

Technologies of Physics of Systems will help to realize ToxCast mission

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ABSTRACT

Technologies of Physics of Systems (TPS) are known to EPA through Project ISTC 3476p. TPS automatically extracted objective system knowledge about chemical toxicity from ToxCast data and provided (without human experts) system expertise, scientific understanding and rational explanation of generated knowledge.

Results:
1080 typical toxicity forms² (TTF) are obtained. Every TTF describes one definite **systemic toxicity effect** (STE). 784 of 1080 TTF are verified by ToxCast data¹, 296 are potentially possible¹. For every verified TTF, group of chemicals which are the TTF's carriers is established.

Complete toxic spaces' system reconstructions of all ToxCast data chemicals are constructed¹. TTF's number which represents complexity of reconstruction estimates varies from 25 to 164¹. Sections over dominant target organs, severity, potency and significance define reconstruction properties of every chemical's toxic space¹.

Perspectives:
TPS will provide scientific model reconstructions' automatic generation of STEs for thousands of chemicals across thousands of characteristics³ and will open the way to the new analysis and understanding of chemicals toxicity.

COMMENTS on ABSTRACT

1. Project ISTC#3476p «Unified Method of State Space Modeling of Biological Systems», 2006–2009. (Project Coordinator of US EPA – PhD Chao W. Chen, e-mail: (www.istc.ru)). ISTC– The International Science and Technology Center

2. Typical Toxicity Forms (TTF) is the scientific reconstruction (system model) of system's standard state. System covers a variety of biological toxic effects and is given by empirical description of ToxCast data. System has 1080 standard states.

3. Systemic Toxicity Effect (STE) is standard state's model which is the description of a TTF and presents unique qualitative definiteness of toxic effect.

4. ...784 of 1080 TTF are verified by ToxCast Data. For every TTF of this set the specific group of chemicals causing respective STE is established.

5. ...296 (TTF) are potentially possible. Every TTF of this set possesses scientifically stated potential of belonging to a specific chemicals group. For this group's detection, the TPS's special tools intended for work with TTF of high complexity level will be applied.

6. ...complete toxic spaces' system. The system itself presets boundaries in which toxic effect of every specific chemical is being manifested completely. Within these boundaries the chemical's complete toxic space is being situated. For each chemical from ToxCast its complete toxic space is represented by scientific reconstruction (system model). Such reconstruction describes intrasystem "assembling mechanism" synthesized out of TTF's set specific for this concrete chemical.

7. ...from 25 to 164. Complexity of chemical's complete toxic space is being characterized by the number and composition of TTFs which are involved in this chemical's "assembling mechanism". The chemical possesses least complex toxic space if its "assembling mechanism" is synthesized out of 25 TTF. Most complex toxic space is synthesized out of 164 TTF.

8. ...reconstruction properties of every chemical's toxic space. Scientific reconstructions of chemicals' complete toxic spaces are being transformed into scientific reconstructions of each chemical's different toxic profiles.

9. ...for thousands of chemicals across thousands of characteristics. Scientific methods and technologies of Physics of Systems have no structural restrictions on the size of an empirical system.

PHYSICS OF SYSTEMS

Physics of Systems is the post-cybernetic paradigm which created an apparatus for understanding and explanation of complexity of open natural, social science and industrial systems on the basis of scientific knowledge.

Creators:

Prof. Dr. Fomin B.F., Prof. Dr. Kachanova T.L.

Institutions:

Saint-Petersburg State Electrotechnical University "LETI"
Saint-Petersburg State Polytechnical University
Consortium "Institute of Strategic Developments", Saint-Petersburg
Research centre of innovative technologies "Laboratory of Generation of System Knowledge", Saint-Petersburg

Functionality:

Automatic generation of scientific knowledge based on empirical descriptions of complex systems;

Automatic scientific understanding and rational explanation of generated knowledge;
Automatic qualimetry of completeness, reliability, actuality, sufficiency, applicability and significance for received scientific knowledge;

Production of completed scientific reconstructions of states and variability mechanisms for natural, social science and industrial open systems in real scale and real complexity;
Automatic solutions generation of systemic tasks on scientific knowledge's base;
Overcoming of fundamental technological gaps of interdisciplinary interaction.

Informational technologies of Physics of Systems:

* Have no analogues;

* Algorithms are proprietary.

* Constitute analytical kernel of software-based technological cluster of Physics of Systems.

Experience:

Technologies of Physics of Systems were successfully applied in more than 50 projects in the fields of biology, medicine, health care, ecology, heliophysics and geophysics, planetary physics, economy, sociology, national security and government management.

EXAMPLES of PHYSICS OF SYSTEMS APPLICATION

1. Project "Global system reconstructions of the models of solar activity and related geospheric and biospheric effects"

Generation of scientific knowledge over problems of solar physics and geophysics on the base of global monitoring multiyear data of the system "Sun – Interplanetary medium – Earth".

Publications:

Prediction of Solar Flaring and CME Activity by Means of Conceptual Modelling (COMOD) Technology for the Reconstruction of Complex Systems/ B.F. Fomin, H. Lammer, A. Hansmeier et al./ "CITS-2004", Communications, Information & Control Systems, Technologies & Applications, IIS, Orlando, Florida, USA, PP. 161–166, 2004.

2. Project "Tension"

Generation of scientific knowledge about civil society's state in constituent entities of the Russian Federation.

Publications:

Ageev V.O., Araslanov A.V., Kachanova T.L., Fomin B.F., Fomin O.B. Global Reconstructions for States and Existence of Open Systems: Social Tension in Districts and Regions of the Russian Federation // Proc. of the VI Intern.Conf. "System Identification and Control Problems" SICPRO'07, Moscow: Inst. of Control Sciences, 2007. PP. 1–17. (In Russian).

3. Project "Physiological and etiopathogenic formation mechanisms of bronchi obstruction"

Revealing, scientific understanding and explanation of bronchi obstruction formation mechanisms for patients with bronchial asthma. Pathogenesis research of a disease on molecular, sub-cellular, cellular level and on organ and body levels.

Definition of bronchial obstruction's mechanisms for patients with bronchial asthma in consideration of interplanetary medium's influence and meteorological factors.

Composition of data system:

No	Research procedures	Number of parameters
1	Medico-biological researches (such as microbiological, immune, etc.)	1089
2	Heliogeophysical researches (such as sun activity, etc.)	75
3	Meteorological researches (such as ozone, etc.)	33
Total		1197

Data system includes 546 complex studies of patients with bronchial asthma

Results:

A detailed systemic picture of bronchial asthma's pathogenesis has been constructed. System solution's space covers the 1172 models of standard states. Nature of really observed characteristic features of bronchial asthma's manifestation (heterogeneity, polymorphism, multifactorial and multivariate aspects) has been disclosed. Base of System knowledge has been constructed. Owing to that the development of valid and scientifically proven models (the models of common and special pathogenetic mechanisms of disease, conceptual models of disease course in small groups of patients and also the individual models of disease course and disease's course forecasting) has been actualized.

Publications:

1. General allergology. V.1. / Ed. Fedoseev G.B. SPb: «Nordmed-Izdat», 2001, 816 p. (in Russian).
2. Private allergology. V.2. / Ed. Fedoseev G.B. SPb: «Nordmed-Izdat», 2001, 464 p. (in Russian)
3. Inflammation mechanisms of bronchuses and lungs and anti-inflammatory therapy. / Ed. Fedoseev G.B. SPb: «Nordmed-Izdat», 1998, 688 p. (in Russian)
4. Bronchial asthma. / Ed. Fedoseev G.B. SPb: Medical news agency, 1996, 464 p. (in Russian)
5. Fedoseev G.B. Mechanisms of bronchial obstruction. SPb: Medical news agency, 1995, 336 p. (in Russian)

4. ISTC Project No. #3476. "Unified Method of State Space Modeling of Biological Systems"

System models' automatic generation for biosystems' states space over empirical data. New knowledge's obtaining, scientific understanding and rational explanation of biosystems states.

Reports:

1. Concept of technologies application of Physics of Systems for scientific knowledge's generation about states space and existence of biosystems, 83 p.
2. Automatic release's patterns of standard documentary reports for scientific knowledge's generation about states and existence of biosystems on the basis of empirical contexts, 161 p.
3. Automatic generation's templates of normative documentary reports «Solution Quality», «Solution Volume» and «Solution Essence», 30 p.
4. Standard documentary report "Solution Essence" generated by virtue of database "Dynamics" for locality DAYS_ALL, 106 p.
5. Solution Base «Carcinogenic risk. Dynamics», 164 p.

Scientific Paper:

System analysis of working conditions' influence onto personnel health status of hazardous chemical production // Proc. of the IV Intern.Conf. "Parallel Computations and Control Problems" (PACO'2008). Moscow: Inst. of Control Sciences, 2008, 22p. (In Russian).

Problem "Gene Expression Changes in the Rat Nasal Epithelium Following Formaldehyde Exposure"

Estimation of TPS's application perspectives for research of genes' states under chemical influence. Estimation of doses causing cellular processes' changing.

Composition of data system:

GO-category	Name of GO-category	Number of parameters
GO:0008565	Protein transporter activity	67
GO:0003924	GTPase activity	100
GO:0003777	Microtubule motor activity	55
GO:0003774	Motor activity	116
GO:0045182	Translationregulator activity	118

Number of research objects is 90 rats. Each category was reviewed as the whole system responsible for certain functions in the living organism.

Intermediate results:

For five GO-categories the scientific reconstructions of all standard states are obtained: 260 models for GO:0008565; 372 models for GO:0003924; 120 models for GO:0003777; 384 models for GO:0003774; 436 models for GO:0045182.

Base of scientific knowledge about systems is constructed. It is being supposed that the mechanisms of genes' activity changes under different formaldehyde concentrations will be disclosed and explained by virtue of this base.

Technologies of Physics of Systems for ToxCast

Empirical description of system:

The system is being defined as event of animals' toxic effect due to chemicals exposure. Empirical description of system is being given in observations table format. Rows are the regulated chemicals, columns are the sets of toxic effect's parameters and cells are the parameters values.

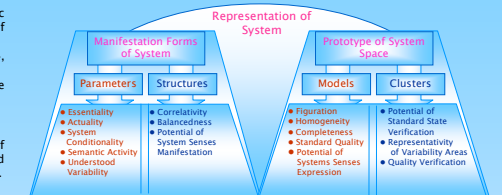
Ontological modeling:

Reconstruction of system senses over its empirical description. Result is the system knowledge.



Communicative modeling:

Scientific understanding and rational explanation (on language of systems) of qualities and properties of TPS's objects, namely of empirical description (base of system knowledge's generation), of models of interactions and states, their elements and parts (formalized system knowledge). Quantitative estimations of qualities and properties for manifestation forms of system (categories "Parameters" and "Structures") and for prototype of system's semantic space (categories "Models" and "Clusters")

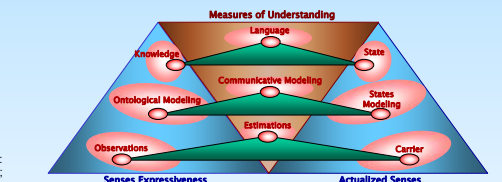


Complete qualimetry of TTF, CTS and formation mechanisms models of TTF and CTS. TTF verification.

Definition of chemicals groups specific to each STE and which form the base for scientific classifications' construction of chemicals and toxic effects.

States modeling:

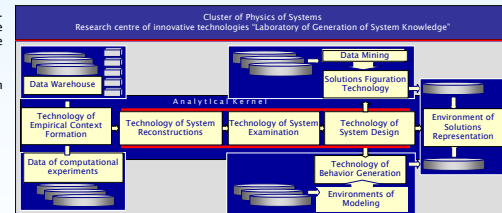
System has semantic form; holistic image of system has been synthesized. The unity of the whole for the system is expressed and explained through understood and qualitatively and quantitatively estimated properties and laws of system's semantic organization.



Are being carried out:

- Construction of target states' reconstructions over profiles of toxic effects;
- Analysis of target reconstructions;
- Toxic effects' certification for each chemical;
- Benchmarking of chemicals over toxic effects.

Technological platform:



1. Fomin B.F., Kachanova T.L. Foundations of the systemology of phenomena. SPb.: Publishing Centre SPbGLETU (St.Petersburg Electrotechnical University "LETI"), 1999, 180 p. ISBN 5-7629-0293-5. (in Russian).
2. Fomin B.F., Kachanova T.L. Meta-technology of system reconstructions. SPb.: Publishing Centre SPbGLETU (St.Petersburg Electrotechnical University "LETI"), 2002, 336 p. ISBN 5-7629-0439-3. (in Russian).
3. Fomin B.F., Kachanova T.L. Technology of system reconstructions. In: Problems of innovation development, issue 2, Publishing Centre Politehnika, St.Petersburg, 2003, 146 p. ISBN 5-7325-0772-8. (in Russian).
4. Fomin B.F., Kachanova T.L. Introduction into Language of Systems. SPb.: Publishing house "Science", 2009, 340 p. ISBN 978-5-02-025360-5. (In Russian).