УДК: 576.311.3+57.085.2+576.32.34

IS IT POSSIBLE TO CONSIDER «KINETOMICS» AND «ARGYROMICS» AS NOVEL TRENDS OF FUNCTIONAL MORPHOLOGY AND SYSTEMS BIOLOGY OF PARASITIC AND NONPARASITIC *PROTOZOA*? A BRIEF ANALYTICAL REVIEW

Oleg V. Gradov

Institute for Energy Problems of Chemical Physics, Russian Academy of Sciences; Institute of Biology and Chemistry, Moscow Pedagogical State University, Moscow, Russia

O.V. Gradov
38/2 Leninsky prospekt, Moscow, Russia 119334
E-mail: gradov@chph.ras.ru, gradov@center.chph.ras.ru, gradoff@bioinformatics.ru

Abstract. This paper considers argyrophilic (i.e. stained by the silver nitrate) fibrils visualized by the well-known Klein method and later called neuroformative system of *Protozoa*, or neuroformium. Klein described the excitation wave propagation and coordination of the cilia moving by this network, as well as the main role in localization of the peristomes and the ciliar apparatus on the topographic microanatomy map of *Protozoa* before and after the cell division. However, in early 1930-th the advanced staining techniques revealed two components in the above mentioned fibrill network with the similar morphobiochemical parameters (within the limits of the silver nitrate staining selectivity), one of which provides the mechanical stabilization of the *Protozoa* body (a number of *Paramecium* species were found to possess even a third selectively-stained fiber system). This resulted in the introduction of the term "argyrome" by Chatton in 1936 for the complex of the argentophilic fibrils and a term "cinetome" for the subpellicular infraciliature. It is therefore more appropriate to speak about "kinetomics" and "argyromics" rather than of a single "omics" for all the intracellular networks of *Protozoa*. We consider the principles of introduction of the novel "-omics" in modern science and from the above standpoint discuss whether it is possible to consider "kinetomics" and "argyromics" as the novel trends of functional morphology and systems biology of *Protozoa*.

Keywords: systems biology, kinetome, argyrome, *Protozoa*, *Ciliata*, "-omics" approaches, subpellicular infraciliature, neurophanes, neuromotor apparatus, neuroformative system, neuronemes, neuroformium, history of biology, history of protozoology.

Introduction: What is "omics"?

There is a general tendency in the contemporary cell biology to divide sub-disciplines in accordance with the morphological / ultrastructural and biochemical (selective staining) criteria. This classification considers the type of the compartments, organelles or subcellular localizations / morphobiochemical targets of the sighting study. This means that for any cytophysiological and ultrastructural unit one can introduce a corresponding sub-discipline, and hence, discover a "new field of science". A special name is given to every newly introduced branch of cell biology. This gives rise to the so-called "omic trend" in the cellular biology, because it is conventional to assign such areas and fields of research as "…-omics". The Oxford English Dictionary (also abbreviated as OED) distinguishes between the different meanings of the -ome suffix, including "a part of an animal or plant with a specified structure" for zoology and "all constituents considered collectively" for cellular and molecular biology. Consequently, it may be classified into the two types by the morphological / ultrastructural criteria (the first type) and biochemical selectivity (the second type). This classification will help us to understand the meaning of the applicability of new types of "omics" for protistology.

For example of morphological classification units see: membranomics for membranous structures (Ghosh, 2008; Shimanouchi, 2012); plastidomics or plastomics for plastids (Laukers, 2004; Navarro, 2004); chromonomics for chromosomes (Willard, 1999); mitochondriomics for redox-active interactions in chondriome (Reichert, 2004) and mitointeractomics for protein interactions in chondriome (Reja, 2009); cellomics (Taylor, 2007; Yasuda, 2012) and cytomics (Kriete, 2005; Valet, 2005; Schubert, 2006) for cells and cellular systems biology; histomics or tissomics for different living tissues (Ecker, 2005; Kriete, 2006); and, furthermore, phenomics – for phenotype and its physiological and morphological lability and reactivity (Furbank, 2011; Berger, 2012; Matsubara, 2012; Naika, 2013).

Many professional morphologists object to this classification. They point out that "no forward-looking biological meaning can be attached to this trend and to the new sciences", because "the results of our morphological investigation are not affected if our disciplines will be called as an "-omics" in a new fashion" and "strictly speaking, such a renaming is meaningless". But such a view is clearly a misunderstanding of the contemporary systems biology approaches and the methodology of the semiautomatic data mining in the computational biology and, consequently, in the peculiarities of the novel biological data which can not be processed using non-automatic, non-computational and non-mathematical research techniques. But novel complicated experimental techniques have made it possible and thus, we have a necessary and sufficient condition for an "omics trend" usability in biology (when other data processing methods are impossible or pointless). Nevertheless, there are many dangers in the use of the indiscriminate "omics" introduction into the general biology, when it is unreasonable in accordance with the above criteria. One source of confusion is the tendency for single structure emphasizing for any omic promotion without taking into account the relationships and interactions between different structures and processes in the living cell. This tendency contradicts to the system biological approach. Currently there is no satisfactory definition of systems biology, but we can now perform a more systematic study of the objects of different "omics" using multiple "omics" approaches (Zhang, 2010; Droste, 2011; Kayano, 2013; Kohl, 2014).

Consequently, to avoid any possibility of confusion we shall verify the morphological "omics" conclusions using biochemical "omics" antecedents. The best and the most complex conclusion for "omics" data mining is that obtained from the morphobiochemical data using colocalization studies and selective morphometry of spatial distributions and singular localizations of biochemical agents in cells. Early investigators used to ignore the spatial distributions of chemical agents in cells, but not in biochemical pathway network hierarchy. Hence, early systematizations of sub-disciplines according to "omic" hierarchy were performed in the frame of the organic chemical / biochemical principles. Such sub-disciplines (omics) were named on the basis of their chemical substrate implementations, such as: chemogenomics (Namchuk, 2002; Bredel, 2004; Wuster, 2008; Cheung-Ong, 2012; Wang, 2014; Brown, 2014), which is not fully

equivalent to chemical genetics (Carlson, 2012; Jung, 2014); interferomics – a science about interfering RNAs (Reddy, 2013); lipidomics – a science about lipids and cellular fats (Lagarde, 2003; Kagan, 2004; Wenk, 2005); eicosanomics – a science about eicosanoids (Balazy, 2004); glycomics – a science about sugars (Kheronsky, 2003; Lubner, 2003; von der Lieth, 2004; Mrksich, 2004); ionomics – a science about ions in living cells (Salt, 2008; Baxter, 2009; Baxter, 2010; Danku, 2013); metalloproteomics – a science about metalloproteins (Shi, 2008; Barnett, 2012; Fu, 2014; Roberts, 2014) and similar metallomics as a science about the metal functions in living cells (Szpunar, 2004; Lopez-Barea, 2006; Szpunar, 2006; Mounicou, 2009); proteomics – a science about proteins (Geisow, 1998; Persidis, 1998; Müllner, 1998); kinomics – a science about enzymes-kinases (Johnson, 2005; Gomase, 2008; Vieth, 2005); phytochemomics – a science about phytochemical bioactive agents (Amigo-Benavent, 2014). Many principles of similar sciences can be automatically extended to the case of protistology – as complex principles for comparative colocalization morphology of the *Protozoa* species. In this paper we prove a generalization of this approach on *Protozoa* cytology / protistology using a conventional morphobiochemical approach based on the selective staining of the compartments of living cell.

Requirements on the protistological "omics"

Our first concern is to describe the systematic methods for distinction between the types of the stained microstructures in the frame of the "omic" approaches. Generally, there are various reactions for an accurate determination of different biochemical agents (as the objects of different "omic's" studies) in the living cells, based on the selective staining principles. For example, immunofluorescence can visualize and semi-quantitatively determine different types of biochemical agents using general coordination and supramolecular chemistry principles, such as non-covalent interactions and complementarity (the "lock-key" principle in its "antigen-antibody" implementation), etc. Similar determination methods are analogous in some aspects to the "mapping of the immunomic functions and the immunogenomic agents (or complements)" (Klysik, 2001; Brusic, 2003; Schönbach, 2003). This technique provides a rational basis on which the morphologists can make conclusions about different cell components. This approach can be extended by the simple general-biological interpolations to the *Protozoa* morphology not only because immunofluorescence staining methods are applicable for protistological / protozoological studies from 1960 till now (Zaman, 1965; Zaman, 1966; Dzbenski, 1966; Hauser, 1980; Kovac, 1980; Ohba, 1986; Brugerolle, 1988; Olins, 1989; Allen, 1990; Turkewitz, 1992; Dohra, 1994; Hanyu, 1995; Hanyu, 1996; Clerot, 2001; Santangelo, 2001; Strzyzewska-Jówko, 2003; McLaughlin, 2004; Itabashi, 2004; Kissmehl, 2004; Ramoino, 2004), but also because the simplest inorganic staining agents may be used for visualization of several compartments and constituents of the *Protozoa* cells (even without the antibodyome agents (Mohebbi, 2009; Zhu, 2013)). Notwithstanding, there is no case of determination of the different "omics" characteristics using inorganic dyes. In the microscopy practice, the investigator cannot always predict whether the staining agents are really specific for the stained compartments compositions or ROI (i.e. regions of interests) when using an inorganic dye without the "imbedded" molecular selectivity site(s). From the above we conclude that morphological "omics" based on the inorganic or bioinorganic determination (staining) agents can be used as the alternatives for the immunomics or other antibodyome-based dyes if and only if the visualization of the target compartments or biochemical constituents in the stained cell is equivalently effective both for inorganic-stained samples or living cells as well as for bioorganic-stained samples or living cells.

According to the hypothesis of colocalization microchemistry of the analyzed indicators, the cell components and the property / activity maps with the involved systems biology descriptors and pathways (Gradov, 2014; Orehov, 2014; Orehov, 2016) which form the basis of the "omics" targets, it is of great interest to consolidate the above listed descriptors using the principles of multimodal imaging morphochemistry (Vogler, 2010) and morphophysiology (Welsh, 1994). Thus one can speak about the morphochemistry-based "omic", when the physiological and biochemical basis of ROI is taken into account and considered in the frame of the methodologies and techniques of

systems biology. A comprehensive approach must account for the integration of the biological hierarchy levels from proteins to compartments and organs / organoids in the frame of physiomics (Hunter, 2003; Gomase, 2008) for bio-mathematical model representations, implementations and interpretations based on the data mining principles (Britten, 2013). Also this approach must be modified in order to explain the fact that both internal and external regulation is the basis of physiological functions and, therefore, a quantitative imaging of ROI must be based on the quantitative mapping of the "metabo-regulome" (Okumoto, 2008) in the frame of regulomics of life as the form of existence of the protein bodies (Werner, 2003) (but without immunofluorescence this approach can not be applied for immunoregulomics (Tassinari et al., 2008)). However, these approaches do not explain the effects of the environmental agents and factors despite their significant and irremovable action on the morphology and physiology of *Protozoa*, as well as *Metazoa* (also as Plants). It also must be borne in mind that protistological objects are exposed to those factors and thus one can speak about the *Protozoa* exposome and the *Protozoa* exposomics (Buck Louis, 2012; van Tongeren, 2012; Miller, 2014; Vrijheid, 2014) at phylogenetic (including the local adaptations or / and microevolution) and genetic levels, including biobehavioral and geospatial (in the frame of population biogeography) aspects (Stahler, 2013; Lyon, 2014). But even at this stage we can project the phenomic phenomena of the "normal" physiomics modified by exogenous exposomic factors influence on the morphology of single cell or *Protozoa* organization using the analytic morphomics (Engelsbe, 2012; Englesbe, 2012a; Miller, 2014) and the timing-based analytic morphomic methodologies and approaches (Rinkinen, 2013; Ranganathan, 2014), interpolated from the human / animal (*Metazoa*) organization level to *Protozoa* considered both as the organisms and as single cells.

Which of the morphological and ultrastructural *Protozoa* compartments or organelles / organoids is most suitable for this novel "omics" as a proof of concept of the "morphophysiologically selective staining" (except from the objects of antibodyomics and immunomics)? The result of considerations depends on the fact that unicellular organisms in contrast to multi-cellular ones can not be analyzed by means of the standard "organomics", such as connectomics for neurosciences (Lichtman, 2008; Kennedy, 2010), epithelliomics (from "epitheliome") for covering tissues (Walker, 2004) etc., but their functional equivalents should inevitably be integrated into protistology, because the functionally corresponding structures really exist. Furthermore, it's generally known that some early classical protistologists developed a number of similar hypotheses / theories about the physiological correspondence between the compartments or organoids of the *Protozoa* cells and the multi-cellular organs of *Metazoa*. In accordance with the approach outlined in the first section of this article, we propose that each element of the *Protozoa* compartmentalization can be assigned to a one or more multi-cellular organs of *Metazoa* and each element can be characterized by two "omic" descriptors from morphology and biochemical physiology.

From kinetome and argyrome towards kinetomics and argyromics

The simplest example of such a hybrid morpho-physiological mapping and imaging data mining is the mapping of a pool of the contractile fibrills and conductive strands of *Protozoa*. The problem of existence of the special system of conductive fibrills in *Protozoa*, which are partially similar in their function to the nerve fibers of *Metazoa* and capable of coordination of the organoid activity in *Protozoa,* was comprehensively studied at the beginning of the XX century, although as early as in 1890 a detailed description of a myonem system in *Stentor* was given, which demonstrated a rapid reaction / response to different stimuli via a quick body contraction (Schuberg, 1890). The basis for the neural-like structure-coupled activity mapping was laid out at the beginning of the XX century when the novel staining method revealed a new system of fibrills – neurophanes which were expected to function as the conducting nerve fibers (Neresheimer, 1903). In *Stentor* they diverge at an angle and are parallel to the myonems, but differ from them in the affinity to different dyes, which allows to distinguish between them in the course of the mapping procedure. The same substances which are known to be the paralyzing agents for the nervous system of

Metazoa cause a similar effect in *Stentor*, since they affect the neurophanes. There is also a similarity between the neuromuscular relations in the topographic anatomy of higher animals: the neurophanes were shown to possess branches contacting with the myonems. Other *Protozoa*, such as *Diplodinium (Epidinium) ecaudatum* (a ciliate from the order *Enlodiniomorpha*) possess a fiber system, directed to the myonems as the moving organs. The above system was called motorium, and together with the fibers with the outcoming fiber bundle it was called a neuromotor apparatus (Sharp, 1914). The fiber bundle from the motorium goes to the point providing a sensitive character of the above apparatus. Sometimes there is also a number of additional centres (described at 1933 (Powers, 1933) for the first time) which sustain the functional activity of the general motorium.

Only motorium and micronucleus can be visualized by Mallory staining, although Mallory's trichrome stain (aniline blue + acid fuchsin + orange G) provides visualization of other cellular structures. A combination of the three different stains in precise amounts applied in the correct order reveals the structural details selectively. This results from more than just electrostatic interactions of the stain / dye with the tissue and the stain can not be washed out after each step. Collectively the stains complement one another (a so-called spectrozonal colocalization). We are already familiar with the fact that different Mallory staining method variations can be used for a large number of cellular constituents and tissues, different in their biochemical characteristics: keratin (Ayoub, 1963) and keratin aggregation products (Nan, 2006); inorganic agents, including heavy metals, such as lead and copper (Mallory, 1939); genetic molecules – RNAs (Chieffi Baccari, 1992); conductive nervous media components (Schümperli, 1977); electrostatic inert, inactive connective tissue matrixes (Cason, 1950) and secreting glands (Gude, 1953), etc. Thus, there is a close analogy between the classifications of various Mallory stained tissues and the possible "omics" for descriptor-based distinction and mapping-based differentiation of these tissues.

As an example of practical importance we consider a comparative projection of descriptors of the secreting cells (or tissues) to the subspace of the micro-colorimetric measurement results of the Mallory stained sample analysis in the frame of the secretome expression concept (Zwickl, 2005; Martinez, 2006) and comparative "secretomics" (Lamonica, 2005; Sibbald, 2006) which can also be used for the parasitic protozoa-related phenomena (Przyborski, 2004). A less trivial example is the relation between metallomics or microelementomics (Li, 2008) and an old Mallory method of lead and copper determination (Mallory, 1939), because to the best of our knowledge the methods of cellular metallomic and elementomic mapping have not yet been developed. A more intriguing example is the correlation between connectomics (Lichtman, 2008; Kennedy, 2010) and the topography of neurophanes (Neresheimer, 1903) and similar elements of the *Protozoa* body (as a simple example of the convergence or parallelism or pseudo-homology between *Protozoa* and *Metazoa* organizations), based on the semblances or propinquities of the Mallory staining results of the nervous media (Schümperli, 1977) and a neuromotor apparatus of *Protozoa*, as well as the relations between histomics or tissomics (Ecker, 2005; Kriete, 2006) of the synaptic neuromotor connections and the complexes of *Metazoa* and the neuromotor apparatus conjunctions or the branches of neurophanes, contacting with the myonems or spasmonems (Febvre, 1981). "The first point favoring the idea that the neuromotor apparatus is of a truly nervous character comes from animals stained with Mallory's connective-tissue stain" (Barrows, 1935). This illustrates our thesis about the necessity and inevitability of the development of new specialized "omic" for the systematic description of the *Protozoa* elements, functionally equivalent to the elements of the nervous "connectomics" of *Metazoa* or the neuromotor apparatus "physiomics".

If we introduce new terms for defining new research sub-branches, we cannot avoid multiple verification of our understanding of the subject under investigation, using alternative methods. Actually, it is not quite true to say that we have a new object of the analytic morphomics (Engelsbe, 2012; Englesbe, 2012a; Miller, 2014) if we use only one method for its structure determination. But the only method available to us from the foregoing text is Mallory staining. Although this is a reasonable visualization for our region of interest (ROI) as a morphomic descriptor, it would be wrong to postulate that it is not only necessary but also sufficient for the introduction of a novel entity, such as new "omics". It follows historically from the fact that the understanding of the

neuromotor apparat, neurophanes and motoriums, since their first introduction have been sometimes criticized by a number of morphologists (Ten Kate, 1927; Ten Kate, 1928; Bretschneider, 1934) and then confirmed by the other ones (Fernandez-Galiano, 1949; Noirot-Timothée, 1958; Noirot-Timothée, 1960) in a different from the initial meaning and morphophysiological sense. Besides, we need purely inorganic methods of the structure visualization, since the selectivity of the most staining methods using the organic dyes can be attributed to the specific bioorganic interactions. Therefore the control staining method should avoid any biochemical interactions but it should also provide an effective visualization of the ROI.

An alternative approach to the visualization of the subpellicular microtubules or subpellicular infraciliature is either Ag or Au impregnation using the corresponding metal salts. This method was also developed at the beginning of the last century (Schuberg, 1905). Argyrophilic (i.e. stained by the silver nitrate) fibrils visualized by the well-known Klein method (Klein, 1926; Klein, 1927) and later called neuroformative system of *Protozoa*, or neuroformium (Klein, 1943), together form a kind of network similar to the connectome of *Metazoa*. Klein described the excitation wave propagation and coordination of the cilia moving by this network, as well as the main role in localization of the peristomes and the ciliar apparatus on the topographic microanatomy map of the *Protozoa* before and after the cell division. However, in early 1930-th the advanced staining techniques revealed two components in the above mentioned fibrill network with the similar morphobiochemical parameters (within the limits of the silver nitrate staining selectivity) (von Gelei, 1932; von Gelei, 1937), one of which provides the mechanical stabilization of the *Protozoa* body (a number of *Paramecium* species were found to possess even a third selectively-stained fiber system). This resulted in the introduction of the term "argyrome" by Chatton in 1936 for the complex of the argentophilic fibrils and a term "cinetome" for subpellicular infraciliature (Chatton, 1936; Chatton, 1937). It is therefore more appropriate to speak about "kinetomics" and "argyromics" rather that of a single "omics" for all intracellular networks of the *Protozoa*.

The initial idea of combination of all the argentophilic structures into the argyrome without considering the recent physiological, biochemical and ultrastructural data could lead to a simplified understanding of these structures as a mechanical network. According to the first electron microscopic observations of those structures (Metz, 1953; Sedar, 1955), the bundle fibrillar structure morphostructurally corresponds to the neuronemes or kinetodesmes, but there was no synapse-like connection observed between them in the pioneer works, while the other workers (Randall, 1958; Ehret, 1959; Yagiu, 1959) argued that many fibrils from several neighbouring kinetosomes can be connected to the kinetodesmic fibril. Coordinated motor activity of the cilia (Párducz, 1954) with the high level of reactivity to the electrostatic and electrodynamic sources and monovalent cations until the reverse movement of the cilia, provided by the fibrillar ectoplasmic structures with the system acetylcholine + cholinesterase localized within the ROI (Seaman, 1951; Seaman, 1951a; Seaman,1952), indicates the presence of a kind of similarity between some network structures in *Protozoa* and their neurophysiological / electrophysiological homologs and "hierarchical prototypes" of the high level connectome self-assembly in *Metazoa*. For a more detailed understanding of this discussion, see a fundamental Dogel's handbook (Dogel, 1965).

We do not present here a systematical development of this subject, but just propose a new approach and sub-disciplines ("omics"). A detailed discussion of such problems is beyond the scope of this paper, but we expect to publish our further results and considerations within several years. The structural changes of "argyrome" and "kinetome" ("cinetome" in French) induced by "regulomics" and "enviromics" are of special interest (Neiderhiser, 2001; Texiera, 2011). It is well known that "according to the A. Lwoff's (Lwoff, 1990) hypothesis the modifications of the argyrome pattern … are associated with the rearrangement of the cortical proteins" (Dovgal, 2002) and, priory, that "the ontogeny took place in any Ciliates and began from the moment of anlage the fragment of tomit kinetom" (Jankowski, 1972). Little is known about the role of the kinetome and argyrome morphogenesis in the formation and stabilization of the "neuromorphic" functions of *Protozoa*. The topology and topography of "kinetomes" undergo evolution in the course of the

development and the adaptive changes in *Protozoa*. The topology of kinetomes was determined using the silver impregnation method (Chatton, 1930; Corliss, 1953) which used to be rather popular not only in France where it was initially developed, but also in Germany as "protargolimprägnation" based on the principle of the "protargolaffines" of the dried ciliates to the protargol, which results in the stained sample (protargolpräparaten) with the inactivated ciliates (Krainer, 1995). Despite the fact that the above method was widely used until recently in the CIS and Russian Federation (Alekperov, 2006), as well as in Asia and Africa (Quyen, 2014), the dry sample preparation by the Klein method described above is not a vital staining method. Only recently a number of woks have appeared describing the novel modifications of protargol impregnation staining for live observations (Hu, 2001). This previously existing limitation corresponds to the fact that Ag^+ ions and clusters in certain concentrations are very strong and active toxins and biocides. It should not be overlooked that "kinetome" is a term from "physiomics" (because dynamical elements, as well as kinetids are physiologically active), while "argyrome" is a biochemical and morphometrical (i.e., morphobiochemical) term from "morphomics". Consequently, "kinetomics" + "argyromics" = "dynamomics" + "localomics" according to the Parkinson systematics (Gradov, 2014). It is obvious that both dynamics and localization can be studied simultaneously only within the living object. Although vital Ag^+-based staining methods may affect the "dynamomics" leading to the artifacts, for the "localomics" studies non-vital methods produce much more artifacts due to the postmortem effects. Modern histochemical methods, such as FISH (fluorescence *in situ* hybridization) allow to study the kinetome and "kinetomics" *in vivo* (Modeo, 2013), but the full correspondence between the terms "kinetome" and "argyrom" in the old papers and in the recent works can be achieved only if the old staining methods using inorganic protargol staining on the one hand and the Mallory staining on the other hand) and the new visualization techniques (FISH and immunofluorescence) result in the colocalization in the ROI visualization (i.e. the ROI of the corresponding "omics").

Prospects of the development of the new "**-omics**"

With the development of the novel comparative system-biological (omical) approach the earlier classical papers considering kinetoms (cinetomes) and argyroms (argyromes) (for example, see: (Kaczanowski, 1970; Sapra, 1970; Ky, 1971; Wilbert, 1986; von Foissner, 1989; Wasik A, 1994) etc.) will still remain relevant and one will be able to revise them in the frame of the structure and function unity, i.e. both from the standpoint of statics and dynamics. At the same time the conventional silver staining method which has been standard for many years will also remain useful regardless of the further developments. This can be provided by the implementation of the alternative non-optical forms of the analytical signal registration. The simplicity and wide applicability of such methods as protargol impregnation staining and the Mallory method variations (Cason, 1950; Gude, 1953; Roque, 1953; Churg, 1956; James, 1961; Mazzugo, 1982; van Leeuwen, 1990) allows to expand the boundaries of the detection principles for the stained samples. A comprehensive analysis of the above possibilities based on the physical descriptor mapping (Orekhov, 2014; Orekhov, 2016), such as the redox state (Gradov, 2013), determining the staining intensity through the medium acidity and the plasmon resonance on the small Ag clusters, is beyond the scope of this paper and will be partly considered in our forthcoming papers. Since mass-spectrometry is known to be a routine analytical method for the biochemical "omics" (Di Girolamo, 2013) with the highest accuracy in detection of the biochemical analytes, especially for the spin-labeled ones, this method is expected to be a final "diagnosis" for the introduction of kinetomics and argyromics. In this case both Ag and other inorganic non-immunochemical agents for morphological staining can be used as MS labels for colocalization analysis. The above fact is consistent with the existing analytical procedures where Ag^+ labeling is applied for characterization of hydrogen-bonded supramolecular assemblies by MALDI-TOF mass spectrometry (Timmerman, 2000), as well as the silver nanoparticles (Shrivas, 2008), while for ESI MS detection Ag-staining is useful as a complementary method for Coomassie-staining (Winkler, 2007), and for the MS analysis combined with gel-electrophoresis combined radiolabelling and silver staining can be

successfully applied for visualization, localization, and identification of proteins or peptides (Westrook, 2001).

Due to their compatibility with the modern staining methods for MS and other "omics" methods, kinetomics and argyromics are expected to be useful not only in the morphological protistology, but also in the physiological and biochemical studies, such as classification and monitoring of the populations and communities of *Protozoa*, together with the other "omics" method – fingerprinting and the advanced analysis of the genetic polymorphism, introduced from genomics (Skotarczak, 2004; Przyboś, 2005; Zhang, 2006; Zhang, 2012).

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