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Principle Generalized Net Model of a Human Stress Reaction

Vihren Chakarov[1], Anthony Shannon[2], Krassimir Atanassov[1*]

[1]*Centre of Biomedical Engineering "Prof. Ivan Daskalov"– Bulgarian Academy of Science*
105 Acad. G. Bonchev Str., Sofia 1113, Bulgaria
E-mails: vihren@clbme.bas.bg, krat@bas.bg

[2]*Warrane College, University of New South Wales,*
Kensington 1465 & Raffles College,
North Sydney, NSW 2060, Australia
E-mail: tony@warrane.unsw.edu.au,

[*] *Corresponding author*

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Abstract: *The present study was aimed at investigating the mechanism of a human stress reaction by means of Generalized Nets (GNs). A principle GN-model of the main structures, organs and systems of the human body taking part in the acute and chronic reaction of the organism to a stress stimulus is generated. A possible application of the GN-model of the human stress reaction for testing the effect of known or newly synthesized pharmacological products as well as of food supplements is discussed.*

Keywords: *Generalized net, Modelling, Stress.*

Introduction

Each phenomenon or stimulus surpassing the sensitivity threshold of one or several different senses can be regarded as a source of stress [4]. The stress reaction physiological effects, being a product of long evolution, are profound and wide ranging. It starts by excitation of one or several senses as a result of a change in the environment (external or internal). This information reaches the deep brain structure named thalamus, where raw sense data are processed and information is further transmitted to the brain cortex and to the limbic system (mainly to its hippocampus and amygdala) simultaneously. The brain cortex extracts the data from the past experience stored in the memory and exchanges information with the limbic system, thus giving the stimulus emotional meaning depending on its biological importance already established as to what extend it is a "threat" to the organism. If the stimulus causes fear (threat), two systems are involved in effecting the organism's reaction. The first one ensures the immediate response of the organism in an acute, often life threatening situation. It involves the sympathetic nervous system (part of the autonomous nervous system) and the medulla of the adrenal glands. They produce several mediators and hormones, the most important of which is adrenaline. It causes heart rate increase, constriction of the blood reservoirs and of medium size and small blood vessels, thus ensuring increased blood flow to the muscles and brain. Adrenaline also causes elevation of blood sugar level, thus ensuring the energy source for the fast stress reaction. The changes in the organism caused by adrenaline are fast, strong and usually quickly reversible as the triggering stimulus is eliminated.

The stress reaction redistributes the priorities of the processes taking place simultaneously in the organism. It can increase the brain's cognitive and attention-related functions as well as peripheral muscle performance at the expense of slowing down digestion and sexual activity.

If the stress situation is long lasting (the so called chronic stress) the second system of stress reaction is activated. The limbic system sends a signal to the hypothalamus which activates the hypophysis to release adrenocorticotropic hormone, thus activating the adrenal cortex. It releases cortical steroid hormones which control carbohydrate, fat and protein metabolism, maintain the water-salt balance and affect the external sexual characteristics. The most important adrenal cortical hormone is cortisol. High cortisol levels on a long-term basis have a number of adverse effects: elevated blood pressure, metabolic changes including constantly elevated blood sugar, even brain toxicity, especially on the hippocampus, which can be irreversibly damaged.

Stress reaction is a fast mechanism for solving an urgent, life-threatening task. When it is too strong or is maintained too long however, it can lead to considerable damage of organs and systems, even death from acute or chronic diseases. For example, coronary constriction causes damage to the coronary vessels themselves, as well as heart muscle ischemia, i.e. myocardial infarction.

In the general model we present below a lot of details are skipped or simplified. For example the different anatomical parts of the adrenal gland and all the human body systems are considered as one position. We do not consider the difference between the acute and chronic stress reaction, which will be the purpose of a future study.

GN-model of stress reaction

Tokens α enter the GN (see Fig. 1) through place l_1 with initial characteristic:

x_0^{α} = "*events from the environment* (*external and/or internal*)"

Below, each one of α-tokens with be marked by α without indices.

Tokens β, γ, δ, ε, ζ, η, θ permanently stay, respectively, in places l_7, l_{12}, l_{16}, l_{18}, l_{23}, l_{25}, l_{27} with initial and current characteristics:

x_{cu}^{β} = "*current status of the nervous system* (*including especially: thalamus, hypophysis, limbic system, cerebral cortex*) *and sensory receptors*";

x_{cu}^{γ} = "*current status of the suprarenal gland*";

x_{cu}^{δ} = "*current status of the heart*";

x_{cu}^{ε} = "*current status of the muscles and fat depots*";

x_{cu}^{ς} = "*current status of the vascular system*";

x_{cu}^{η} = "*current status of all other human body systems* (*respiratory, endocrine, gastrointestinal, reproductory, excretory, skin, hematopoetic, etc.*)";

x_{cu}^{θ} = "*current status of the liver*".

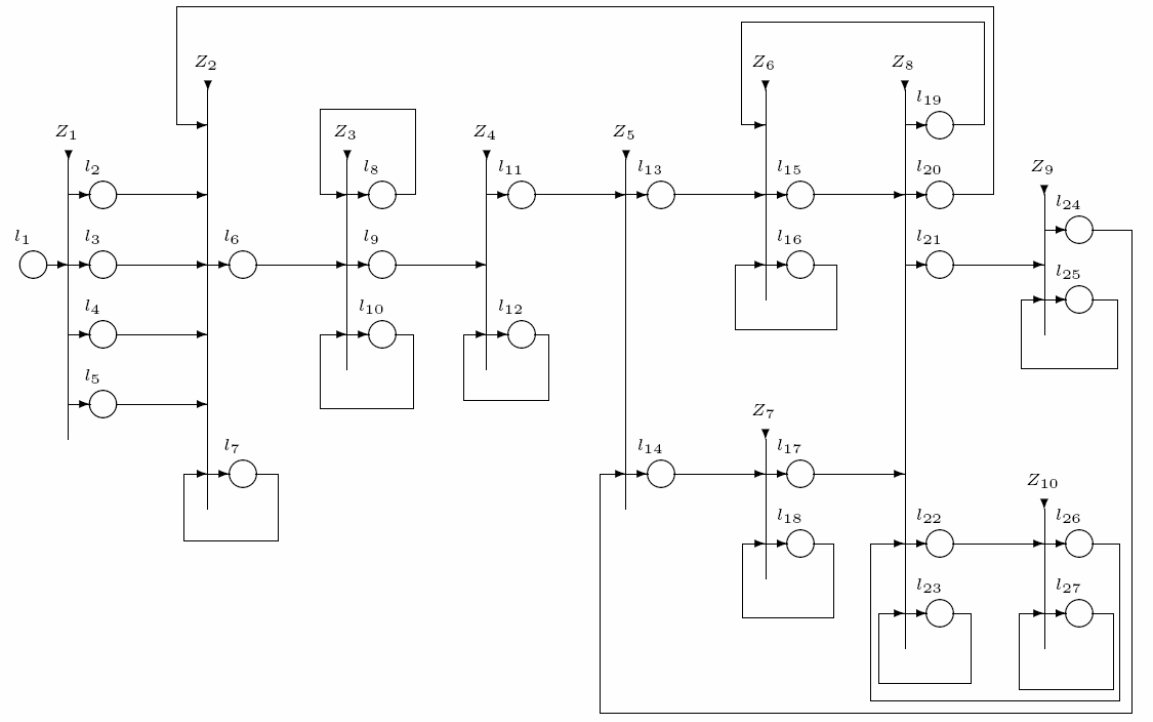

Fig. 1 GN-model of a human stress reaction (explanation in the text)

$$Z_1 = <\{l_1\}, \{l_2, l_3, l_4, l_5\},$$

	l_2	l_3	l_4	l_5
l_1	$W_{1,2}$	$W_{1,3}$	$W_{1,4}$	$W_{1,5}$

$>$,

where

$W_{1,2}$ = "the event from the environment is over the hearing threshold",
$W_{1,3}$ = "the event from the environment is over the visual threshold",
$W_{1,4}$ = "the event from the environment is over the olfactory threshold",
$W_{1,5}$ = "the event from the environment is over the somatosensor threshold".

Token α can splits to four, three or two tokens or can continue to be only one token, entering the output places of Z_1 with characteristics:

"*the event is sound, voice, music, etc; level, direction, duration, etc.*"

in place l_2,

"*the event is light; form, distance, etc.; luminescence, brightness, contrast, color, duration, etc.*"

in place l_3,

"*the event is smell and/or taste; intensity, type, duration, etc.*"

in place l_4,

"*the event is touch, heat, pain, etc.; intensity, location, duration, etc.*"

in place l_5.

$$Z_2 = <\{l_2, l_3, l_4, l_5, l_7, l_{20}\}, \{l_6, l_7\},$$

	l_6	l_7
l_2	*false*	*true*
l_3	*false*	*true*
l_4	*false*	*true*
l_5	*false*	*true*
l_7	$W_{7,6}$	*true*
l_{20}	*false*	*true*

$>$,

where

$W_{7,6}$ = "the stimulus is over the sensory threshold of the respective sensor input".

All α-tokens unite with token β (as token β) in place l_7, obtaining there the above mentioned characteristic. When predicate $W_{7,6}$ is true, token β splits to two tokens – the same β-token and a new α token that enters place l_6 with characteristic:

"*current status of the thalamus; effect of its activation after sensory input*".

$$Z_3 = <\{l_6, l_8, l_{10}\}, \{l_8, l_9, l_{10}\},$$

	l_8	l_9	l_{10}
l_6	*true*	*false*	*true*
l_8	*false*	*false*	$W_{8,10}$
l_{10}	$W_{10,8}$	$W_{10,9}$	*false*

$>$,

where

$W_{8,10} = W_{10,8}$ = "the emotional estimation of the stimuli characteristics shows stress situation" and "on the previous step the current α-token arrived from place l_6".

The second conjunctive term in the later predicate is true when the respective α-token was in place l_8 or l_{10} on its previous step.

Token α from place l_6 splits to two tokens that enter (for the first time) places l_8 (that represents the cerebral cortex) and l_{10} (that represents the limbic system) with characteristics:

"*information processing related to the signals from thalamus after an above threshold sensory stimuli*"

and

"*level of activation related to the signals from thalamus after an above threshold sensory stimuli*",

respectively.

The α-tokens from place l_8 and l_{10} enter (for the second time) places l_{10} and l_8 with characteristics:

"*emotional estimation of the stimuli characteristics from the limbic system*"

and

"*command from the cerebral cortex to the limbic system depending on the emotional estimation of the stimuli characteristics*",

respectively.

On the third step, token α from place l_9 enters place l_8 with a characteristic

"*impulse from the limbic system to the hypophysis*".

Of course, next α-tokens enter in all other previous mentioned places for some time period and they generate the simultaneous functioning of each one of these transitions. The next transitions will be activated only in the case, when at least one α-token enters place l_9.

$$Z_4 = <\{l_9, l_{12}\}, \{l_{11}, l_{12}\},$$

	l_{11}	l_{12}
l_9	*false*	*true*
l_{12}	*true*	*true*

$>$.

The α-tokens from place l_9 enter place l_{12} and unite with γ-token, staying only there. The later one obtains the above mentioned characteristic. On the next step it splits to two tokens – the same γ-token and a new α-token that enters place l_{11} with characteristic:

"*adrenaline production from suprarenal gland entering the blood in the vascular system; quantity, quality*".

$$Z_5 = <\{l_{11}, l_{24}\}, \{l_{13}, l_{14}\},$$

	l_{13}	l_{14}
l_{11}	*true*	*true*
l_{24}	*true*	*true*

$>$.

Each one of tokens α from place l_{11} and l_{24} splits to two tokens, that enter the output places of Z_5 and there they unite with characteristics:

"*adrenaline entering the heart; quantity, quality*"

in place l_{13},

"*adrenaline entering the muscles and fat depots; quantity, quality*"

in place l_{14}.

$$Z_6 = <\{l_{13}, l_{16}, l_{19}\}, \{l_{15}, l_{16}\},$$

	l_{15}	l_{16}
l_{13}	*false*	*true*
l_{16}	*true*	*true*
l_{19}	*false*	*true*

$>$.

Token from places l_{13} and l_{19} enter place l_{16}, where they unite with token δ, that obtains the above mentioned characteristic. On the other hand, token δ splits to two tokens – itself, remaining in place l_{16} and a new one (we will continue to mark it by α) that enters place l_{15}, where it obtains characteristic:

"*blood from the heart with higher arterial pressure* (*parameters*)".

$$Z_7 = <\{l_{14}, l_{18}\}, \{l_{17}, l_{18}\},$$

	l_{17}	l_{18}
l_{14}	*false*	*true*
l_{18}	*true*	*true*

$>$.

The token from place l_{14} enters place l_{18}, where it unites with token ε, that obtains the above mentioned characteristic. On the other hand, token ε splits to two tokens – itself, remaining in place l_{18} and a new α-token that enters place l_{17}, where it obtains characteristic:

"*blood from muscles and fat depots with elevated glycogen level*".

$$Z_8 = <\{l_{15}, l_{17}, l_{23}, l_{26}\}, \{l_{19}, l_{20}, l_{21}, l_{22}, l_{23}\},$$

	l_{19}	l_{20}	l_{21}	l_{22}	l_{23}
l_{15}	*false*	*false*	*false*	*false*	*true*
l_{17}	*false*	*false*	*false*	*false*	*true*
l_{23}	*true*	*true*	*true*	*true*	*true*
l_{26}	*false*	*false*	*false*	*false*	*true*

$>$.

Tokens from places l_{15}, l_{17}, l_{26} (all from α-type) are united with token ζ in place l_{23} and it obtains the above mentioned characteristic. On the next step it splits to five tokens – itself and four α-tokens, that enter the output Z_8-places (without place l_{23}) with characteristics:

"*blood for the heart needs, quality, quantity*"

in place l_{19},

"*blood to the nervous and sensory system needs, quality, quantity*"

in place l_{20},

"*blood to the needs of all human body systems, except heart, nervous system and liver, quality, quantity*"

in place l_{21},

"*blood for liver needs, quality, quantity*"

in place l_{22}.

$$Z_9 = <\{l_{21}, l_{25}\}, \{l_{24}, l_{25}\},$$

	l_{24}	l_{25}
l_{21}	*false*	*true*
l_{25}	*true*	*true*

$>$.

The token from place l_{21} enters place l_{25}, where it unites with token η, that obtain the above mentioned characteristic.

Token η splits to two tokens – itself and α-token that enters place l_{24} with characteristic:

"*blood from all human body systems, except heart, nervous system and liver,quality, quantity*".

$$Z_{10} = <\{l_{22}, l_{27}\}, \{l_{26}, l_{27}\},$$

	l_{26}	l_{27}
l_{22}	*false*	*true*
l_{27}	*true*	*true*

$>$.

The token from place l_{22} enters place l_{27}, where it unites with token θ, that obtains the above mentioned characteristic. On the other hand, token θ splits to two tokens – itself, remaining in place l_{27} with the above mentioned characteristic and a new token (we will continue to mark it by α) that enters place l_{26}, where it obtains characteristic:

"*blood from liver, quality, quantity*".

Conclusions

The so-constructed GN-model can be used for simulation of processes related to stress reaction of human body. For example the effect of known drugs like anxiolythics or newly synthesized pharmacological products can be tested on such model. A lot of food supplements like coffee, alcohol or B-vitamins also act on different stages of the human stress reaction. Their combination in different proportions can also be estimated on such model.

If we use the hierarchical operators defined over the GNs (see, e.g., [1, 2]) we can further develop the model in more details. In this case we can substitute each places of the GN-model (from [3, 5]) with new GN that will be a subnet of the whole GN. It will show in depth the relations between the human body systems during the stress reaction.

Appendix: Generalized Net

The concept of a *Generalized Net* (GN) is described in the books [1, 2].

First, we shall give some notations:

- $N = \{0, 1, 2, \ldots\} \cup \{\infty\}$;
- $pr_i X$ is the i-th projection of the n-dimensional set, where $n \in N$, $n \geq 1$ and $1 \leq k \leq n$.

More generally, for a given n-dimensional set $X (n \geq 2)$

$$pr_{i_1, i_2, \ldots, i_k} X = \prod_{j=1}^{k} pr_{i_j} X$$

$(1 \leq i_j \leq n, 1 \leq j \leq k, i_{j'} \leq i_{j''}$ for $j' \neq j'')$;

- card(X) is the cardinality of set X.

Formally, every transition is described by a seven-tuple:

$Z = \langle L', L'', t_1, t_2, r, M, \Box \rangle$,

where:

(a) L' and L'' are finite, non-empty sets of places (the transition's input and output places, respectively); for the transition in Fig. 2 these are

$L' = \{l'_1, l'_2, ..., l'_m\}$

and

$L'' = \{l''_1, l''_2, ..., l''_n\}$

(b) t_1 is the current time-moment of the transition's firing;

(c) t_2 is the current value of the duration of its active state;

(d) r is the transition's *condition* determining which tokens will transfer from the transition's inputs to its outputs. Parameter r has the form of an Index Matrix (IM):

$$r = \begin{array}{c|c} & l''_1 \quad \ldots \quad l''_j \quad \ldots \quad l''_n \\ \hline l'_1 & \\ \vdots & r_{i,j} \\ l'_i & (r_{i,j} \text{ – predicate}) \\ \vdots & (1 \le i \le m,\ 1 \le j \le n) \\ l'_m & \end{array}$$

where $r_{i,j}$ is the predicate which gives the condition for transfer from the i-th input place to the j-th output place. When $r_{i,j}$ has truth-value "*true*", then a token from the i-th input place can be transferred to the j-th output place; otherwise, this is impossible;

(e) M is an IM of the capacities of transition's arcs:

$$M = \begin{array}{c|c} & l''_1 \quad \ldots \quad l''_j \quad \ldots \quad l''_n \\ \hline l'_1 & \\ \vdots & m_{i,j} \\ l'_i & (m_{i,j} \ge 0 \text{ – natural number or } \infty) \\ \vdots & (1 \le i \le m,\ 1 \le j \le n) \\ l'_m & \end{array}$$

(f) □ is called transition type and it is an object having a form similar to a Boolean expression. It may contain as variables the symbols that serve as labels for a transition's input places, and it is an expression built up from variables and the Boolean connectives $\wedge$ and $\vee$ determining the following conditions:

- $\wedge(l_{i_1}, l_{i_2}, ..., l_{i_u})$ – every place $l_{i_1}, l_{i_2}, ..., l_{i_u}$ must contain at least one token,
- $\vee(l_{i_1}, l_{i_2}, ..., l_{i_u})$ – there must be at least one token in all places $l_{i_1}, l_{i_2}, ..., l_{i_u}$, where $\{l_{i_1}, l_{i_2}, ..., l_{i_u}\} \subset L'$.

When the value of a type (calculated as a Boolean expression) is "*true*", the transition can become active, otherwise it cannot.

The ordered four-tuple

$E = \langle\langle A, \pi_A, \pi_L, c, f, \theta_1, \theta_2\rangle, \langle K, \pi_K, \theta_K\rangle, \langle T, t^o, t^*\rangle, \langle X, \Phi, b\rangle\rangle$

is called a *Generalized Net* (GN) if:

(a) A is a set of transitions (see above);

(b) π_A is a function giving the priorities of the transitions, i.e., π_A: $A \rightarrow N$;

(c) π_L is a function giving the priorities of the places, i.e., π_L: $L \rightarrow N$, where $L = pr_1A \cup pr_2A$. Obviously, L is the set of all GN-places;

(d) c is a function giving the capacities of the places, i.e., c: $L \rightarrow N$;

(e) f is a function which calculates the truth values of the predicates of the transition's conditions (for the (ordinary) GNs, described in this section, function f obtain values "false" or "true", or values from set {0, 1}. If P is the set of the predicates used in a given model, then we can define f as f: $P \rightarrow \{0, 1\}$;

(f) θ_1 is a function giving the next time-moment for which a given transition Z can be activated, i.e., $\theta_1(t) = t'$, where $pr_3Z = t$, $t' \in [T, T + t^*]$ and $t \leq t'$. The value of this function is calculated at the moment when the transition terminates its functioning;

(g) θ_2 is a function giving the duration of the active state of a given transition Z, i.e., $\theta_2(t) = t'$, where $pr_4Z = t \in [T, T + t^*]$ and $t' \geq 0$. The value of this function is calculated at the moment when the transition starts functioning;

(h) K is the set of the GN's tokens. In some cases, it is convenient to consider this set in the form

$$K = \bigcup_{l \in Q^I} K_l,$$

where K_l is the set of tokens which enter the net from place l, and Q^I is the set of all input places of the net;

(i) π_K is a function giving the priorities of the tokens, i.e., π_K: $K \rightarrow N$;

(j) θ_K is a function giving the time-moment when a given token can enter the net, i.e., $\theta_K(\alpha) = t$, where $\alpha \in K$ and $t \in [T, T + t^*]$;

(k) T is the time-moment when the GN starts functioning. This moment is determined with respect to a fixed (global) time-scale;

(l) t^o is an elementary time-step, related to the fixed (global) time-scale;

(m) t^* is the duration of the GN functioning;

(n) In all publications on GNs (see, e.g., [1, 2]) it is defined that X is the set of all initial characteristics that the tokens can receive when they enter the net. Here, for a first time another interpretation of X will be introduced: X is a function which assigns initial characteristics to every token when it enters input places of the net;

(o) Φ is the characteristic function which assigns new characteristics to every token when it makes a transfer from an input to an output place of a given transition;

(p) b is a function giving the maximum number of characteristics a given token can receive, i.e., b: $K \rightarrow N$.

A given GN may not have some of the above components. A GN without some components is called a reduced GN. The present GN is a reduced one.

The static structure of a given GN is determined by the elements of the set $pr_{1,2,6,7}A$, i.e., the static structure of a GN is determined by the collection of the following elements for each transition: the input and output places, the index matrix of the arcs and the transition type. The dynamical character of the net is due to the GN's tokens and the transitions' conditions (pr_5A), the temporal character comes from the components T, t^o, t^* and from the elements of the set $pr_{3,4}A$. Finally, the components Φ, X and b play the role of a memory in the GN.

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Vihren Chakarov, Md, Ph.D.
E-mail: vihren@clbme.bas.bg

Born: 3rd of November 1955 in Sofia, Bulgaria.

University: Medical Academy, Sofia, Faculty of Medicine 1976-1984.

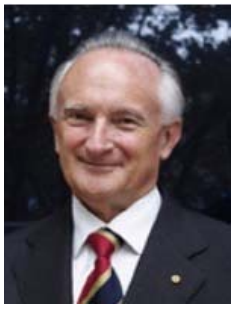
Special courses: Psychometrics, 1992;
EEG and clinical electrophysiology, 1993.

Professional experience and interests: Assistant professor in Brain Research Institute, Department of electrophysiological correlates of behavioural reactions 1985-1995; Centre of Biomedical Engineering, Department of Analysis and Modelling of the Excitation of Biological Structures, Bulgarian Academy of Sciences, Sofia since 1995.

Electrophysiological correlates of auditory information cognitive processing in normal subjects and in patients with neurological and psychiatric disorders (Ph.D. Thesis, 2000).

High resolution EEG, 3D reconstruction depending on the individual anatomy and electrophysiological frequency domain analysis during motor tasks in normal subjects and neuropathology, Neurology Clinic, Karl-Ludwig University, Freiburg, Germany, 2001.

Anthony G. (Tony) Shannon, Prof., Ph.D., Ed.D., D.Sc.
E-mails: tony@warrane.unsw.edu.au



Professor A.G. (Tony) Shannon AM is an Emeritus Professor of the University of Technology, Sydney, where he was Foundation Dean of the University Graduate School and Professor of Applied Mathematics, and where he is currently Chair of the Key University Research Centre for Health Technologies.

He holds the degrees of Ph.D., Ed.D. and D.Sc. He is co-author of numerous books and articles in medicine, mathematics and education. His research interests are in the philosophy of education and epidemiology, particularly through the application of generalized nets and intuitionistic fuzzy logic. He has taught and mentored at all levels from primary school to post-doctoral.

Prof. Shannon is a Fellow of several professional societies and a member of several course advisory committees at private higher education providers. He is on the Board of Trustees of Campion College, a liberal arts degree granting institution in Sydney. In June 1987 he was appointed a Member of the Orden of Australia for services to education.

He enjoys reading, walking, theatre, number theory, and thoroughbred racing.

Krassimir Atanassov, Prof., D.Sc., D.Sc., Ph.D.
E-mail: krat@bas.bg

Professor Krassimir Atanassov was born on 23 March 1954. He studied in Department of Mathematics in Sofia University and defended dissertations for PhD in 1986, Doctor of Technical Science in 1997 and Doctor of Mathematical Sciences in 2000. Since 1998 he is a Professor in the Centre of Biomedical Engineering "Prof. Ivan Daskalov" of the Bulgarian Academy of Sciences. Editor-in-Chief of four international journals and member of the Editorial Boards of eight others. His research interests are in the areas of fuzzy sets (he introduced the object of "Intuitionistic Fuzzy Set" and investigated its basis properties and some of its applications in expert systems, systems theory, decision making, medicine and others), Petri nets (he introduced the object of "Generalized Net" and investigated its basic properties, as well as some of its applications in artificial intelligence, systems theory, medicine, economics, transportation, chemical industry and others) and number theory. He has about 500 papers in journals, 200 conference reports and 24 books.