INVESTIGATION OF MEDICINE QUALITY BY RAMAN SPECTROSCOPY AND MACHINE LEARNING METHODS

IGOR GOLYAK[1], DMITRIY ANFIMOV[1], PAVEL DEMKIN[2], IGOR FUFURIN,[1] AND ANDREY MOROZOV[1]

[1]Bauman Moscow State Technical University, Moscow, Russia
[2]BMSTU Center of Applied Physics, Moscow, Russia

igorgolyak@yandex.ru

ABSTRACT

Raman spectroscopy is a method of optical spectroscopy that allows you to get a kind of “fingerprint” of a sample. As an optical method, Raman scattering of light allows non-destructive analysis of the chemical composition of various molecular compounds. The use of Raman spectroscopy in pharmaceutical and biomedical analysis has increased dramatically over the past three decades with the improvement of laser sampling technology and registration methods [1-5]. Thanks to these technological advances Raman spectroscopy is a practical method of analysis both inside and outside the laboratory. At the same time the relevance of quality control of medicines is increasing due to their huge variety and the complexity of choosing an effective method of treating patients. In this paper a study of medicine quality was carried out on the example of aspirin from various commercial manufacturers, available for sale, using Raman spectroscopy.
To register the Raman scattering spectra of test substances, an experimental setup was created. The scheme is shown in Fig. 1. The setup consists of an Ocean Optics Ventana 785L (3) spectrometer, a laser source with a wavelength of 785 nm. The spectrometer is paired with a laptop (4) via a USB.

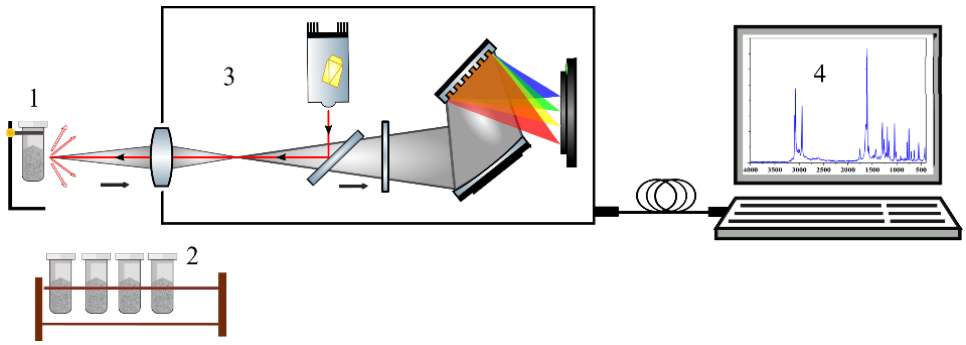
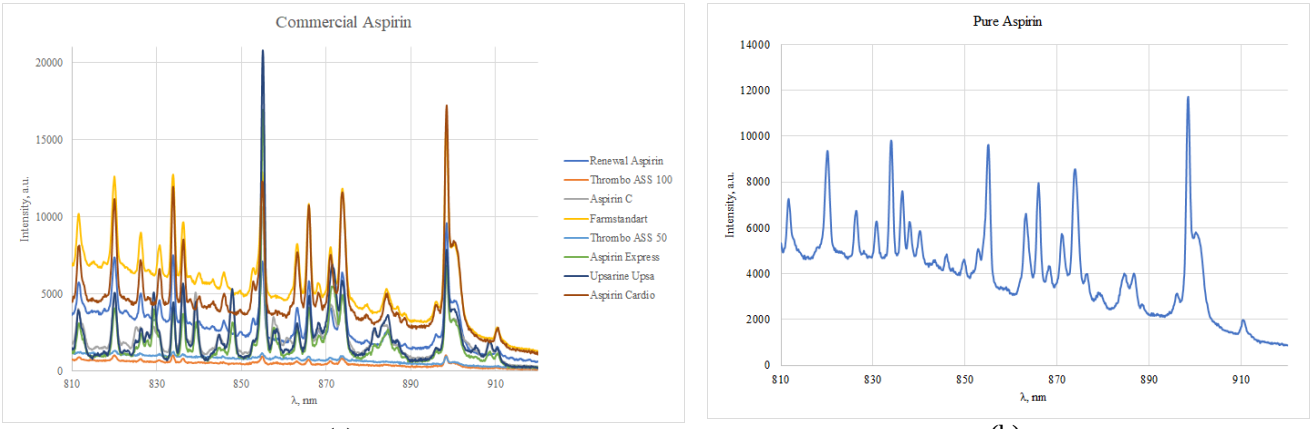


Figure 1: *Experimental setup scheme.*

Aspirin samples from the following manufacturers available in pharmacies were selected as test substances: Renewal Aspirin, Thrombo ASS 50, Thrombo ASS 100, Aspirin C, Farmstandart, Aspirin Express, Upsarin Upsa, Aspirin Cardio. The experimental spectra are shown in Fig. 2a.



(a) (b)

Figure 2: *Raman spectra of commercial aspirin (a) and pure aspirin (b).*

The Raman spectrum of pure aspirin was used as a reference spectrum (Fig. 2b). The experiment was carried out as follows. For each type of aspirin, Raman scattering spectra were recorded with the exposure changed from 10 msec to 1 sec with 10 msec step, and the laser power from 10 mW to 100 mW with 10 mW step. At the same time, all test samples were extracted from the shell to ensure the purity of the experiment. As a result, 100 spectra were recorded for each test substance. A shallow convolutional neural network was used to process the data obtained [6]. The neural network model

is shown in Fig. 3. Neural network training took place on the pure aspirin samples, and quality control on Raman spectra of commercial aspirin. The search for optimal parameters was carried out using the following grid:

- number of kernels of the convolutional layer: k ∈ 24, 48};
- size of kernels of the convolutional layer: N ∈ [64, 256];
- stride for the convolution and max-pooling: s ∈ [1, 2];
- momentum in the SGD updating rule: momentum ∈ [0.1, 0.9];
- number of neurons in FCL: neurons ∈ [128, 256];
- learning rate: lr= 10^n, n ∈ [−3, −4];
- number of epochs: epochs ∈ [100, 300].

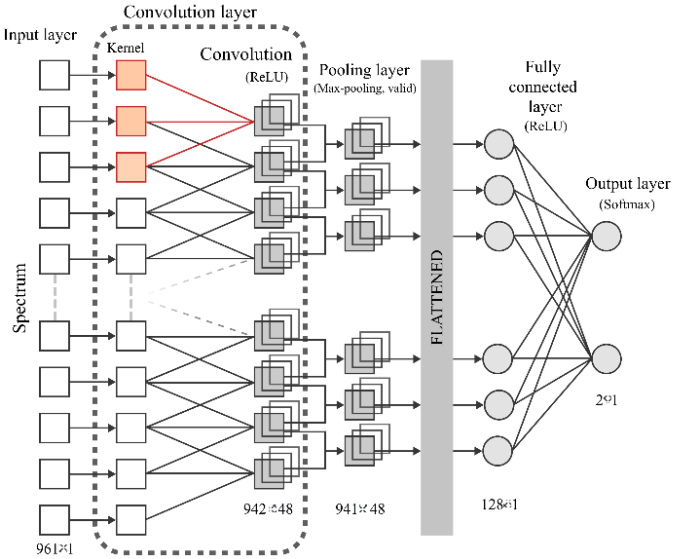
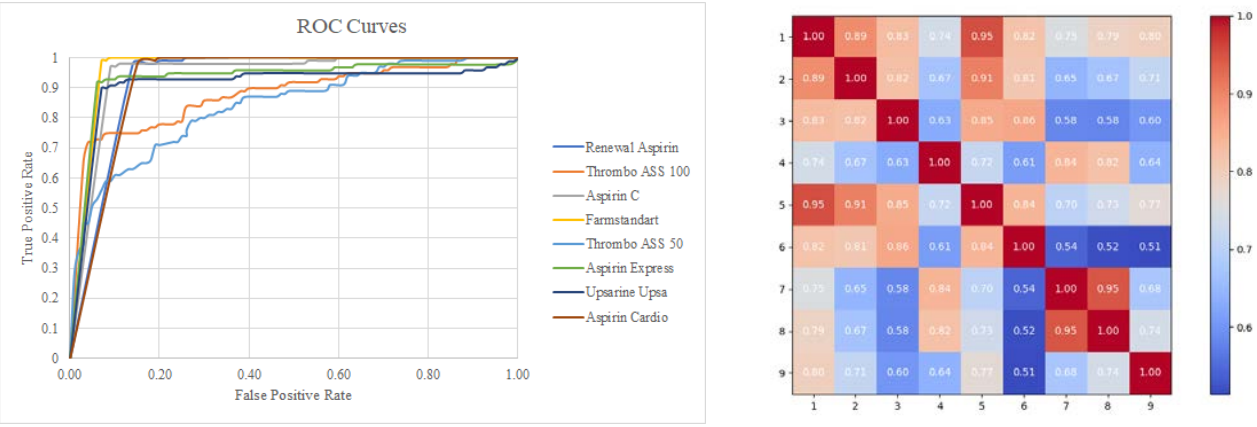


Figure 3: *Shallow neural network scheme.*

As a result of the experiment, the following ROC curves were obtained (Fig. 4a). Numerical results are presented in Table 1.



(a) (b)

Figure 4: *ROC curve analysis of commercial types of aspirin (a) and cross-correlation matrix (b). The numbers in figure correspond to the numbers from the Table 1.*

To compare the effectiveness of deep learning methods and classical methods of comparing spectra, a cross-correlation matrix of the obtained data is constructed (Fig. 4b). From the results presented in Fig. 4b and Table 1, neural network shows a higher result.

Table 1. *Area under the ROC curve for test substances.*

No.	Test Substance	ROC AUC score	Correlation
1	Renewel Aspirin	0.93	0.80
2	Thrombo ASS 100	0.88	0.71
3	Aspirin C	0.94	0.60
4	Farmstandart	0.96	0.64
5	Thrombo ASS 50	0.84	0.77
6	Aspirin Express	0.93	0.51
7	Upsarine Upsa	0.91	0.68
8	Aspirin Cardio	0.92	0.74
9	Pure Aspirin	1.00	1.00

From the results of Table. 1 all types of aspirin are comparable to the quality of the reference. However, the best result was shown by aspirin produced by Farmstandart with a ROC AUC score of 0.96.

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