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# Models of specialization in multicellular systems

PhD Dissertation summary
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**Statement of the problem**

Systems, containing a finite number of elements that can carry out one or several functions such that an increase in the performance of one function leads to a decrease in the performance of at least one of others (we will call these systems as multicellular systems), emerge when studying objects of completely diverse nature. In particular, aforementioned systems are widespread in economics, sociology, social anthropology, educational sphere, evolutionary and system biology. A possibility of specialization emergence is a core issue when studying the systems under consideration. An element is specialized in the performance of a certain function if it makes all its efforts on this function performance and does not invest in the performance of other functions. The system is called specialized if at least one of its elements is specialized.

A wide variety of theoretical and empirical works in different fields of science show that environmental factors, different importances of the functions performed, positional effects and heterogeneity of elements, as well as the number of elements in the system have a great influence on the possibility of specialization emergence. It is worth noting that not all aspects of these factors effect on the possibility of specialization emergence in systems are well-elaborated. This issue is investigated in the dissertation in a more general level in terms of abstract systems theory.

**Degree of results availability**

A specialization emergence issue in multicellular systems is studied in fundamental work of Rueffler and co-authors. There are a number of works by Russian researchers covering various aspects of the problem under consideration. In particular, the problem of modeling the emergence of specialization in multicellular systems can be attributed to the class of problems studied in the framework of system optimization. R. Michod, C. Solari, A. Nedelcu, S.

Gavrilets, Y. Ispolatov, M. Willensdorfer provide theoretical models for studying the emergence of specialization in multicellular individuals. One notice the wide recognition of the importance of the labor division phenomenon in the economic theory and social sciences, and highlight a number of works concerned the problems the labor division emergence modeling in various socio-economic systems.

**Objectives and goals of the research**

**Objective of the research**. The purpose of the research is to construct a new mathematical model of the specialization emergence in multicellular systems, taking into account the set of various factors that have a direct impact on the system.

**Goals of the research:**

1. to analyze foreign and domestic studies on the specialization emergence modeling in multicellular systems;
2. to construct a mathematical model capturing the influence of different environmental factors on the specialization emergence in multicellular systems;
3. to study the influence of a resource constraint type on the emergence of specialization;
4. to analyze a joint influence of elements' heterogeneity and environmental factors on the emergence of specialization in a system;
5. to investigate the influence of trade-off constraints and a number of elements in a system on the specialization emergence in the system;
6. to get biological interpretations of the obtained results.

**Relevance of the dissertation**

Systems containing a finite number of elements that are capable to fulfill one or several functions so that an increase in the performance of one function leads to a decrease in the performance of at least one of others, are common in different fields of study. The problem of the labor division emergence in aforementioned systems is fundamental. In particular, the emergence of cell specialization is one of the core issues in evolutionary biology, since the emergence of differentiated cell types leads to a structural complication of organisms and an increase in biological complexity. In evolutionary anthropology, the emergence of the division of labor in primitive communities is the engine for economic development. The issue of specialization may also arise at the level of a university system, when the problem of optimal distribution of tasks between universities is solved.

One infers that the identification of factors affecting the emergence of specialization in multicellular systems, as well as the development of theoretical approaches for this phenomenon investigation, is an important problem.

**Personal contribution of the author to the development of the problem**

All the results presented in this dissertation research have been obtained by the author personally. Propositions 1-3, presented in Chapter 2 of this work, have been formulated and proved in collaboration with Professor F.T.Aleskerov (NRU HSE) and with Professor V.Makarenkov (Université du Québec à Montréal). Propositions 4–12 presented in this research have been formulated and proved by the author personally. The results analysis and its interpretations in the framework of theoretical biology have been made by the author personally as well.

The results of the research were presented by the author as reports at the following scientific conferences, workshops and seminars:

1. All-Russian seminar „Expert evaluation and data analysis“, ICS RAS, Moscow, Russia. Topic „Evolution and the origin of multicellularity: a case of different types of cells“, September 24, 2014.

2. World Congress on Global Optimization, Gainesville, Florida, USA. Topic „Global optimal solutions and the origin of multicellularity: differentiation of types, energy constraints, curvatures of trade-off functions“, February 22-25, 2015.

3. All-Russian seminar "Mathematical modeling and system biology“, ICS RAS, Moscow, Russia. Topic „Evolution and the origin of multicellularity: a case of different types of cells“, March 04, 2015.

4. All-Russian seminar „Automatic control theory“, ICS RAS, Moscow, Russia. Topic „Models of specialization in abstract systems“, March 29, 2016.

5. Conference BIOMAT 2017, Steklov Mathematical Institute of RAS, Moscow, Russia. Topic „Modeling functional specialization of a cell colony under different fecundity and viability rates and resource constraint“, October 30 - November 3, 2017.

6. Conference „MOISEEV 100“, Dorodnicyn Computing Centre of RAS, Moscow, Russia. Topic „Models of specialization in abstract systems“, November 9, 2017.

7. All-Russian seminar „Mathematical methods of decision analysis in economics, finance and politics“, NRU HSE, Moscow, Russia. Topic „Modeling functional specialization of a cell colony under different fecundity and viability rates and generalized resource constraint“, December 20, 2017.

8. Workshop „Evolutionary Emergence of Life Cycles“. Max Planck Institute for Evolutionary Biology, Ploen, Germany. Topic: „Modeling functional

specialization of a cell colony under different fecundity and viability rates and generalized resource constraint“ October 26-29, 2018.

9. Autumn school „Current trends in decision-making analysis“, NRU HSE, Moscow, Russia. Topic: „Modeling functional specialization of a cell colony under different fecundity and viability rates and generalized resource constraint“, November 9, 2018.

**Description of the research methodology**

The methods of optimization theory, mathematical programming, convex analysis and calculus of functions of many variables are used in the dissertation research. The problems obtained within the framework of the dissertation research represent problems of mathematical programming with two types of constraints imposed: trade-off and resource constraints, and with a Cobb-Douglas type objective function. Resource constraint is defined in the form of inequality. Trade-off constraints can be specified both in the form of equalities and in the form of inequalities. The solution of the obtained problems is analyzed with the help of classical methods of finding the extremum of functions of several variables and the properties of convexity (concavity) of functions that define trade-off constraints.

**Theoretical significance of the research** consists in:

1. the development of new mathematical models of specialization in multicellular systems;
2. identifying the conditions leading to the emergence of specialization in multicellular systems;
3. the generalization of the form and the type of constraints affecting the functioning of the system.

**Practical significance of the research** consists in the fact that, the proposed mathematical models can be used in various fields of knowledge, such as evolutionary biology, economics, social anthropology, medicine, state and municipal management, both to increase the efficiency of system operation and to predict the evolution of these systems.

**Basic results presented to be defended:**

1. a new model of specialization in multicellular systems has been presented;
2. conditions (including those related to the external environment) that affect the emergence of specialization in the systems under consideration have been investigated;
3. modifications of the proposed specialization model, allowing to consider and investigate a wider class of restrictions imposed on the systems, have been developed.

**Scientific novelty of the work**

The following new scientific results have been obtained in the dissertation research:

1. a new model of specialization in multicellular systems, based on classical models and allowing to take into account the influence of various factors on the possibility of the specialization emergence, has been developed;
2. a comprehensive study of the environmental factors influence on the system efficiency and the specialization of elements in optimal states has been performed;
3. modifications of specialization models in multicellular systems, based on systems restrictions generalization, arising both at the level of an individual element and at the level of the system as a whole, have been elaborated.

**General research conclusions**

1. Within the framework of the dissertation research, a new model of the specialization emergence in multicellular systems has been proposed. The model allows to identify the influence of the following factors on the efficiency of the system: the different importance of performing functions at the system level, the amount of resource available to the system, the amount of resource required for the colony to carry out the first (the second) functions, heterogeneity of elements. The solutions structure of the formulated mathematical programming problem has been investigated. Three different cases of solving the problem under consideration have been highlighted. Moreover, it has been shown how the solution of the problem is changing for various forms of trade-off functions.

- It has been shown that Case 1 implies that the system can achieve the highest possible level of efficiency obtained if there is no resource constraint. It has been also shown that the optimum will contain no more than one unspecialized element, both with the homogeneity of all elements of the system and with the existence of elements of different types in the case of convex trade-off functions. The number of elements specializing in a particular function depends on the parameter of the relative importance of this function. Under the condition of trade-offs concavity and the absence of positional effects, specialization will not arise in the optimum at any values of function importances parameters. If all trade-off functions are concave and positional effects are presented, specialization can arise in the system with certain values of the model parameters. In particular, the necessary and sufficient condition for the emergence of specialization in the systems under consideration was obtained.

- It has been shown that Case 2 implies that the set of optimal strategies of the system is a set of states, characterized by the fact that each of these states

requires the system to have fix performance levels of functions. The set of solutions to the problem under study provide the system a wide range of possibilities for adaptation. It is also worth noting that the entire amount of the resource available to the system is fully consumed by this system.

- Case 3 is characterized by a large range of opportunities for specialization. A formal solution search algorithm has been obtained in Case 3 for concave and linear trade-off functions. For convex trade-off functions, the problem is reduced to a simpler optimization problem of a linear function on a certain compact set. Illustrative examples, highlighting some of the most interesting situations with specialization arises, have been presented.

Propositions that shed lights on the solution structure of the problem, as well as the conditions for the labor division emergence in some of the cases have been presented. Proofs of the presented propositions have been presented, and the results have been interpreted.

An interpretation of the results in terms of evolutionary biology has been proposed. One of the most interesting results is the large number of cellular phenotypes emergence in the presence of only two biological functions in the framework of Case 2. This question is closely related to the so-called size-complexity rule, which implies that the complexity of an organism increases as its size increases, and an assessment of the biological complexity of living beings.

2. Two modifications of the basic specialization model have been formulated and investigated. The first modification concerns the generalization of trade-off constraints. It has been proposed to consider trade-off constraints not in the form of rigid functional dependencies between the levels of functions performances of elements, but in the form of inequalities, when for a given fixed performance level of one function, an element can have a level of performance of another function

less than or equal to a certain value defining according to a trade-off function. The second modification concerns the generalization of the resource constraint, when the possibility of adding the so-called opportunistic behavior costs into the resource constraint has been considered.

Results on the structure of the posed problem mathematical programming problem solution with structural constraints in the form of inequalities have been obtained. Various cases solutions comparison of a problem with constraints in the form of inequalities and the corresponding problem with trade-off constraints defined as equalities has been made. In particular, it has been shown how the solution structure of the problem to be changed during the transition from structural constraints in the form of equalities to structural constraints defined by inequalities. Theoretical results, describing how the solution structure changes in a model with structural constraints in the form of inequalities depending on changes in the amount of resources available to the system, have been obtained.

A model modification has been developed, taking into account elements costs of the opportunistic behavior. The costs of opportunistic behavior imply the expenditure of system resources on combining the performances of both functions at a non-zero level within each element. The corresponding mathematical programming problem has been formulated, the solution structure of the problem has been identified in the case of a linear trade-offs. For the model with identical elements, a complete analysis of the problem has been carried out, the solution has been found in general form for all possible values of the resource constraint parameters. The cases with the emergence of specialization have been identified, it has been established how the structure of the solution changes when the total resource available parameter changes.

**List of publications in the topic of the dissertation**

The main results of the dissertation research are presented in the following publications:

Publications from the list of journals indexed by Web of Science and Scopus international citation bases (quartile Q1):

1. Tverskoi D., Makarenkov V., Aleskerov F. Modeling functional specialization of a cell colony under different fecundity and viability rates and resource constraint // PLoS ONE 13(8): e0201446/ doi: 10.1371/journal.pone.0201446. 2018.

Publications from the list of journals recommended by NRU HSE:

2. Tverskoi D. N. Mathematical model of the process of specialization emergence in colonial organisms. The case of different types of cells // Journal of Information Technologies and Computing Systems. 2017. № 2. PP. 24-32.

3. Aleskerov F.T., Tverskoi D.N. Modeling the influence of external factors on the emergence of specializatiom in abstract systems // Control Sciences. 2019. № 1. C. 26-31.

Other publications:

4. Aleskerov F. T., Tverskoy D. N. Life history evolution and the origin of multicellularity / NRU Higher School of Economics. Series WP7 "Mathematical methods of decision analysis in economics, finance and politics". 2014. No. WP7/2014/05.

5. Tverskoy D. N. Life history evolution and the origin of multicellularity: differentiation of types, energy constraints, non-linear curvatures of trade-off functions / Cornell University. Series arXiv:1512.04471 "q-bio.PE". 2015.

6. Aleskerov F. T., Tverskoy D. N. Life history evolution and the origin of multicellularity: the case of different types of cells / Cornell University. Series arXiv:1506.01985 "q-bio.PE". 2015.