# Use of the Green Function in the Study of Morpho-structural Changes in Tissues

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*Abstract:* - Currently, automation and robotization of research is being introduced into all areas of medicine and veterinary medicine, including histological analysis. At the same time, it is necessary to provide an automated decision-making system for quality control of histological images preparation. The technological process of histologic analysis running in spatial and temporal basis has been studied. The process of histologic analysis is a complex dynamic system including the stages of biomaterial preparation and study of morphostructural changes in tissues. The problem of process flow description is based on the law of mass conservation during biosphere transfer, which takes into account the equation of flow continuity in Euler and Lagrange variables. In controlling the histologic process, the errors associated with process failure were taken into account. The solution was obtained using an impulsive transient Green's function. In the period 2000-2023, according to statistical data, an increase in the number of cancer cases was observed, which makes the development of an automated histological analyzer relevant. **The aim of the study** was to build a control model for the automated process of histological analysis. **Research Methods**. The approaches to the device design were based on the theory of histologic analysis, application of continuum mechanics methods, methods of solving differential equations using Green's function. Results. The technique of histologic analysis was studied. The analytical solution describing the control of the automated technological process of histological analysis in conditions of possible disturbances caused by perturbations, such as "marriage" and time delay in the preparation of histological specimens has been obtained. Preparation of high-quality histological images will accelerate the diagnosis in the study of morphostructural changes in tissues, which will help to reduce the risks of developing not only cancer, but also other diseases. **Conclusion**. Express analyzer of histological analysis will reduce the time of preparation of histological images and the burden on highly qualified medical personnel.

*Key-Words:* - histologic analysis, automated system, Green's function.

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## 1 Introduction

Currently, much attention is paid to the automation of histologic analysis [1, 2]. Histologic examination is widely used in the study of morpho-structural changes in tissues [3, 4]. In the preparation of histological preparation, the technological process is automated in a fragmentary way, the known equipment is mainly foreign. Within the framework of import-substitution strategy, the issue of automation of histologic analysis management becomes especially urgent. The technological process of histologic analysis includes many operations [5] (Figure 1). Histologic analysis is a deterministic, multi-parameter system, which creates a number of difficulties for the development of an automatic control system.

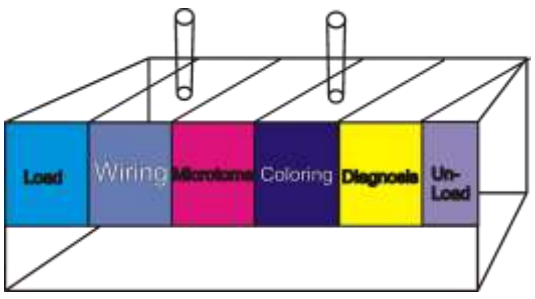


Fig. 1: Structural diagram of the robot histologist

The processes of automation and modeling of technological flows and resources in the preparation of histological images and diagnosis in medicine and veterinary medicine are currently an urgent task.

The classification of models used in histologic analysis can be divided into flow-continuous, discrete-logic, network, neural network, wavelet technology, macro and microanalysis, and others.

Flow-continuous models describe a spatially distributed operational flow, the realization of which guarantees the fulfillment of the specified planned indicators of product preparation (histological images) within the stipulated period [6].

Discrete-logic models are characterized by a combinatorial approach [7]. Models describing the step-by-step process of histological image preparation and pathology analysis based on tree-structured indicators are presented in [8].

Network models are represented as graphs, the vertices of which are technological operations, and the arcs represent biomaterial movements.

Neural network methods have now found application in recognizing pathologies in cancer and diseases caused by chlamydia infection [9].

The application of macro and micro analysis models in histological express diagnostics is considered on the example of diagnosing oncologic diseases realized in the ATLANT diagnostic complex. The results of laboratory experiments allowed us to identify the parameters of histological analysis processes and gave us an opportunity to develop and build a model of automated control when designing a histological analyzer.

## 2 Materials and Methods

Methods of histological analysis, characteristics of systems with distributed parameters, methods of continuum mechanics, theory of automatic control, methods of mathematical and simulation modelling were used to substantiate methods and algorithms of control of histological process.

## 3 Results of the study

### 3.1 Description of the technological process

To describe the technological process of moving the biosphere during histological analysis, let us define the spatial and temporal basis ($l$, $t$). Let us denote conjugate variables characterizing the local place ($l$, $\xi$) on the technological route and instantaneous time ($t$,$\tau$) of histological analysis processing.

In the process of biomaterial passage on the technological route, disturbances may occur due to processing failure at technological operations causing non-critical A($l$, $\tau$) (Figure 2) and gross errors leading to biomaterial sample loss C($\xi$, $t$) (Figure 3).

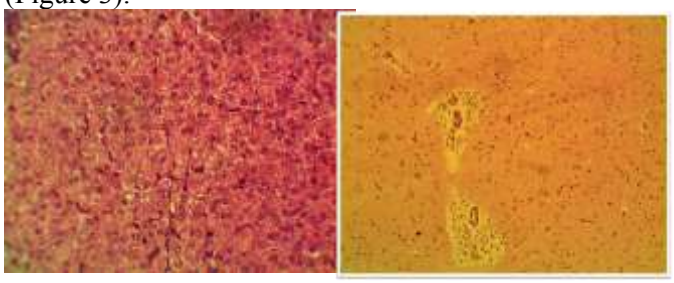

Fig. 2: Uneven coloring

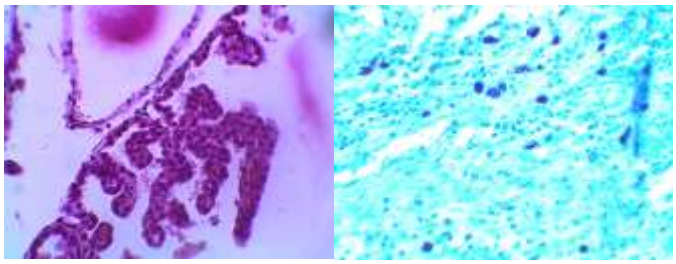

Fig. 3: Faulty staining leading to loss of histologic section

Interference correction on the process route will be by controlling the biomaterial flow $q(l,t)$ and the processing rate v($l$,$t$) (Figure 4).

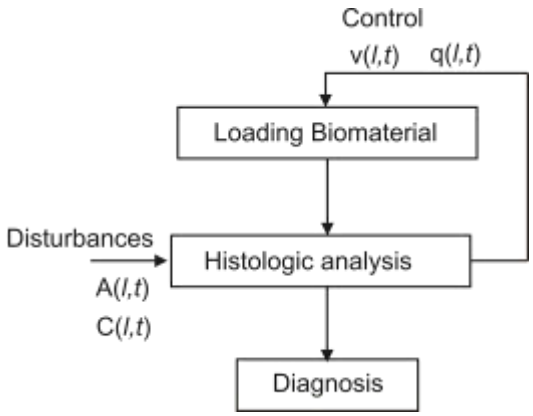


Fig. 4: Management system

We replace the Lagrangian coordinates of biomaterial passage by Euler variables, in this case we can use differential-integral calculus, in particular the Green's function [10], to describe the technological process.

As criteria for controlling the technological process of histologic analysis, we can use the indices of relative deviation of processing speed and biomaterial flow:

$$\int_{t_0}^{t_k}\int_{l_0}^{l_k}|v(l,t)|\mathrm{d}l\mathrm{d}t \to \min;$$
$$\int_{t_0}^{t_k}\int_{l_0}^{l_k}|q(l,t)|\mathrm{d}l\mathrm{d}t \to \min, \quad (1)$$

where $v(l,t)$ is the biomaterial velocity, $q(l,t)$ is the biomaterial flux ($l$, $t$), $l_0$ ($l_k$), $t_0$ ($l_k$) are the boundary conditions.

Let us write down the biomaterial flow control by the integral expression

$$v(l,t) = -z_1\int_{t_0}^{t_k} q(l,t)dt, \quad (2)$$

where $z_1$ is the dimensional normalizing factor of the biomaterial flow.

The regulation of biomaterial movement control on the technological route with respect to biomaterial distribution density $\rho(l,t)$, let us write down by the integral expression

$$q\ (t) = -z_2\int_{l_1}^{l_2}\rho(l,t)\mathrm{d}l, \quad (3)$$

where $z_2$ is the dimensional normalizing coefficient of biomaterial flow density at the site ($l_1$, $l_2$).

The system of equations characterizing the state of biomaterial processing is described by the mass conservation equation (Euler equation) taking into account biomaterial rejects (losses) on the technological route and the control equation [6]:

$$\begin{cases} \dfrac{\partial\rho(l,t)}{\partial t} = -\dfrac{\partial q(l,t)}{\partial l} - C(l,t) \\ v(l,t) = A(l,t) - z_1(t)z_2(l)\int_t q(l,t)dt \end{cases}$$
under initial conditions: (4)
$$l_0 \le l \le l_k, t \ge t_0,\ q(l_0,t) = q_0(t),$$
$$q(l_k,t) = q_k(t), \rho(l,t_0) = \rho_0(l).$$

## 3.2 Synthesis of analytical solution

At known initial and boundary conditions system (4) has an analytical solution based on the use of Green's function (G):

$$q(l,t) = \int_{t_0}^{t}\int_{l_0}^{l} G(l,\xi,t,\tau)\omega(\xi,\tau)\mathrm{d}\xi\mathrm{d}\tau, \quad (5)$$

where $G(l, \xi, t, \tau)$ is the transition function of the system (Green's function);

- $\omega(\xi,\tau)$ standardizing function of external influences.

The expression for the Green's function will take the following form

$$G(l,\xi,t) = \frac{1}{\beta}\exp\left[-\frac{d}{\beta}(l-\xi)\right]\delta\left[t-\frac{\alpha}{\beta}(l-\xi)\right]1(l-\xi).$$

The standardizing function has the form

$$\omega(l,t) = \alpha\, d(l)\delta(t) - \beta\, q(t)\delta(x) + f(x,t), \quad (6)$$

where $\alpha = 1 - z_1, \beta = z_2$.

In the one-dimensional (scalar) case the delta function is described by the expression

$$\delta(f(l)) = \sum_k \frac{\delta(l-l_k)}{|f'(l_k)|}.$$

When interference is given as a polynomial form of the Dirac function

$$C(l,t) = \frac{\delta(t)}{l^2+1},$$
$$A(l,t) = \frac{\delta(l)}{t^2+1}. \quad (7)$$

the solution of the problem of controlling the flow and distributed density of biomaterial from the failure causing rejection will be written by expressions

$$q(l,t) = \frac{\alpha\, z_2}{(\alpha l - \beta t)^2 + \alpha^2},$$
$$\rho(l,t) = \frac{\alpha(1-z_1)}{(\alpha l - \beta t)^2 + \alpha^2}, \quad (8)$$

where $\alpha = 1 - z_1,\ \beta = z_2$.

The solution of the control problem taking into account the technological failure causing time delays on the operating line is described by the equations

$$q(l,t) = \frac{2t}{\sqrt{(\alpha l - \beta t)^2 + \alpha^2}}\ \mathrm{arctg}\frac{\alpha t}{\sqrt{(\alpha l - \beta t)^2 + \alpha^2}},$$
$$\rho(l,t) = \frac{2(\alpha l - \beta t)}{\sqrt{(\alpha l - \beta t)^2 + \alpha^2}}\ \mathrm{arctg}\frac{\alpha t}{\sqrt{(\alpha l - \beta t)^2 + \alpha^2}}, \quad (9)$$

where $\alpha = 1 - z_1,\ \beta = z_2$.

The analytical expressions (8) and (9) express the control of flow and distributed density of biomaterial advancement taking into account the interference caused by equipment failure on the process route, which will contribute to the development of control systems for automated histological analysis processes.

## 3.3 Numerical modelling

In order to analyze the solution (9) of the set problem and the formation of the control action, numerical simulation was carried out at coefficients $z_1 = 2$, $z_2 = 1$ (Table 1).

Table 1. Numerical modelling

| *t* | Stage of technological operation, *l* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 1 | -0.38 | -0.71 | -0.91 | -1.04 | -1.13 | -1.19 | -1.24 | -1.28 | -1.31 |
| 2 | -0.19 | -0.44 | -0.63 | -0.76 | -0.87 | -0.95 | -1.02 | -1.07 | -1.11 |
| 3 | -0.12 | -0.29 | -0.45 | -0.58 | -0.69 | -0.77 | -0.85 | -0.92 | -0.96 |
| 4 | -0.08 | -0.21 | -0.34 | -0.46 | -0.56 | -0.64 | -0.72 | -0.78 | -0.83 |
| 5 | -0.05 | -0.16 | -0.26 | -0.37 | -0.46 | -0.54 | -0.61 | -0.68 | -0.73 |
| 6 | -0.04 | -0.12 | -0.21 | -0.30 | -0.38 | -0.46 | -0.53 | -0.59 | -0.65 |
| 7 | -0.03 | -0.09 | -0.17 | -0.25 | -0.33 | -0.39 | -0.46 | -0.52 | -0.57 |
| 8 | -0.02 | -0.08 | -0.14 | -0.21 | -0.28 | -0.35 | -0.42 | -0.46 | -0.51 |
| 9 | -0.02 | -0.06 | -0.12 | -0.18 | -0.24 | -0.30 | -0.36 | -0.41 | -0.46 |
| 10 | -0.02 | -0.05 | -0.10 | -0.16 | -0.21 | -0.27 | -0.32 | -0.37 | -0.42 |

Figure 5 shows the graph of biological media flow control based on the calculations presented in the Table1.

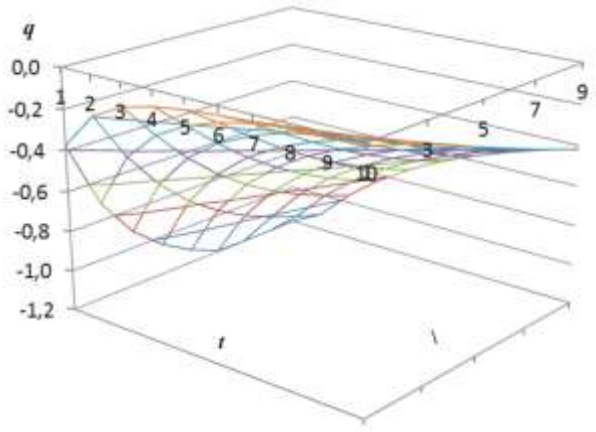


Fig. 5: Biosphere flow control

## 4 Conclusion

The use of mathematical physics methods allowed to formalize the control system of biomaterial movement on the technological route of histological analyzer taking into account perturbations at operations. The analytical solution of the system of differential equations in deterministic formulation formalizing the control model of histological analysis is given. At introduction of the automated line at histological analysis it is possible to realize control functions for minimization of disturbances caused by loss (rejection) of biomaterial and failure of technological equipment causing time delays that will improve the quality of morpho-structural diagnostics of tissues at diagnosis.

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The authors have no conflicts of interest to declare that are relevant to the content of this article.