Hybridization of COBAC, QSPR / QSAR and SBGN Technologies: The Unity of Theory and Practice for Biomedical Technique Design and Biochemical Diagnostic Information Analysis

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***Abstract*—A current global trend in the development of biomedical and pharmaceutical chemistry is the use of computerized analytical technologies like COBAC, typically followed by the comparison with the action of the known alalytes using QSAR / QSPR methods. The clinicians are interested not in the results of the primary measurements, but in representative results of the physiological and biochemical tests compared with the preceding drugs and their analogs. In this case a direct conversion of numerical data into the QSAR / QSPR descriptor values with their subsequent transformation to the qualimetric results is necessary, which is described in this paper. We would also like to underlie that the innovation of our work is in the concept proposed which for the first time combines the principles of COBAC, QSPR / QSAR and SBGN, but not in the technical realization or program code itself.**

***Index Terms*—QSAR / QSPR, COBAC, SBGN, SCADA, GUI, SPECTRAL-SAR, automation, control engineering**

I. Introduction

A known trend in the development of biomedical and bioanalytical chemistry since early 1980-th is the application of COBAC (Computer Based Analytical Chemistry) approach [1], [2], although the first steps towards multifactor using of digital computers in analytical chemistry were made as early as middle 1960-th [3]-[5]. Modern COBAC technologies allow to obtain statistically reliable information during measurement result interpretation for further comparison with databases. In biomedical chemistry, toxicology and pharmaceutics it is usually followed by a physico-chemical, physiological and biochemical comparison with the action of the known agents - toxins, pharmaceuticals, allosteric regulators, etc by means of QSAR and / or QSPR (Quantitative Structure-Activity Relationships / Quantitative Structure-Properties Relationships) technologies [6]-[8]. In this case a clinician is usually interested not in the results of the primary measurements, but mostly in a reliable medical result of the physiological or biochemical test compared to the results of the previous drugs / agents and their analogs. In other words, a practical physician wonders "whether this substance will be toxic or not", or "will this drug be active in this particular case (e.g. interact with the proper receptors)", according to the similarity databases.

Thus, laboratory diagnostics does not need the pure spectra and quantitative measurements, (though SPECTRAL-SAR also exists [9]), but the comparative data, such as determination of the ratio between the acting agent and its potential antagonists or the stoichiometry of their complexation; the comparison of action of the unknown pharmacological or toxicological agent with the known ones in order to predict the processes that could be induced by it; determination of the acting agent dynamics (pharmacodynamics, toxicodynamics, etc.) or the reaction kinetics - comparative efficiency criteria of drugs with different rates of incorporation into the metabolic networks; automatic classification of the new substances to a corresponding class of biochemical or biologically active compounds; the study of biochemical, biophysical and thus pharmaceutical properties of the analyte without its full spectral and structural analysis based on statistically reliable analogies within a reasonable time range for the particular medical case. It is obvious that such a practical approach requires from the data acquisition and processing system a clear numerical and graphical representation [10], [11] of the above criteria instead of the primary pure chemometric information, which is aimed to help a standard clinician without any special skills in molecular diagnostics to come to the plausible and statistically representative conclusions.

Therefore in some special areas there is a current need in designing of specialized setups for the direct receiving of this information without converting of any file formats and measurement units. In other words, it is necessary to

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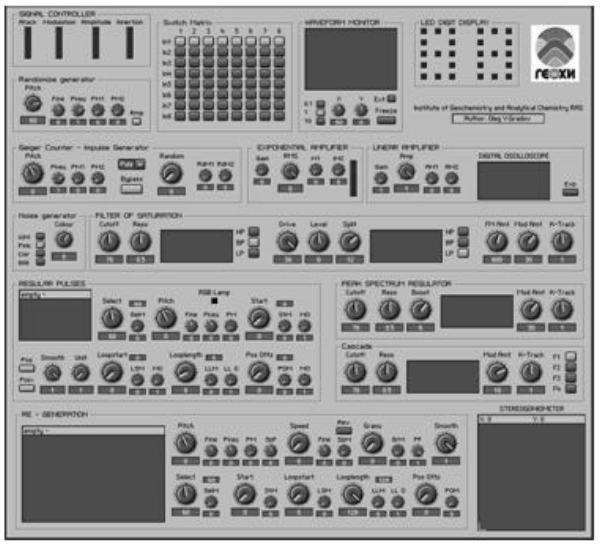
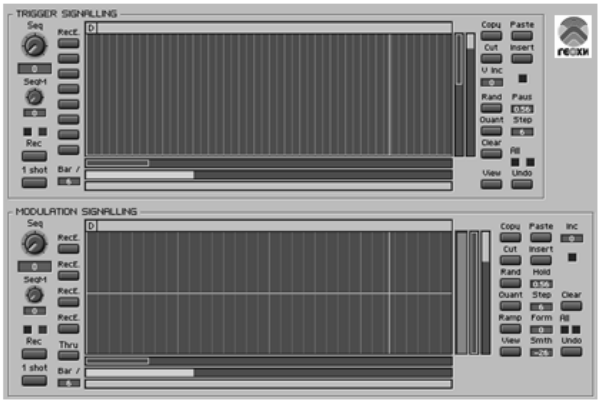
develop measuring tools which can directly provide the values required, such as QSAR / QSPR variable values in a similar way as modern setups in molecular biology do, i.e. using SBGN (System Biology Graphical Notation) notation [12] supporting all the necessary libraries and databases [13]. The latter notation can be also used in the analysis of biomedical analytes if they are considered in the framework of the special system biology areas, such as proteomics, lipidomics, glycomics, etc. This paper describes the possibility of implementation of the above approach and its introduction into the variety of modern biomedical and bioanalytical chemistry methods.



a



b

Figure 1. Virtual devices («descriptometers») created using «Reactor» graphical programming system for data acquisition from different types of analytical devices with optron switching (Institute of Geochemistry and Analytical Chemistry of Russian Academy of Sciences, Laboratory of Carbon Geochemistry, «O.V. Gradov student subgroup», 2010).

II. Early Preliminary Results

We developed systems which performed a direct conversion of the data obtained from the measuring equipment into the relevant molecular descriptors or their ratios, including the tracking mode monitoring of single analyzing channels and descriptor conversion in time (the working title of the virtual instruments was "descriptometers"). From arithmetical parameter correlation it is possible to establish indirect ratios between quantitative / numerical descriptors. For this purpose a GUI interface of the multichannel instrument controlled by LabView or its analog includes a virtual channel, corresponding to the known analog device like «ratiometer» [14]-[22] or «dual channel rate-meter». Direct comparison of the channels with the corresponding single interacting stoichiometric units allows to use the setup as an automatic "stoichiometer" capable of detecting supramolecular and non-stoichiometric coordination (this can be achieved due to the fact that "it is all the same for the virtual device what to measure" in arbitrary units.

Figure 2. The earliest CAMAC-based descriptometric complex (hardware was assembled in the 1980-1990; new measurement technique ideology was proposed and new software program was written in the 2000s by «O.V. Gradov student subgroup»).

The possibility to analyze the process kinetics / dynamics (including kurtosis - the probability distribution sharpness, spectral analysis of the process dynamics and the mode detection, including normalization according to their polarity with a separate classification of the antimodal distributions) allows to distinguish between a number of complicated cases similar in some key variables by means of comparing their kinetic parameters with the known data and existing pharmacokinetic models.

Therefore, we propose to perform "fingerprinting" of the time-frequency distributions (pseudospectra) complementing the standard spectroscopic [23] or mass-spectrometric [24] QSAR-related data obtained by analytical methods of primary control. Thus, the way from an automatically generated hypothesis (e.g. by JSM method [25-27]) to the primary mathematical model underlying a biochemical basis for pharmacokinetics and pharmacodynamics, can be easily performed automatically [28].

We have attempted research efforts in this area since 2010. In 2010 a complex system for integrated

registration of data streams from multiple devices was developed on the basis of converters with an optron switching (we applied the early Russian developments in this area [29]-[32]). Fig. 1 shows graphic user interfaces (GUID – Graphic User Interface of Device) of such «descriptometers». Now we are working on their hardware implementation, a project of which is given in Fig. 3. Since 2013 the invited students developed the software and create similar systems for QSAR, QSPR and SBGN hybridization using LabView, ZetView and some other platforms. The complex system designed is capable of reproducing the interfacing functions of the above mentioned virtual devices using the optron switching techniques. We ceased to develop such complex systems based on CAMAC a few years ago for the reason of the obsolescence of this hardware platform. The last setup targeted for the design of descriptometers based on CAMAC is shown in Fig. 2. Nowadays we have already launched a data station for mass-spectrometer based on National Instruments PXI chassis, which is planned to be applied for data acquisition from mass-spectrometric and other equipment including temporal schemes based on ELVIS station) for real-time «descriptometric» computer processing using handmade software, such as LabView-based descriptometric GUI.

III. Perspectives

To date, a number of works have been started on the creation of novel virtual descriptometers for systems biology, capable of qualimetric code analysis [33] according to the formal features, including synthetic semantides, which is of great interest for synthetic biology, abiogenetic research and the creation of alternative code forms [34]. An automation scheme was proposed for the analysis of GC-auxanometric and GC-MS-auxanometric data [35] using complex automatic data mining of descriptors' sets and descriptor mapping in the framework of systems biology (in a primitive case – of «gas biology» [36,37]). One of the schemes developed by our group for the real-time patch-clamp lab-on-a-chip automation [38] has also provided an opportunity of descriptometric approach realization and automation for quantitative research in membranomics and channelomics (using MATLAB + SIMULINK). Currently the work of our group is aimed at the development of a descriptographic lab-on-a-chip / imager, which after the completion of the scheme design will provide the descriptor distribution mapping and allow to obtain information about the objects investigated in a symbolic form.

Appendix A

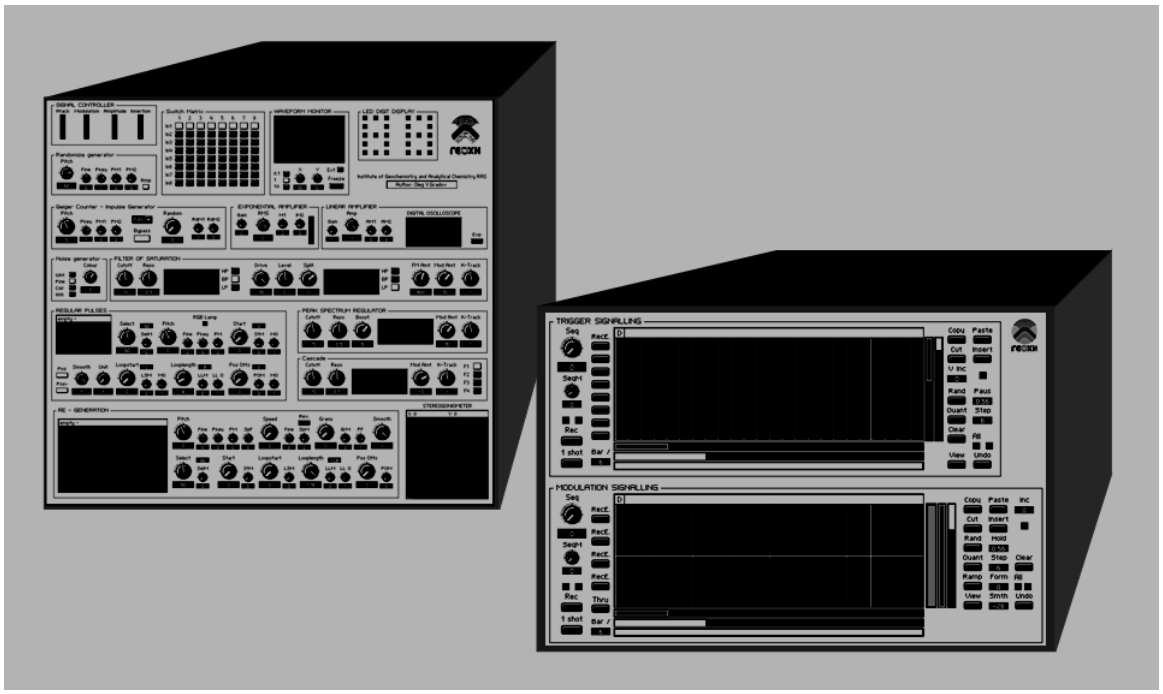


Figure 3. Project of the hardware implementation of virtual descriptometric stations based on various physical measuring instruments with the optron switching.

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2. Chemometric microscopy and mapping
   DOI: 10.13140/RG.2.1.3272.5602
3. Electro-morphological mapping of neural structures
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