Creation of the automatic machine of the cell pathology recognizer

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Abstract. The histology is carried out for studying of fabrics of different bodies and systems. The histologic research helps to define existence of pathological cells and new growths with high precision. Modern examinations of an organism are conducted in the different ways: surveys, analyses, ultrasonography, but not always these methods allow to make precisely the diagnosis or to find pathological processes at the cellular level. This method is often applied in various fields of medicine and veterinary science. We conducted pilot laboratory studies pathologically of the changed cells with use of a technique of the histologic analysis. Qualitative and quantitative characteristics pathologists of the changed cells, with identification of indicators are defined. The module of support of decision-making for the preliminary diagnosis of pathologies is developed. The table of the validity of communication of indicators and group of pathologies is developed. With use of the theory of finite-state machines minimization of disjunctive normal form is carried out. On the basis of the received logical equations ladder charts for programming of logical matrixes of the microcontroller of OMRON are constructed. Experiments on reliability of results of the automatic machine - the recognizer of pathology of cells, the shown satisfactory results are made.

1. Introduction
In the nearest future the quantum leap of application of robotics in numerous fields of activity, including in medicine and veterinary science is expected [1, 2]. Approaches to development of the automated system of the histologic analyzer were described in work [3]. This article is devoted to development of the module on recognition of pathologies on the basis of the analysis of certain indicators. When carrying out the histologic analysis three main groups of pathologies were allocated: Core pathology, Cell wall pathology, Mitochondria pathology including changes of morphological structure of a cell wall and ribosome’s, changes of the size, forms and quantity of kernels and kernels, emergence of various nuclear inclusions and changes of a nuclear envelope with the subsequent death of a kernel which is shown by a karyopyknosis, a karyorrhexis and a karyolysis [4, 5].
2. Equipment and devices used in studies
For performance of a histologic research the following equipment is used: technical and analytical scales, rn-meter, microtomes (sled, rotational, freezing), the cryostat or a cryowhale, the water bath, a table for fusion of paraffin sections, a set of automatic pipets, the thermostat, the refrigerator, a microscope, the automatic machine for conducting. In work approaches of the theory of the system analysis, theory of chains and signals and also finite-state machines were used.

3. The results of the study and their discussion

3.1. Physical modeling
Carrying out laboratory experiments was executed by means of the equipment: technical and analytical scales, rn-meter, a sledge microtome, the cryostat, the water bath, a table for fusion of paraffin sections, the thermostat, the refrigerator, a microscope, the automatic machine for conducting which purpose was a definition of indicators of three main pathologies of cells: Core pathology, Cell wall pathology and Mitochondria pathology. Experiments were made on 218 samples with a certain type of the pathologies shown in table 1.

Table 1. Preparation of samples for a research.

| №   | Pathology          | Quantity of samples |
|-----|--------------------|---------------------|
| 1.1 | Core pathology     | Karyopinocnosis     | 25      |
| 1.2 |                    | Carirexis           | 32      |
| 1.3 |                    | Karyolysis          | 27      |
| 2.1 | Cell wall pathology| Permeability increase| 30      |
| 2.2 |                    | Cell swelling       | 15      |
| 3.3 |                    | Cell wall rupture   | 17      |
| 3.1 | Mitochondria       | Mitochondria swelling| 22      |
| 3.2 | pathology          | Crystal structure   | 24      |
|     |                    | change              |         |
| 3.3 |                    | Crystal death       | 26      |

Results of experiments on the analysis of pathologies are shown in figures 1–9.

Core pathology

Figure 1. Atypical cells at cancer. Coloring by hematoxylin and eosine. x 200.

Figure 2. Karyopyknosis, disintegration of kernels. Coloring by hematoxylin and eosine. x 400.

Figure 3. Lysis of nuclear substance. Coloring by hematoxylin and eosine. x 400.
Investigating photos of models of destruction of a cell and having carried out the analysis of pathology of a condition of a cell, it is possible to reveal indicators of extent of destruction of a cell: disturbance of integrity Cell wall (a), core (b), existence of mitochondrions (c) and ribosomes (d).

3.2. System development “Indicators-Cell-Pathology”
For the analysis of development of the mechanism of destruction of a cell we will consider the Indicators – the Cell Pathology system (ICP) (figure 10).

We will describe pathology of a cell the two-dimensional massif P (Y$_{1N}$, Y$_{2N}$, Y$_{3N}$), where Y$_{1N}$ – Core pathology (y$_{11}$ – karyopicnosis, y$_{12}$ – carirexis, y$_{13}$ – karyolysis); Y$_{2N}$ – Cell wall pathology (y$_{21}$ – permeability increase, y$_{22}$ – cell swelling, y$_{23}$ – cell wall rupture); Y$_{3N}$ – Mitochondria pathology (y$_{31}$ – Mitochondria swelling, y$_{32}$ – Structure change crista, y$_{33}$ – Granular dystrophy).

We will describe indicators of pathology of a cell the massif I (a, b, c, d).

3.3. Design of the analyzer of pathology of a cell
For identification of pathology of a cell we will use binary code: 0 – there is no pathology, 1 – there is pathology. By means of the entered indicators I (a, b, c, d) it is possible to define a functional linkage and to construct the table of the validity of pathologies of a cell (table 2).
To obtain logical equations of the equipment operation we have received a minimal disjunctive normal form using Karnaugh map. The example of calculation of logical function for pathology of $y_{11}$ is shown in figure 11.

| Indicators | Core pathology | Cell wall pathology | Mitochondria pathology |
|------------|----------------|---------------------|------------------------|
| a b c d    | $y_{11}$ $y_{12}$ $y_{13}$ | $y_{21}$ $y_{22}$ $y_{23}$ | $y_{31}$ $y_{32}$ $y_{33}$ |
| 0 0 0 0    | 0 0 0 0 0 0 0 0 0 0 0 0 | 0 0 0 0 0 0 0 0 0 0 0 0 | 0 0 0 0 0 0 0 0 0 0 0 0 |
| 0 0 0 1    | 0 0 0 0 0 0 0 0 0 0 0 0 | 0 0 0 0 0 0 0 0 0 0 0 0 | 0 0 0 0 0 0 0 0 0 0 0 0 |
| 0 0 1 0    | 0 0 0 0 1 0 0 0 1 0 0 1 | 0 0 0 0 1 0 0 0 1 0 0 1 | 0 0 0 0 1 0 0 0 1 0 0 1 |
| 0 0 1 1    | 0 0 0 0 1 0 0 0 1 0 0 1 | 0 0 0 0 1 0 0 0 1 0 0 1 | 0 0 0 0 1 0 0 0 1 0 0 1 |
| 0 1 0 0    | 1 0 0 0 0 0 0 1 0 0 1 0 | 1 0 0 0 0 0 0 1 0 0 1 0 | 1 0 0 0 0 0 0 1 0 0 1 0 |
| 0 1 0 1    | 1 0 0 0 1 1 0 1 1 1 1 1 | 1 0 0 0 1 1 0 1 1 1 1 1 | 1 0 0 0 1 1 0 1 1 1 1 1 |
| 0 1 1 0    | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 |
| 0 1 1 1    | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 |
| 1 0 0 0    | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 |
| 1 0 0 1    | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 |
| 1 0 1 0    | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 |
| 1 0 1 1    | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 | 0 1 0 0 0 1 1 0 1 1 1 1 |
| 1 1 0 0    | 1 0 0 0 1 0 1 1 1 1 1 1 | 1 0 0 0 1 0 1 1 1 1 1 1 | 1 0 0 0 1 0 1 1 1 1 1 1 |
| 1 1 0 1    | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 |
| 1 1 1 0    | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 |
| 1 1 1 1    | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 | 1 0 0 0 1 1 1 1 1 1 1 1 |

$y_{11} = a \lor b$

**Table 2.** Table of truth diagnosis of a cell.

**Figure 10.** System "Indicators-Cell-Pathology" (ICP).

**Figure 11.** Karnaugh map ($y_{11}$).
The received minimal disjunctive normal form of the logical equations are given in table 3. As the hardware-software providing which is widely used in medicine and veterinary science the OMRON CP1L controller was chosen [6].

Table 3. Logical equations of definition of the diagnosis of a cell.

| Logical equation | Diagnosis                      |
|------------------|-------------------------------|
| \( y_{11} = a \lor b \) | Karyopicnosis                 |
| \( y_{12} = bc \lor ab \lor a\overline{c}\overline{d} \) | Carirexis                     |
| \( y_{13} = abd \lor bcd \lor a\overline{b}\overline{c}\overline{d} \) | Karyolysis                    |
| \( y_{21} = \overline{a}c \lor \overline{a}bd \lor bcd \lor a\overline{b}\overline{e} \lor ab\overline{d} \lor b\overline{c}\overline{d} \) | Permeability increase         |
| \( y_{22} = \overline{a}b \lor bc\overline{d} \lor a\overline{c}\overline{d} \lor ab\overline{e} \lor ab\overline{c} \lor bcd \) | Cell swelling                 |
| \( y_{23} = abd \lor bcd \lor ab\overline{c}\overline{d} \) | Cell wall rupture             |
| \( y_{31} = c \lor ab \lor a\overline{d} \) | Mitochondria swelling         |
| \( y_{32} = bc \lor ac\overline{d} \lor a\overline{b}\overline{e} \) | Crystal structure change      |
| \( y_{33} = abc \lor a\overline{c}\overline{d} \) | Crystal death                 |

On the basis of the received logical equations the contact-relay scheme with use of program CX-Programmer [7, 8] (figure 12) is developed.

Figure 12. Ladder diagram fragment for pathology of "Core pathology".

At creation of the screen of the operator of the laboratory assistant of the histologist program CX-Designer is used (figure 13).

Figure 13. Panel of the Histologic Analyzer device.
Results of experiments of simulation of the program are shown in table 4.

**Table 4.** Results of experiments of simulation.

| Ladder Diagram Simulation | Quit | Diagnosis |
|---------------------------|------|-----------|
| ![Diagram](image1)         | ![Diagram](image2) | ![Pathologies](image3) |

Results of experiments on recognition of diagnoses were estimated by the laboratory assistant - the histologist. The quality of recognition of diagnoses was defined by amount of encoding of information of n and noise level of an image of sh (the number of the changed bits) $L = f(n, sh)$. In our case, according to the table of the validity of $n = 9$. Resistance to a noise was estimated by recognition of the received image. The algorithm of recognition consisted in imposing of pathologies of the table of the validity on a noisy image with use of the correlation analysis of pair values of Boolean variables. Results of an experiment on definition information / noise are given by amount of coding in table 5.

**Table 5.** Results of dependence on recognition of an image (length bearing sequence / noise).

| n length, bit | Noise of sh, bit | Coefficient correlations | Level recognitions |
|--------------|------------------|--------------------------|--------------------|
| 9            | 0                | 1                        | Excellent          |
| 9            | 1                | 0.89                     | Good               |
| 9            | 2                | 0.78                     | Satisfactory       |
| 9            | 3 and more       | <= 0.67                  | Unsatisfactory     |

Results of experiments on recognition of diagnoses are shown in table 6. Results of experiments on recognition of images showed satisfactory definition of diagnoses. The best recognition of images was shown by pathology of "Karyopcniosis", satisfactory recognition of images was shown by pathologies of "Cell wall rupture" and "Mitochondria swelling". The most important structural unit of a cell are
mitochondrions, their changes demonstrate breath dysfunction, it leads to pathology of exchange processes in all cell, not only their own structure, but also structure of a cell wall and kernel respectively falls apart. Thus, detection of pathology of a kernel, first of all, is very informative indicator of the existing cell pathology in general.

Table 6. Results of experiments on recognition of diagnoses.

| №  | Pathology                | Recognition | Coefficient successful recognitions |
|----|--------------------------|-------------|-------------------------------------|
| y_{11} | Karyopicnosis          | 15 8 3     | 0.92                                |
| y_{21} | Carirexis              | 20 7 5     | 0.84                                |
| y_{31} | Karyolysis             | 16 7 4     | 0.85                                |
| y_{22} | Permeability increase  | 22 4 4     | 0.86                                |
| y_{22} | Cell swelling           | 10 3 2     | 0.86                                |
| y_{23} | Cell wall rupture       | 11 3 3     | 0.82                                |
| y_{31} | Mitochondria swelling   | 14 4 4     | 0.82                                |
| y_{32} | Crystal structure change| 17 5 2     | 0.92                                |
| y_{33} | Crystal death           | 18 5 3     | 0.88                                |

4. Conclusions
Pathology of a cell are changes of its components and ultrastructures in relationships of cause and effect. At the same time, it is about identification of the general regularities of damage of a cell and its reaction to damage. Here can be carried: reception of pathogenic information cell and reaction to damage, disturbances of permeability of cellular membranes and circulation of intracellular liquid; disturbances of metabolism of a cell, death of a cell (necrosis), cellular dysplasia and metaplasia, hypertrophy and atrophy, pathology of the movement of a cell, its kernel and genetic device. For definition of pathological processes at the cellular level and also for decrease in an error when performing histologic manipulations, we developed approaches to design of the robot histologist. Laboratory experiments on identification of indicators of pathologies on the basis of which the table of the validity is constructed are made. The software is developed for the microcontroller of OMRON. The analysis of work of the scheme showed satisfactory results.

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