# QFM Contribute in Fabrication of Brain with more Abilities

Tigran Ghevondyan Laboratory of Electron Microscopy and Quantitative Functional Morphology, L. A. Orbeli Institute of Physiology NAS RA, Yerevan, Republic of Armenia e-mail: tigranghevondyan@yahoo.com

Abstract—This paper presents the course of further development of the new research and diagnostic methodology "Quantitative Functional Morphology", which is an original type of system-based multivariate analysis of structured biological systems. A number of fundamental principles underlying the methodology are presented. Some results obtained in the study of the heart muscle, cardiomyocyte, lungs, and brain are presented.

In histological and ultrathin sections of small samples of these tissues under a microscope, the values of the main functions of these tissues were measured: the degree of oxygen supply, the maximum contractile potential and the maximum value of the brain power. Some "pitfalls" have been identified that significantly impact on the accuracy of research results by the new methodology. Ways to overcome these obstacles are discussed.

*Keywords*—Brain supercomputer relation, brainpower measuring, Quantitative Functional Morphology.

## I. INTRODUCTION

With the advent of a new paradigmatic research methodology "Quantitative Functional Morphology" (QFM), new horizons have opened in biomedical morphological research. This became possible thanks to a new type of systemic multivariate analysis, developed and named by us as "Quantitative Functional Morphology" methodology.

In the original, narrowest sense, the QFM used in biomedical research can be characterized as: "A complex-set of morphological methods, methods of quantitative analysis of an image, a method of mathematical modeling that allows to measure the entire reserve, the entire volume of the magnitude of the main function of an organ, tissue, cell using a meager volume already "dead" - lifeless biological tissue (small sample or biopsy), and this is performed outside the body[4, 9, 13] . Later it became clear to us that QFM is, in fact, a universal method of systems analysis, and that it is applicable and can be applied to almost all organs, tissues, cells. This approach can be used to determine the margin of safety, the volume of the compensatory reserve of various systems: physical, even political, social and economic.

### II. MATERIAL AND METHODS

The studies were carried out on tissue samples of the heart, lungs, liver, kidneys, skeletal muscles, placenta and the brain of humans and experimental animals: mouse, rat, cat, dog, and on the flight muscles of a house fly, wasp, and dragonfly [Figures 1,2,3,4,5]. The studies were carried out by methods of electrophysiological recording of the brain, perfusion fixation of organs, histological, electron microscopic, semithin sections, ultraviolet irradiation of sections, morphometry, stereology, image analysis, statistics and mathematical modeling. Image analysis was performed using specially developed eyepiece grids and the ImageJ2x computer program. A number of patented or know how techniques have also been used [5].

Apparatus used: installation for perfusion fixation with controlled perfusion pressure, sled microtome, ultramicrotome LKB III, ultraviolet lamps, electron microscopes EMV-100L, Tesla BS500, Siemens, computer Samsung.



Figure 1. Cross cut pattern of the human heart muscle band from left ventricular wall. Small circles are myocardial capillaries. Light microscopy, 1500x. Stained with modified PAS method.



Fig. 2. Cross section of rat's healthy heart muscle cell surrounded by capillaries. Dark spots are mitochondria. Electron microgram, 5000x.



Fig 3. Longitudinal section of swam rat's heart muscle cell. Alternation of mitochondrial (darker) and myofibrillar (light grey) columns. Electron microgram, 25 000x.



Figure 4. Cross cut muscle cell of wasp flying muscle. Dark areas are mitochondria. Electron microgram, 6000x.



Figure 5. Single healthy human placental villi. Three circles inside of villi are capillaries. Electron microgram, 5000x.

## III. THE MAIN PRINCIPLES OF METHODOLOGY

The known Swiss scientist Ewald Weibel developed a method for measuring the diffusion capacity of the lungs on histological sections [21, 23, 24]. The method is described in paper over 12 pages. Later, we developed independently first for myocardium, then for lungs and other organs, methods for which the goal is the same - measuring the functional capacities of organs in histological sections under a microscope. In the end, we both came to the same result, but in completely different ways. Our method was first developed and tested on the myocardium, cardiomyocyte and received the title of Quantitative Functional Morphology [5].

The QFM foundation is based on at least ten main principles, of which, for example, some can be listed.

In mathematical modeling, the role of the system-forming factor is played by time.

A virtual simplification is applied to the system.

The model takes into account the parameters of both static structures and the values of the indicators of dynamic functional processes.

The model considers the system under study as an open dynamic system that is - functioning in equilibrium.

The mathematical model has a modular structure. The number of modules can be increased if necessary.

Each module can be strengthened, enriched with new indicators, which, on the one hand, provides a higher

measurement accuracy, and on the other hand, it can complicate the module and make it cumbersome.

In the basic mathematical model, an essential, not all unambiguously perceived method of replacing the values of functional parameters with digital coefficients is used. These coefficients reflect the ratio of the magnitude of each functional indicator to the value of the functional indicator which is located and acts at the very beginning of the system.

The application of this principle has proven itself in practice. They helped to make the model practical, easy to apply.

The studies of some organs and tissues have revealed that the logic and algorithm for applying the QFM approach are universal for many biological structural systems, tissues: for example, the heart muscle at the tissue level, in other words: the "capillary-myocardial fiber" system, cardiomyocyte, skeletal muscle, lung tissue, placenta, liver, brain [4,6-8,9,13-18], [Figures: 1-5]. The most detailed method was developed for the cardiac muscle and cardiomyocyte.

At present, the brain is also the object of our research. Specialists in information technology, neurophysiology, and neuropathologists are seriously interested in the first results of these studies [16, 17, 20]. Certain parallels can be traced between the biological brain and supercomputer between the rates of the processes of obtaining and accumulating information, its processing, storage, reproduction, in the synthesis of new knowledge, in the creation of new types of logistic, prognostic, futurological knowledge and conclusions.

Our studies have shown the efficiency of the QFM methodology on the brain of humans, laboratory rats and mice in normal conditions and under various effects on the body: chronic alcohol poisoning, exposure to various doses of snake venom. Normally, the results of measurements of "brain power" through the QFM study positively correlate with the value of the total specific electric potential per unit volume of the gray matter of the cortex, hypothalamus, and hippocampus of the brain. In pathological conditions, the positive correlation of the decreased indicators of "brain power" measured using the QFM method and with the help of electrophysiological measurements is preserved.

## IV. PITFALLS

In the course of research, various "pitfalls" are periodically discovered that impede their conduct, affecting the accuracy of research. These obstacles must be circumvented, overcome. This is especially obvious in the QFM study of the brain, when the shape, diameter of the lumen of the capillaries, their walls strongly react to the effects of external and internal factors, such as the cause of human death, experimental factors, and the type of slaughter - euthanasia of animals [Figures: 6-7]. We are currently working on this issue.



Figure 6. Cross cut healthy rat heart muscle band of left ventricle. Semithin section stained with methylene blue, 100x.



Figure 7. Cross cut healthy rat heart muscle band of left ventricle. The animal was perfused under control pressure. Semithin section stained with methylene blue, 100x.

Along with this, the tasks of achieving complete and simultaneous optimal visualization of the structures of a neuron, its axon, dendrites, synapses, for their further stereological study are also important. In the case of the model brain, due to the multiplicity of levels of organization and the multiplicity of structures involved at each level, the mathematical equations are more likely to be grouped into two or three independent, but complementary equations.

### V. WHAT MAY "GIVE" QFM TO FUTURE BRAIN?

The capabilities of QFM in tissue engineering of myocardium, organ fabrication of the heart were shown earlier [18]. The QFM methodology can take on the role of an architect of tissue engineering and organ fabrication of the brain, when it can represent those parameters - characteristics of individual brain structures (vessels, neurons, neuropil, axons, dendrites, synapses) and their spatial relationships, which ensure the maximum functional capacity of a given biological structural system, in particular the whole brain or its distinct parts: cortex, hippocampus, amygdale.

### REFERENCES

- G. Avtandilov, "Fundamentals of quantitative pathological anatomy". *M. Medicine*, 2002, 238 p.
- [2] Bertalanffy L. von, *General systems theory*. Foundations, development, applications, 2 ed., N.Y., 1969.
- [3] Bertalanffy L. von, Trends in general systems theory, N.Y., 1972.
- [4] T. Ghevondyan, "Mathematical model of heart muscle cell". All-union 2-nd conference on actual problems of informatics and computer techniques, pp. 175-176, Yerevan, Armenia, 1987.
- [5] T. Ghevondyan, "A method for evaluating the contractility of a cardiomyocyte". Author's certificate of invention, No. 1446523, 1988, Bull. Discoveries and Inventions No. 47, Moscow, Russia, 1988.
- [6] T. Ghevondyan, "Systemic morphofunctional assessment of ultrastructural organization and pathology of myocardial cells". *Gegenbauers Morphologisches Jahrbuch* 1989, 135/1, 195-197.
- [7] T. Ghevondyan, "To the problem of liver quantitative functional morphology". In the book: *Modern aspects of reconstructive surgery*, pp. 103-104, Yerevan, Armenia 1994.
- [8] T. Ghevondyan, "Quantitative functional morphology of lungs". In Materials of the Annual Conference of the Yerevan Scientific Research Institute of Experimental and Clinical Surgery, pp. 231. Yerevan, Armenia, 1995.
- [9] T. Ghevondyan, "Quantitative Functional Morphology. Fourdimensional assessment of the morphofunctional state and pathology of the cell". *In materials of the 6-th All-Russian Conference on Cell Pathology* (with international participation), pp. 50-51. Moscow, Russia, 28-30 November, 2000.
- [10] T. Ghevondyan, K. Ghevondyan, "To the question of applicability of main principles of "Quantitative Functional Morphology" for placenta". In Annual Congress of Armenian Society of Electron microscopy, pp. 36, Yerevan, Armenia, 2000.
- [11] T. Ghevondyan, "Quantitative functional morphology of heart muscle", Abstract of a thesis for doctor of medical sciences, Yerevan, Armenia, 2001. 21p.
  [12] T. Ghevondyan, "A novel method of Quantitative Functional "in method."
- [12] T. Ghevondyan, "A novel method of Quantitative Functional Morphology, assessing contractile reserves of myocardium using histological sections", 20-th European Congress of Pathology. Abstracts. Virchows Archiv, August vol. 447, no. 2, p. 462, Paris, France, 3-8 September, 2005.
- [13] T. Ghevondyan, "Quantitative functional morphology neologism, method or way of thinking"? *Proceedings of the 2-nd Congress of the Russian Pathologists Society*, p. 312-314, Moscow, Russia, 2006.
- [14] T. Ghevondyan, "New opportunities of Quantitative Functional Morphology in the light of virtual microscopy and telepathology". Book of abstracts. VIII European Congress on Telepathology and 2-nd International Congress on Virtual Microscopy, p. 47, Budapest, Hungary, 6-8 July, 2006.
- [15] T. Ghevondyan, H. Ghevondyan, "A step towards mathematical modeling of neuromuscular junction". *Abstract in Materials of the XVI Congress of the International Society of Ultrastructural Pathology*, p. 149. Regensburg, Germany, 06-12 August, 2012.
- [16] T. Ghevondyan, Developing cognitive models by stereological measurements of cerebral cortex. *Proceedings of the Conference* "Computer science and information technologies", Yerevan 2017, pp. 71-73.
- [17] T. Ghevondyan, A step closer to measuring "brain power" under a microscope in histological preparations. *The new Armenian Medical Journal*. vol. 11, (2017), no. 3, Supplement, p.19.
- [18] T. Ghevondyan, «Quantitative functional morphology as an architect for tissue engineering and organ fabrication in the field of preventive cardiology». *Abstract Book of the 5th International Medical Congress* of Armenia. pp. 55-6, 2019.
- [19] T. Ghevondyan, New paradigm, its place in science and practice. *Proceedings of the Georgian National Academy of Sciences*, vol. 45, no. 3-4, pp. 91-92, 2019.
- [20] T. Ghevondyan, Is there a key for unlocking the Mechanisms of the futurological Abilities of the human brain. *Abstract in Materials* 5th Neurological Disorders Summit (NDS-2019), p 57.
- [21] T. Mattfeldt, Stereologic methods in pathology. Norm Pathol Anat (Stuttg). 1990; 52:1-300. PMID: 2195466 Review.
- [22] S. Saltykov, Stereometric metallography, M. Metallurgy, 1976, 271 p.
- [23] E. Weibel, Morphometric estimation of pulmonary diffusion capacity. I.Model and Method. Respiration Physiology, 1970/71, vol. 11, pp. 54-75.
- [24] E. Weibel, Stereology a bridge between morphology and physiology. Acta stereol. SFRI, 1982, vol.1, no.1, pp. 23-33.