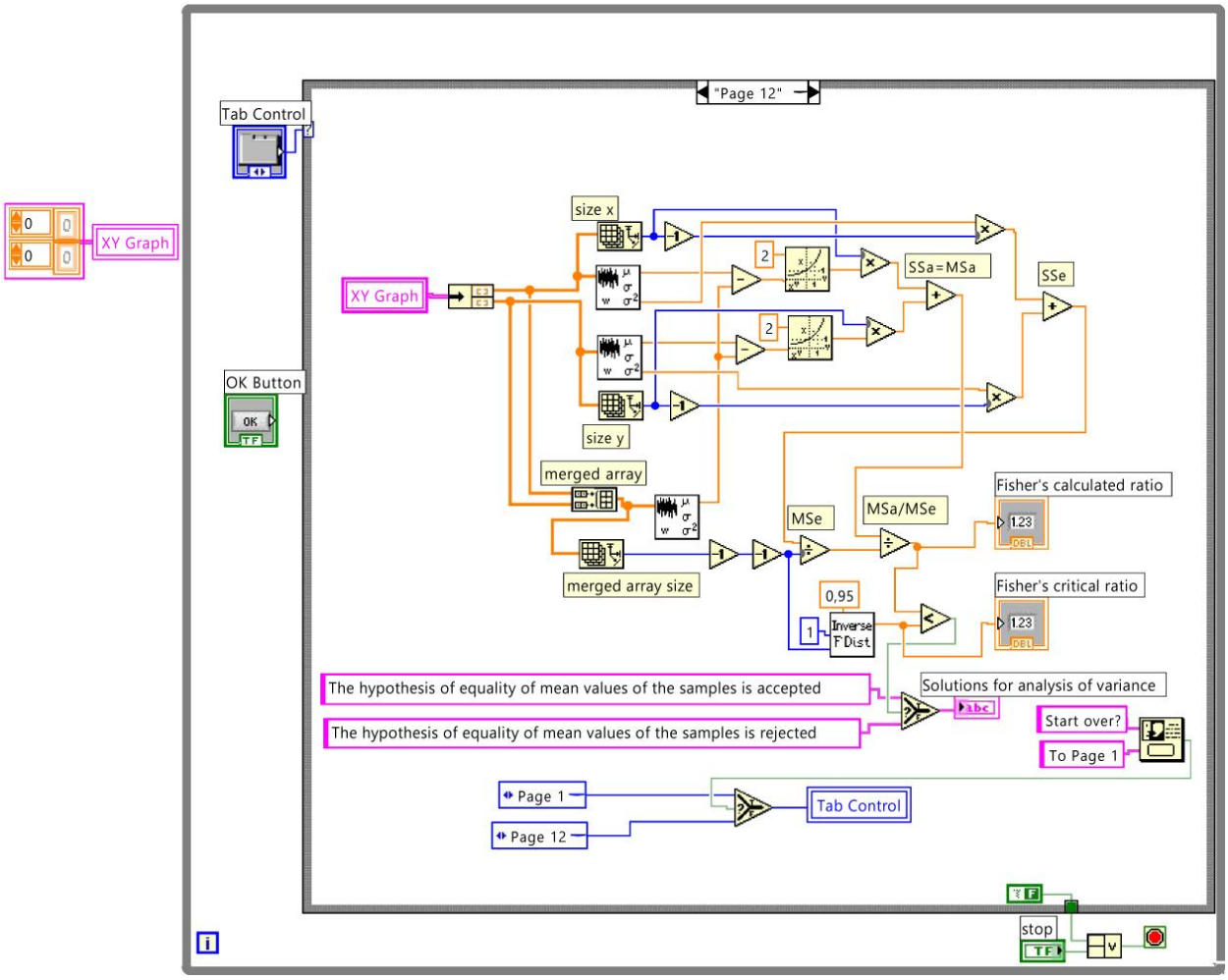

Figure 3.27 – Block diagram of the twelfth module

It should be noted that the module of analysis of variance seems to duplicate the results of previous modules, i.e. determines the presence of a statistically significant difference between the average values of two samples, only by another method. But, first, the verification of important conclusions by two independent statistical methods increases the reliability of obtained results, and secondly, the analysis of variance is less sensitive to errors associated with a small amount of data in the samples.

Conclusions to the section 3

The implementation of software system modules demonstrates the principles of achieving formulated goal of work. The main distinguishing feature of system is automatic check of criterias for applicability of the corresponding statistical methods, as well as tree structure of the system, where decision on branching is made at the nodes in accordance with the results of the check.

SECTION 4
SAFETY AND PRECAUTIONS

This section discusses the norms and measures for labor protection and safety, which will be aimed at eliminating potentially harmful and dangerous production factors that under certain conditions may adversely affect the human body during the development and operation of this software.

4.1 Object characteristics

Table 4.1

Characteristics of premises and decoration

№	Name	The main characteristics of the room	Quantity	Position
1	Room parameters	dimensions: 4500 x 3500 x 2700 mm; S - 4.5 * 3.5 = 15.75 m ^{2}; V - 4.5 * 3.5 * 2.7 = 42.525m ^{3}		-
2	Number of employees	Doctor, patient	2	-
3	Natural lighting	Folding window VEKO SM - 2080 1200 x 1500 mm	1	4
4.	Lamplight	Lamp of the LPO-01 series dimensions 1240x145x52mm; power 18.0 W; armature material: steel material of plafonds and pendants: plastic	1	15
5.	Ventilation	Locally	-	-
6.	Floor type	VH linoleum	-	-
7.	Ceiling	Drywall covered with water-based paint	-	-
8.	The walls	Alkyd paint	-	-
9.	Doors of LAZIO BLK "RODOS"	dimensions: 1090 x 2500 mm; material - MDF board	1	1
10.	The ceramic sink	• dimensions: 500 x 570 x 155 • material: composite - cast mixture of dolomite and resin	1	3

Table 4.2

Equipment and facilities

№	Name	Main characteristics	Quantity	Position
1.	HEACO ECG1201 electrocardiograph	• size: 315 x 215 x 77 mm; • voltage 220V, 50 Hz; • complete set: ECG device, ECG cable (on 10 assignments), pear electrode (6 pieces), hitch electrode (4 pieces), grounding cable	1	17

Continuation of table 4.2

2.	HP Pavilion All-in-One PC is 24-xa1008ur	• size: 540 x 160 x 442 mm; • power supply 120 W; • voltage 220V, 50 Hz; • housing material: plastic	1	9
3.	Wall conditioner COOPER & HUNTER CH-S07RX4	• dimensions: 730 x 254 x 184 mm; • voltage 220V, 50 Hz; • productivity (max) heat kW. 2.43 • consumption (max) cold kW. 0.69	1	5
4 .	Table ON-96-20	• size: 1650 x 900 x 750 mm; • material: chipboard	1	7
5.	Armchair Nowy Styl Bit Gts Chrome (CH) ECO-30 black	• dimensions: 980 x 480 x 475 mm; • product material: leatherette, metal;	1	6
6.	Medical examination couch KP-5	• size: 1900 x 580 x 530 mm; • material: metal frame (painted with powder paint), soft bed (fabric base)	1	11
7 .	Double-leaf metal medical cabinet MP- 958	• size: 1850 x 800 x 400 mm; • material: metal.	1	12
8	Chair stand for the NPO - 34 cardiograph	• size: 1200x500x400 • material: metal	1	16
9.	Medical screen three - leaf HML-526	• size: 2000x10x1800 • material: wood	1	14
10.	HP4532 printer	• size: 540 x 250 x 300 mm; • voltage 220V, 50 Hz; • housing material: plastic	1	10
1 1 .	Radiator steel Brönner 22 type	• size: 1000 x 500 x 120 mm; • material: steel with nanoceramic coating; • max. coolant temperature 110° C • power 2040 W; • connection: lateral;	1	15
12.	Thermal sensor of the fire alarm system IP-105-1 / 2	• size: 100 x 100 x 23 mm; • voltage: from 10 to 30 V • stum (at rest) not more than 30 μa • voltage when transmitting the signal "FIRE" (stum - 20mA) not more than 5.2V • voltage when transmitting the signal "FIRE" (stum - 5mA) not less than 4.2V • case material: plastic;	1	19
13.	Powder fire extin-guisher OPU-10	• size: 420x150x150; • volume: 10 l.	1	16

In Figure 4.1. the scheme of an office is represented.

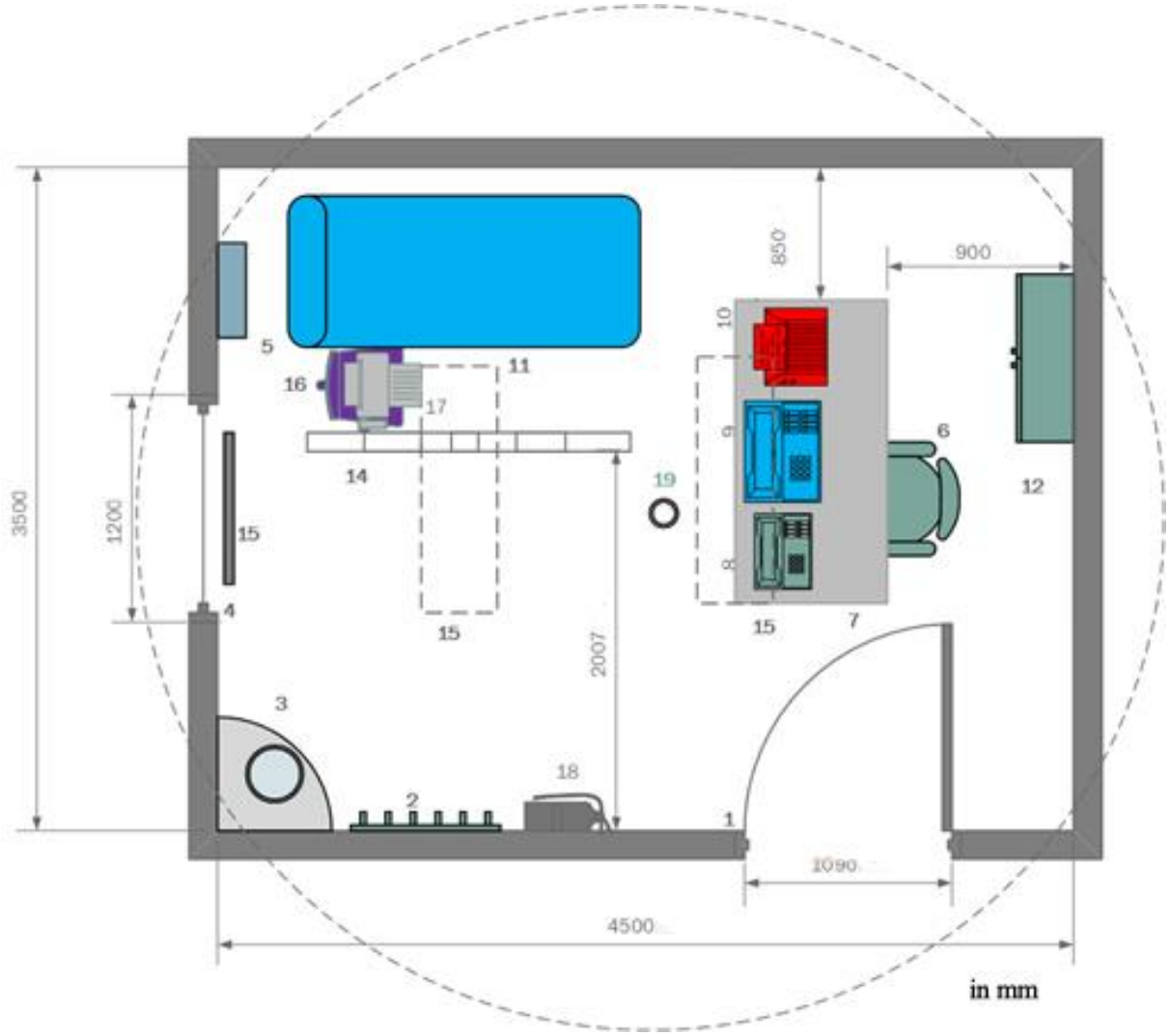

Figure 4.1 – Schematic diagram of the doctor's office

We compare the real data with the normative values given in table 4.3.

Table 4.3

Comparison of factual and normative characteristics

№	Room parameter	Real value	Normative values
1	Area per 1 employee	7.85m ^{2}	6 m ^{2}
2.	Volume per 1 employee	21.26m ^{3}	20 m ^{3}
3.	The minimum width of the passage to the workplace	0.85m	0.7 -1.0 m
4.	The width of the main passages	1.6m	1,5m

After comparison of the actual data of the premises with the norms of DSanPiN 3.3.2.007-98 and DNAOP 0.00-1.31-99 it can be concluded that the premises meet the requirements.

Assessment of key hazards and harmful factors

There are several hazardous factors in the room, which are listed in Table 4.4.

Table 4.4

The main dangerous and harmful factors

№	Physical	Chemical	Biological
1	Microclimate	Disinfecting chemicals	Infections, fungus
2	Electrical hazard	-	-
3	Fire	-	-

There are dangerous factors in the room, but if safety measures are observed, they are not life-threatening.

4.2 Microclimate

This type of work can be attributed to category Ia, the nature of work indoors – constant. Table 4.5 shows the sources of impact on the microclimate and what consequences this may lead to.

Table 4.5

Sources of influence on the microclimate in the room

№	Name of equipment	Source of influence on the microclimate	Causes of influence on microclimate	Consequences of influence on microclimate
1	Radiator steel Brönner 22 type	Heating element	Working heating	In the cold season, the temperature rises
2.	Wall conditioner COOPER & HUNTER CH-S07RX4	Heating / cooling element	Switching the device on / off	Additional temperature rise in the cold season
3.	Window rotary and folding VEKO SM-2080	Cold air penetrating from the outside	Open or insufficiently insulated window	Lowering the temperature

The condition of the premises and the comparison with the normative value are given in Table 4.6

Table 4.6

Real and normative values

№	Microclimate parameters in the cold season	Real value	Normative values
1 .	Air temperature, ^{0}C	22	22-25
2.	Relative humidity, %	45	40-60
3.	Speed of movement, m/s	0.1	0.1

Some measures, developed for normalization of indicators of a microclimate are specified in tab.4.7

Table 4.7

Measures for normalization of microclimate indicators

№	Group of nomenclature measures on SP	View of the event	Selection criterion
1.	Technical measures	Correct radiator intensity	ensuring the temperature is within normal limits
		The air conditioner is in heating mode at insufficient temperature	prevention of hypothermia of the patient
2.	Organizational arrangements	Systematic ventilation	Providing fresh air
3.	Operational	calibration of temperature measuring instruments	reliability of information
4.	PPE	according to the user's position	Control over observance of temperature within norm

The values of the parameters of temperature, relative humidity and air velocity at the workplaces in the workplace do not exceed the normative values, which are considered in accordance with LTO 3.3.6.042-99.

4.3 Chemical and biological hazards

After examination of each patient it is necessary to disinfect the electrodes of the cardiograph and other medical equipment, using disinfectants. In case of

non-compliance with safety requirements, patients may be infected (fungus, infection, etc.)

Table 4.8

Disinfectants

№	Name of equipment	Source of danger	Causes of danger	Consequences of danger
1.	Electrocardiograph cable	Chloramine solution	Contact of the substance with exposed skin	May cause local skin irritation
2.	Electrodes from the electrocardiograph	Glutaraldehyde solution	Contact of the substance with exposed skin	Allergic reactions are possible in case of contact with a concentrated substance

Comparison of normative and real data is given in table 4.9

Table 4.9

Regulatory and real parameters of chemical safety

№	Danger factor	Normative value	Real value
1	Glutaraldehyde solution	0.02 mg / m^3	0.008 mg / m^3
2	Chloramine	10 mg / m^3	4 mg / m^3

The following safety measures must be observed in the office.

Table 4.10

Measures to avoid chemical and biological hazards

№	Group of nomenclature measures on OP	View of the event	Selection criterion
1.	Technical measures	disinfection of devices and (or) their parts in contact with patients	Preventing the spread of biological threats (fungi, infections)
		Replacement of a disposable diaper after each patient	Observance of personal hygiene
2.	Organizational arrangements	admission to work initial instruction on OP	training on safety in the operation of equipment
		Carrying out safety briefings	Regular staff training
3.	Mode	Adherence to the regime and schedule of the cabinet	Providing the opportunity to conduct regular quartz
		preventing the appearance of strangers	Ensuring the reliability of research

Continuation of table 4.10

№	Group of nomenclature measures on OP	View of the event	Selection criterion
4.	Operational	Checking the tightness of the packaging of disinfectants	Follow the instructions
5.	PPE	according to the user's position	individual protection

Doses of chemicals do not exceed the norm, so if you follow safety rules, they do not pose a danger.

4.4 Electrical safety

Table 4.11

Dangers of electric shock

№	Name of equipment	Source of danger	Causes of danger	Consequences of danger
1.	HEACO ECG1201 electrocardiograph	Power cable	Insulation damage	Impressions of the current
		Broken electrode	Careless use	Impressions of the current
		Corps	Short circuit of internal parts of the equipment	The outer parts of the equipment are live. Impressions of the current
2.	HP Pavilion All-in-One PC - 24-xa1008ur	Power cable	Insulation damage	Impressions of the current

The characteristics of the electrical equipment used are given in table 4.12

Table 4.12

Characteristics of electrical safety

№	**Indicator**	**Working conditions**	**Consumer power, kW**
1	HP Pavilion All-in-One PC - 24-xa1008ur	Voltage : 220 V, 50 Hz;	0.3
2	HEACO ECG1201 electrocardiograph	Voltage : 220 V, 50 Hz;	0.15
3	Wall conditioner COOPER & HUNTER CH-S07RX4	Voltage : 220 V, 50 Hz;	0.73 (in cooling mode – 2.0)
4	The ceiling lamp	Voltage : 220 V%, 50 Hz;	0.15

To reduce the likelihood of a hazardous situation, the safety precautions listed in Table 4.13 must be followed

Table 4.13

Means of protection against electric injuries

№	Group of nomenclature measures on OP	View of the event	Selection criterion
1.	Technical measures	the system must only be switched on from a socket with protective earth terminals	Ensuring safe use
		All ECGs connected to the patient - conductors and electrodes, connectors, as well as pre-amplifiers in contact with the patient must be galvanically isolated from other parts of the device and from the "ground".	Ensuring safe use
2.	Organizational arrangements	Before each ECG recording, perform a control examination of the device, wires and electrodes	Ensuring safe use
		Admission to work after the briefing	training on safety in the operation of equipment
3.	Mode	preventing the appearance of strangers	Ensuring security against unauthorized network connections
4.	Operational	Check devices before each use	Follow the instructions
		Disconnect from the network after each use	Follow the instructions
5.	PPE	according to the user's position	individual protection

There is an electrical hazard, but if all electrical safety rules are followed, the risk is minimized.

4.5 Fire safety

The hospital, where the office is located, belongs to the II degree of fire resistance, category B (the room contains non-combustible solid and fibrous materials). Characteristics of non-security sources are given in table 4.14

Table 4.14

Sources of danger

№	Name of equipment	Source of danger	Causes of danger	Consequence
1	HEACO ECG1201 electrocardiograph	Damaged power cable, electrodes, body parts.	Short circuit	Impressions of the current. Occurrence of fire
2	HP Pavilion All-in-One PC - 24-xa1008ur	Damaged power cord	Short circuit	

Characteristics of fire hazard in accordance with ONTP 24-86 are listed in table 4.15

Table 4.15

Characteristics of the room

Classes and subclasses of possible fires	class A (A1 and A2)	Combustion of solids, accompanied and not accompanied by decay
	class E	Combustion of live electrical installations
Combustibility groups of materials and substances that are present in the room	Non-combustible (incombustible) and combustible (combustible). There are no substances that are capable of spontaneous combustion in this room.	
Category of fire danger of the room	category B, class P-zone	Space in the room where solid combustible substances and materials are located.

The following security measures are required in the room.

Table 4.16

Means and measures of fire protection

№	Group of nomenclature measures on PB	Type of protection	Selection criterion
1	Technical	Powder fire extinguishers OPU-10 Automatic PS Thermal BMI	Accordance with the requirements

Continuation of table 4.16

2	Organizational	Conducting briefings, organizing exercises with fire protection. Supervision and control over compliance with fire safety rules. Evacuation plan. Checking the safety of the premises	Training in fire safety rules
3	Personal protective equipment	Respirator (3M 6500; up to 50 MPC) and masks, protective clothing	Accordance with the requirements
4	Mode	Contraindications to the use of open flames	Compliance with fire safety rules
5	Operational	Inspection of electrical devices for their ability to work properly and for the absence of defects	Compliance with fire safety rules

To ensure fire safety in the room there is a fire extinguisher and an automatic thermal fire-fighting system.

Conclusions to the section 4

In this section of the thesis were considered the rules and measures for occupational safety and health in the doctor's office. Possible potential hazards in the workplace and during workplace testing of employees were analyzed.

This room is in acceptable operating values for microclimate, electrical hazards, chemical and biological hazards, subject to the necessary safety precautions. Indoors, the parameters of the area and volume meet the requirements of the standards per employee.

CONCLUSIONS

The goal set in the work has been achieved. An algorithm in the form of a tree structure of modules has been developed and a computer system has been built, which helps to reduce the probability of errors in statistical conclusions in evidence-based medicine. The goal is achieved through the use of automatic verification of the conditions of applicability of specific methods at each stage of statistical analysis. The tree structure of the algorithm allows to automatically select the sequence of modules depending on the characteristics of the analyzed data, making the appropriate statistical conclusion.

The following tasks were solved in the work.

1. An analytical review of statistical methods and algorithms, commonly used in evidence-based medicine, has been done. The complexity of their correct application by specialists without fundamental mathematical training due to the need to check the conditions of applicability at each stage of the analysis is demonstrated.

2. A tree-like algorithm of statistical analysis modules has been developed, the main feature of which is the automatic verification of the criteria of their applicability in tree nodes with the subsequent decision-making on branching to the next possible modules.

3. Software system that corresponds to the developed tree algorithm has been implemented in the NI LabVIEW environment. The scheme of transitions between modules depending on results of check their applicability conditions is constructed. A block diagram and an interface part are built for each module.

The use of an automated system to detect statistical relationships and statistically significant factor effects can reduce the number of erroneous results in evidence-based medicine, especially with widespread access to such a system that can be easily provided on the NI LabVIEW platform.

Prospects for improving the system imply further addition of modules with the implementation of additional methods of statistical analysis, as well as providing easy access to the system by users, for example, via Internet.

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