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Modal Epistemic Łukasiewicz logic with constant and its application in immune system*

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Summary. The theory of three-valued multi modal epistemic Łukasievicz logic with constant, which is an extension of the three-valued Łukasiewicz logic, the language of which is extended by nullary and unary connectives is developed in this paper. The unary connectives are interpreted as modal operators (knowledge operators). We propose to use such logic in studying immune system. A relational system is developed as a semantic of this logic. The relational systems represent the immune system which in its turn is a part of relational biology.

Keywords: Agent, Many Valued Logic, Epistemic logic, Kripke model.

1.1 Introduction

We introduce a new logical system to study a biological system. The first attempt to study systems biology by means of logic (an axiomatic formal system) belongs to H. Woodger [28]. He proposed to discuss biology with precision of statements and reliability of reasoning. Here we also should to mention N. Rashevsky [20] and R. Rosen [21, 22]. N. Rashevsky was founded relational biology that is the study of biology from the standpoint of definition of relations between the parts of a biological system. In this paper we analyze the responses from relational processes when they are represented by relational systems (Kripke frames) which are models of a such biological system as an immune system.

In order to survive, all organisms must use energy sources present in the environment, and avoid dangers that could destroy them. To that end, they must acquire knowledge about the environment. All organisms acquire such knowledge, thanks to which they assume behaviors that, when successful, ensure their survival. Knowledge is a natural phenomenon that occurs in all organisms. Knowledge has a biological role, just like other capacities which ensure the survival of organisms.

Our investigation concerns to study mathematical objects - mathematical logical systems and their semantics - relational systems, with application for immune

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system. In turn the immune system consists of different kind of special cells - B and T lymphocytes. T cells and their subpopulations form some network like relational systems.

Our basic aim is to give to immunologists some useful tools for diagnosis about a state of immune system having some initial data. These data represent some properties, which may estimate, that posses some parts of an immune system, in particular some T cells being fundamental elements of the immune system.

Recent advances in Multiagent Systems and Epistemic Logic within Distributed Systems Theory, have used the Kripke model structure of models for the logic. In [26] examined one of the simpler versions of these models, interpreted systems, and the related Kripke semantics of the logic $S5_n$ (an epistemic logic with n agents).

This paper is a continuation of our previous work [7] where have been introduced multimodal epistemic three-valued Łukasiewicz logic $E\text{Ł}_3(n)$ which is used for estimation of the elements of relational system (Kripke frame) by the elements of adequate three element algebra corresponding to three-valued Łukasiewicz logic Ł$_3$. We introduce new logic - multimodal epistemic three-valued Łukasiewicz logic $E\text{Ł}_3^c(n)$ with constant. The logic $E\text{Ł}_3^c(n)$ is obtained from three-valued Łukasiewicz propositional logic Ł$_3$ by adding nullary connective c interpreted as "unknown" and n 'knowledge operators' ($n \geq 1$), with corresponding axioms. Notice that representing the connectives of this logic by functions (which are given in next section) on three-element set $\{0, \frac{1}{2}, 1\}$ we obtain complete system of functions, i. e. by means of the functions $x \oplus y = \min(1, x + y), x \odot y = \max(0, x + y - 1), x^* = 1 - x$ and constant $\frac{1}{2}$ we can express any function $f : \{0, \frac{1}{2}, 1\}^n \to \{0, \frac{1}{2}, 1\}$, in other words we represent Post functions. The knowledge operators model a community of ideal knowledge agents who have the properties of veridical knowledge (everything they know is true), fuzzy knowledge (everything they know is quasi true, positive introspection (they know what they know) and negative introspection (they know what they do not know) and so on. The knowledge operators permit the following interpretation:

$\Box_i\alpha$ - "the agent i knows proposition α";
$\Diamond_i\alpha$ - "the agent i does not know that proposition α is false".

For detail information on classical and non-classical modal logic we refer to [1, 2, 3, 4, 8, 9, 13, 15, 18, 26, 27].

We will show that 3-valued multimodal Łukasiewicz logic $E\text{Ł}_3^c(n)$ is complete with respect to descriptive Kripke frames and use the ones for representation of immune system. The set of T-cells we can understand as the set of agents. In many ways the immune system is a black box; although many of its inputs and outputs are known, exactly how the system achieves its function is the subject of many investigations. Laboratory experiments provide large quantities of data, allowing components (agents (T-cells), state of the agents (T-cells)) within the black box to be identified, but there remain many details of how the components (agents (T-cells), state of the agents (T-cells)) of the system carry out their functions, or on the nature of interaction between components. There are many variables in such systems that exhaustive testing to establish these details is not feasible. Multimodal logic and corresponding to it Kripke model are ideally suited to describing immune system at this level: they may be represented as a relational system of interacting elements (components), where the components themselves may have complex, non-deterministic, individual behaviour. Moreover, the usage of multimodal logic and Kripke model gives access

to a range of investigatory techniques, including simulation, verification via logical properties.

Let us remark that if $n = 1$, then $E\text{Ł}_3(1)$ coincides with the monadic propositional logic [6], i. e. the modal operator behaves as a quantifier. In other words a monadic propositional logic is connected with the first-order logic with fixed one individual variable x. More precisely, let L denote a first-order language based on $\cdot, +, \to, \neg, \exists$ and let L_m denote a propositional language based on $\cdot, +, \to, \neg, \exists$. Let $Form(L)$ and $Form(L_m)$ be the set of all formulas of L and L_m, respectively. We fix a variable x in L, associate with each propositional letter p in L_m a unique monadic predicate $p^*(x)$ in L and define by induction a translation $\Psi : Form(L_m) \to Form(L)$ by putting:

- $\Psi(p) = p^*(x)$ if p is propositional variable,
- $\Psi(\alpha \circ \beta) = \Psi(\alpha) \circ \Psi(\beta)$, where $\circ = \cdot, +, \to$,
- $\Psi(\exists\alpha) = \exists x\Psi(\alpha)$.

Through this translation Ψ, we can identify the formulas of L_m with monadic formulas of L containing the variable x.

Having as a domain of interpretation some set of T-cells, a monadic predicate is interpreted as some property of a T-cell, say, for example, to possess some geometrical shape. This reasoning can be generalized on $E\text{Ł}_3^c(n)$.

1.2 Multimodal epistemic 3-valued Łukasiewicz logics $E\text{Ł}_3^c(n)$

The unit interval of real numbers $[0, 1]$ endowed with the following operations: $x \oplus y = \min(1, x + y), x \odot y = \max(0, x + y - 1), x^* = 1 - x$, becomes an MV-algebra [5]. It is well known that the MV-algebra $S = ([0, 1], \oplus, \odot, ^*, 0, 1)$ generate the variety **MV** of all MV-algebras, i. e. $\mathcal{V}(S) = \mathbf{MV}$.

Let Q denote the set of rational numbers, for $(0 \neq)n \in \omega$ we set

$$S_n = (S_n; \oplus, \odot, ^*, 0, 1),$$

where

$S_n = \{0, \frac{1}{n}, \ldots, \frac{n-1}{n}, 1\}$.

For any positive integer n, S_n is a subalgebra of S. We are interested by $S_2 = (S_2; \oplus, \odot, ^*, 0, 1)$.

The formulas of Łukasiewicz logic are built from a countable set of propositional variables $Var = \{p, q, ...\}$ using the connectives & (strong conjunction), $\to$ (implication) and $\bot$ (falsity truth constant).

In order to introduce the infinite-valued Łukasiewicz logic we start by considering the standard MV-algebra $S = ([0, 1], \odot, \Rightarrow, 0)$ (which is functionally equivalent to the MV-algebra defined above), where a binary operation $\odot$ called Łukasiewicz t-norm and defined as $a \odot b = max\{0, a + b - 1\}$, for all $a, b \in [0, 1]$; a binary operation $\Rightarrow$ called the residuum (of the t-norm $\odot$) and defined as $a \Rightarrow b = min\{1, 1 - a + b\}$, and $\neg a = a \Rightarrow 0 = 1 - a$, $a \oplus b = \neg(\neg a \odot \neg b) = min(1, a + b)$, for all $a, b \in [0, 1]$.

We extend 3-valued Łukasiewicz logic Ł$_3$ to the 3-valued multimodal Łukasiewicz logic $E\text{Ł}_3^c(n)$ by adding nullary connective c and n unary modal operators $\Box_i$ and $\Diamond_i$

$(i = 1, ..., n)$ to the language of Ł$_3$. The formulas of 3-valued multimodal Łukasiewicz logic $E\text{Ł}_3^c(n)$ are built from a countable set of propositional variables $Var = \{p, q, ...\}$ using the connectives & (strong conjunction), $\to$ (implication) and $\bot$ (falsity truth constant), c (unknown truth constant), and $2n$ unary modal operators $\Box_i$ and $\Diamond_i$ $(i = 1, ..., n)$ in usual way. Denote by Ł$_3^c$ the three-valued propositional Łukasiewicz logic with constant in the language $Var = \{p, q, ...\}$ using the connectives & (strong conjunction), $\to$ (implication) and $\bot$ (falsity truth constant), c (unknown truth constant).

A *propositional evaluation* is a homomorphism e from the algebra of formulas into the algebra S_2, i.e., a mapping e from the set of formulas into $\{0, \frac{1}{2}, 1\}$ such that

- $e(\varphi\&\psi) = e(\varphi) \odot e(\psi)$,
- $e(\varphi \to \psi) = e(\varphi) \Rightarrow e(\psi)$,
- $e(\bot) = 0$,
- $e(c) = \frac{1}{2}$.

A formula φ is said to be *valid* when it is evaluated to 1 in all propositional evaluations. Then, three-valued Łukasiewicz logic Ł$_3^c$ is defined as the set of valid formulas.

We introduce the connectives $\wedge, \vee, \leftrightarrow, \neg, \veebar$ and $\top$ (the semantics counterpart will be denoted, respectively, by $\wedge, \vee, \Leftrightarrow, \neg, \oplus$ and 1, and $\odot$ for &) as the following abbreviations: $\varphi \wedge \psi = \varphi\&(\varphi \to \psi)$, $\varphi \vee \psi = (\varphi \to \psi) \to \psi$, $\varphi \leftrightarrow \psi = (\varphi \to \psi)\&(\psi \to \varphi)$, $\neg\varphi = \varphi \to \bot$, $\varphi \veebar \psi = \neg(\neg\varphi\&\neg\psi), \top = \neg\bot$.

The logic Ł is axiomatized by the following axiom schemata:

Ł1. $\varphi \to (\psi \to \varphi)$,
Ł2. $(\varphi \to \psi) \to ((\psi \to \chi) \to (\varphi \to \chi))$,
Ł3. $((\varphi \to \psi) \to \psi) \to ((\psi \to \varphi) \to \varphi)$,
Ł4. $(\neg\varphi \to \neg\psi) \to (\psi \to \varphi)$.

The inference rule is Modus Ponnens: $\varphi, \varphi \to \psi / \psi$.

3-valued Łukasiewicz logic Ł$_3$ is axiomatized by the axioms of Ł plus the schema: $(\varphi\&\varphi) \leftrightarrow (\varphi\&\varphi\&\varphi)$. 3-valued Łukasiewicz logic Ł$_3^c$ is axiomatized by the axioms of Ł$_3$ plus the schema: $(c\&c) \leftrightarrow \bot$, $(c \veebar c) \leftrightarrow \top$, $(c \wedge \top) \leftrightarrow c$, $(c \wedge \bot) \leftrightarrow \bot$, $\neg c \leftrightarrow c$.

1.2.1 3-valued Descriptive Kripke models

A 3-*valued Kripke frame for agent* i is a pair $\mathfrak{J}_i = (W_i, R_i)$, $i = 1, ..., n$, consisting of a non-empty set W_i of elements called *the states of the agent* i (or *possible worlds of the agent* i); $R_i \subset W_i \times W_i$ is a binary reflexive and transitive relation on W_i (called *the accessibility relation for agent* i).

A 3-*valued Kripke model* for agent i (or simply, Kripke model for agent i, when there is no ambiguity) is a pair $\mathfrak{M}_i = (\mathfrak{J}_i, e_i)$, $i = 1, ..., n$, where $\mathfrak{J}_i = (W_i, R_i)$ is Kripke frame for agent i and $e_i : Var \times W_i \to S_2$ is a function, called *evaluation for agent* i, which maps every propositional variable $p \in Var$ and possible world $w \in W_i$ to the set of truth values S_2, $i = 1, ..., n$, such that if $e_i(p, w) = 1$ and $(w, w') \in R_i$ then $e_i(p, w') = 1$. If φ is a propositional formula of Ł$_3$, then $e_i(\varphi, w) \in S_2$ is a propositional evaluation for agent i; if φ is a modal formula, then $e_i(\Diamond_i\varphi, w) =$

$\bigvee\{e_i(\varphi, w\prime) : (w, w\prime) \in R_i\}$; $e_i(\Box_i\varphi, w) = \bigwedge\{e_i(\varphi, w\prime) : (w, w\prime) \in R_i\}$ for every $w \in W_i$, $i = 1, ..., n$.

A modal formula φ is said to be *modally valid for agent* i when it is evaluated to 1 in all Kripke models for agent i; it is said to be *modally* 1*-satisfiable for agent* i when there is some Kripke model for agent i and some world w such that $e_i(\varphi, w) = 1$; and it is said to be *modally satisfiable for agent* i when it is 1-satisfiable for agent i. A modal formula φ is said to be *modally valid* when it is evaluated to 1 in all Kripke models for every agent i.

A 3*-valued descriptive Kripke frame* is a pair $\mathfrak{J} = (W, R)$, $W = \{W_1, ..., W_n\}$ is the set of n agents (or *possible worlds*); $R \subset W \times W$ is a binary reflexive and transitive relation on W (called *the accessibility relation between agents* $i(= W_i)$).

A 3*-valued descriptive Kripke global model* (or *descriptive Kripke global model*) is a triple $\mathfrak{M} = (W, R, V)$ where $W = \{W_1, ..., W_n\}$ is the set of n agents (or *possible worlds*); $R \subset W \times W$ is a binary relation on W (called *the accessibility relation between agents* $i(= W_i)$); $V(\varphi, W_i) = \bigwedge\{e_i(\varphi, w) : w \in W_i, e_i : Var \times W_i \to S_2\}$, $V(\Box\varphi, W_i) = \bigwedge\{V(\varphi, W_j) : (W_i, W_j) \in R\}$, $V(\Diamond\varphi, W_i) = \bigvee\{V(\varphi, W_j) : (W_i, W_j) \in R\}$, where $\Box\varphi$ and $\Diamond\varphi$ are a abbreviations of $\Box_1\varphi \wedge ... \wedge \Box_n\varphi$ and $\Diamond_1\varphi \vee ... \vee \Diamond_n\varphi$ respectively.

A modal formula φ is said to be *globally modally valid* when it is evaluated to 1 in all Kripke models for every agent $i \in \{1, ..., n\}$; it is said to be *modally satisfiable* when it is 1-satisfiable for some agent $i \in \{1, ..., n\}$.

The logic $E\text{Ł}_3^c(n)$ is defined as the set of its modal formulas that are globally modally valid. It is worth pointing out that for this modal logic the modal operators are interdefinable by means of the modally valid formulas $\Diamond_i\varphi \leftrightarrow \neg\Box_i\neg\varphi$ and $\Box_i\varphi \leftrightarrow \neg\Diamond_i\neg\varphi$.

1.2.2 Axiomatization

We suggest the following schemata of axioms for $E\text{Ł}_3^c(n)$: to the schemata of axioms of Ł_3^c we add

1) $\Box_i\varphi \to \varphi$, $i = 1, ..., n$,
2) $\Box_i\varphi \to \Box_i\Box_i\varphi$, $i = 1, ..., n$,
3) $\Box_i(\varphi \wedge \psi) \leftrightarrow (\Box_i\varphi \wedge \Box_i\psi)$, $i = 1, ..., n$,
4) $\Box_i(\varphi\&\varphi) \leftrightarrow (\Box_i\varphi\&\Box_i\varphi)$, $i = 1, ..., n$,
5) $\Box_i(\varphi\underline{\vee}\varphi) \leftrightarrow (\Box_i\varphi\underline{\vee}\Box_i\varphi)$, $i = 1, ..., n$,
6) $\Diamond_i\varphi \to \Box_i\Diamond_i\varphi$, $i = 1, ..., n$,

inference rules: $\varphi, \varphi \to \psi/\psi$, $\varphi/\Box_i\varphi$, $i = 1, ..., n$.

Notice that mono-modal fragment of the logic $E\text{Ł}_3(1)$ coincides with monadic three-valued Łukasiewicz logic [6]. Extending this result to the $E\text{Ł}_3^c(1)$ we easily obtain three-valued monadic Post logic.

Remark. Notice that the algebra $S_2^c = (\{0, \frac{1}{2}, 1\}, \odot, \Rightarrow, 0, \frac{1}{2}, 1)$ is functionally complete, i. e. any function $f : \{0, \frac{1}{2}, 1\}^n \to \{0, \frac{1}{2}, 1\}$ is expressed by some term on the language $\odot, \Rightarrow, 0, \frac{1}{2}, 1$. In other words it is a Post algebra of order 3. Indeed, it is enough to express the operation $\sim \frac{x}{2} = \frac{x-1 (mod\ 3)}{2}$ in S_2^c, where $x = 0, 1, 2$: $\sim \frac{x}{2} = \frac{1}{2} \odot \frac{x}{2} \vee \neg(\frac{x}{2} \oplus \frac{x}{2})$. It is known that any finite Post algebra is isomorphic to a finite product of algebras S_2^c. Like in monadic Boolean case a finite subdirectly

irreducible monadic Post algebra is an algebra $(A, \Box)$, where A is a finite Post algebra and monadic operator $\Box$ is defined in the following way: $\Box(x_1, ..., x_n) = x_m$ where $(x_1, ..., x_n) \in A$ and $x_m = min\{x_1, ..., x_n\}$. The Post monadic logic is defined as all the formulas of $E\text{Ł}_3^c(1)$ that are valid in all finite monadic Post algebras $(A, \Box)$.

It is well known that the category of Boolean algebras and Boolean homomorphism is equivalent to the category of Post algebras and Post homomorphisms. It is well known that the category of monadic Boolean algebras and monadic Boolean homomorphisms is dually equivalent to the category of $S5$-frames and p-morphisms [4], where $S5$-frame is a Kripke frame (W, R) with equivalence relation R on W. So, we can conclude that the category of monadic Post algebras and monadic Post homomorphisms is dually equivalent to the category of $S5$-frames and p-morphisms. Hence, we have another semantical approach for $E\text{Ł}_3^c(1)$ taking $S5$-frames as 3-valued descriptive Kripke frame. And, following to [26], we can transfer this technic to the multi-modal logic $E\text{Ł}_3^c(n)$.

According to G. Hansoul and B. Teheux's results [13] about completeness theorem of mono-modal Łukasiewicz logic with respect to $n+1$-Kripke completeness and adopting the ones to the multi-modal logic $E\text{Ł}_3^c(n)$ we arrive to the following completeness theorem

Theorem 1. *A formula of $E\text{Ł}_3^c(n)$ φ is a theorem of $E\text{Ł}_3^c(n)$ iff φ is globally valid.*

1.3 On the cells of immune system

The immune system represents a multi-component system which includes a range of cell types with different roles in defending the body against infection agents, damaged tissues and in preventing the uncontrolled growth of rogue cells or cancerous cells. Many of these cells arise in the bone marrow, circulate in the blood and can migrate into solid tissues. Immune responses involve interactions between some of these cells and/or their secreted products. B and T lymphocytes specifically react to microbial antigens: activated B lymphocytes secrete antigenbinding antibodies, and subpopulations of T lymphocytes possess regulatory or cytotoxic functions. Natural killer cells are also cytotoxic cells of the lymphoid lineage, but they do not possess properties of antigen recognition. Different types of cells are antigen presenting cells (APC) present antigens to T lymphocytes. Blood monocytes give rise to tissue macrophages that are phagocytes, as are circulating neutrophils, which are the most plentiful type of granulocyte. Other circulating granulocytes are eosinophils that secrete toxic mediators, and basophils that, in common with tissue mast cells, are important sources of inflammatory mediators. Other cells contribute to immune and inflammatory responses, including endothelial cells, erythrocytes and platelets.

A variety of cell types are important components of the immune system. The main responsible cells are B and T lymphocytes with high specificity. They specifically recognise antigens and are responsible for adaptive, acquired immunity. B lymphocytes recognise native, unprocessed antigens via surface immunoglobulins and produce secreted immunoglobulins called antibodies. T lymphocytes recognise processed antigens, usually peptides associated with MHC proteins expressed on the surface of antigenpresenting cells. Different T lymphocyte subpopulations have helper, cytotoxic or regulatory functions. These subpopulations make a multifunctional network which will be described in this section more detail. T cells can

be categorized based upon cell surface expression of either cluster of differentiation T4 (CD4) or T8 (CD8). CD4+ T cells recognize antigen presented in the context of class II major histocompatibility complex (MHC), while CD8+ cells recognize antigen presented in the context of class I MHC. CD4+ T helper subsets include T helper type 1 (Th1), T helper type 2 (Th2), and T helper type 17 (Th17) cells and some other new described types of Th cells [27], [25].

There is evidence that each of these subsets is involved in the defense against a certain subset of microorganisms. Th1 are pivotal in defense against intracellular microorganisms in general and mycobacteria in particular. Patients with mutations in the interferon-γ (IFN-γ) receptor or interleukin-12 (IL-12) receptor present with recurrent infections with mycobacteria and Salmonella. Th2 cells are integral in expelling parasitic infestations. Th17 seem to play a significant role in defense against extracellular bacteria and some fungi. Th1 and Th17 cells play major roles in autoimmunity, whereas Th2 cells are the hallmark of atopic disease. T regulatory (Treg) cells represent a major subset of CD4+ T cells that may be involved in regulating and attenuating the activity of the three T helper subsets.

T lymphocytes are a major source of cytokines. Cytokines are the hormonal messengers responsible for most of the biological effects in the immune system, such as cell-mediated immunity and allergic type responses. T lymphocytes expressing CD4 are also known as helper T cells, and these are regarded as being the most prolific cytokine producers. This subset can be further subdivided into Th1 and Th2, and the cytokines they produce are known as Th1-type cytokines and Th2-type cytokines.

Th1 cells are characterized by the production of pro-inflammatory cytokines. Th1 cells are involved in cell-mediated immunity. The cytokines produced by Th1 cells stimulate the phagocytosis and destruction of microbial pathogens. Several chronic inflammatory diseases have been described as Th1 dominant diseases. Th2 cells are thought to play a role in allergy responses. Atrophy and allergy are thought to be Th2 dominant conditions. Improved understanding of Th1 and Th2 differentiation will improve our overall understanding of the immune system, its response to infection and aberrant responses that lead to disease.

The immune balance controlled by T helper 1 (Th1) and T helper 2 (Th2) is crucial for immunoregulation and its imbalance causes various immune diseases. Therefore, diagnosis of Th1/Th2 balance in autoimmune diseases including asthma is essential for the application of immune balance regulating drugs. Th1/Th2 balance is not only controlled by Th1 cells and Th2 cells, but also by various regulatory factors including regulatory T cells, sexual factor, chemokines, transcription factors, signal transduction pathway etc. Current research strategies seek to describe these multi-factorial system responsible to keep the Th1/Th2 balance in the body and predict some logical novel targets for regulating this balance which is based on another subpopulations of T cells - T regulatory (T reg) cells and their cytokine profiles. Naturally occurring CD4+ T regulatory cells (nTreg) are derived centrally in the thymus and constitutively express CD25 and other suppressive molecules including CTLA-4. These cells generally appear to exert suppressive effects by direct cell contact rather than cytokine production. The Foxp3 gene appears to be a critical regulator of the development of this subgroup of CD4+CD25+ Trn cells. At a population level, there has been a parallel rise in both Th1-mediated autoimmune diseases and Th2-mediated allergic diseases. At the individual level, there is accumulating evidence that atopy is associated with an increase in both Th1 and Th2

responses. Furthermore, Th1 cells also appear to play a role in allergic inflammation in local tissues, failing to counter balance Th2 responses in airways inflammation. These observations lead to the opinion that the autoimmune diseases may develop as a result of a more fundamental failure of underlying immune regulation, rather than a simple skewing of immune response along a Th1/Th2 homeostasis as previously thought [10], [11].

The nonspecific part of the immune system and different cells involved in the first line defense are also very important components of this system: Natural killer (NK) cells are lymphoid cells that lack antigenspecific receptors, but mediate cytotoxic activity against infected or malignant cells. Dendritic cells (DC) are potent antigen-presenting cells involved in the activation of T lymphocytes, whereas follicular DC present antibodyassociated antigens to B lymphocytes. Monocytes are circulating blood cells that give rise to tissue macrophages with phagocytic and antigen presentation functions. Granulocytes circulate in the blood, migrate into tissues, and include phagocytic neutrophils and eosinophils that secrete toxic mediators, and basophils that release inflammatory mediators; mast cells are tissue cells with similar properties to basophils. A variety of other cell types contribute to the generation and regulation of immune and inflammatory responses, including endothelial cells, erythrocytes and platelets. This multifactorial and multifunctional immune system represents the relational biological system which will be described in this paper by using Modal Lukasiewicz Epistemic Logic.

1.4 Description of immune system by descriptive Kripke frames

In this section we try to represent some simple fragments of an immune system by 3-valued Kripke frame with the following interpretation in immune models. We will consider two cases.

I. Let $\mathfrak{J}_1 = (W_1, R_1)$ be 3-valued Kripke frame for agent 1, where $W_1 = \{MPh, Ag_1, T_c, Th_0, Th_1\}$ and R_1 is the transitive closure of the binary relation $\{(Th_1, MPh), (MPh, Ag_1), (MPh, MPh), (T_c, Ag_1), (Ag_1, T_c), (Th_1, Tc), (Th_0, Th_1), (Ag_1, Th_0), (Ag_1, Ag_1), (Tc, Tc), (Th_1, Th_1), (Th_0, Th_0)\}$; $\mathfrak{J}_2 = (W_2, R_2)$ be 3-valued Kripke frame for agent 2, where $W_2 = \{Ag_2, Th_0, Th_2, B, Y_{Ab}\}$ and R_2 is the transitive closure of the binary relation $\{(Ag_2, Th_0), (Th_0, T2), (Th_2, B), (B, Y_{Ab}), (Ag_2, Ag_2), (B, B), (Th_2, Th_2), (Th_0, Th_0), (Y_{Ab}, Y_{Ab})\}$.

Let $W' = \{W_1, W_2\}$ be system of agents, which is the set of immune system. $\mathfrak{J}' = (W', R')$ is a global immune system represented as a global 3-valued descriptive Kripke frame, where $R' = \{(W_1, W_1), (W_2, W_2)\}$, see Fig. 1. Notice, that $\mathfrak{J}' = (W', R')$ represents a Kripke frame for the classical epistemic multimodal system $S5_2$.

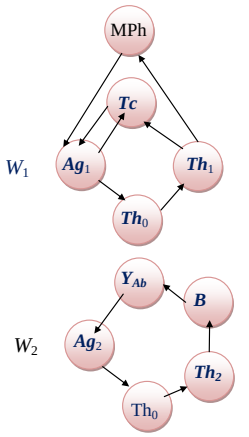
II. Let $W'' = \{W_1, W_2\}$ be another system of agents and $\mathfrak{J}'' = (W'', R'')$ be a global immune system represented as a global 3-valued descriptive Kripke frame, where $R'' = \{(W_1, W_1), (W_2, W_2), (W_2, W_1)\}$, see Fig. 2.

Now we will give some interpretation in models of immune system. Let $\mathfrak{J} = (W, R)$, $W = \{W_1, ..., W_n\}$ is the set of n agents (or *possible worlds*); $R \subset W \times W$ is a binary reflexive and transitive relation on W (called *the accessibility relation between agents* $i(= W_i)$).

A 3-*valued descriptive Kripke global model* (or *descriptive Kripke global model*) is a pair $\mathfrak{M} = (J, V)$ where $V(\varphi, W_i) = \bigwedge\{e_i(\varphi, w) : w \in W_i, e_i : Var \times W_i \to S_2\}$, $V(\Box\varphi, W_i) = \bigwedge\{V(\varphi, W_j) : (W_i, W_j) \in R\}$, $V(\Diamond\varphi, W_i) = \bigvee\{V(\varphi, W_j) : (W_i, W_j) \in R\}$, where $\Box\varphi$ and $\Diamond\varphi$ are a abbreviations of $\Box_1\varphi \wedge ... \wedge \Box_n\varphi$ and $\Diamond_1\varphi \vee ... \vee \Diamond_n\varphi$ respectively.

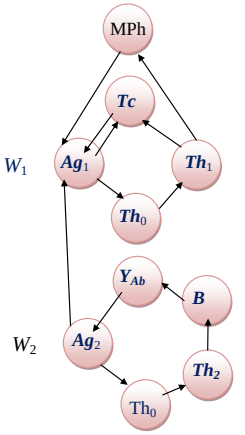
Recall that a modal formula φ is said to be modally valid for agent i when it is evaluated to 1 in all Kripke models for agent i; a modal formula φ is said to be globally modally valid when it is evaluated to 1 in all Kripke models for every agent $i \in \{1, ..., n\}$.

Now we give a naive definition of (global) immune system ImS. A (global) immune system ImS is a set of $Tcells$ with some actions between them. Identifying $Tcell$ with agent (or possible word) and an action between $Tcells$ with the relation between agents we can represent a (global) immune system ImS as a (global) 3-valued descriptive Kripke frame.



Kripke frame $\mathfrak{I}' = (W', R')$

Fig. 1



Kripke frame $\mathfrak{I}' = (W', R')$

Fig. 2

1.4.1 The epistemic aspects of immune system

We say that $w \in W_i$ is activated if $e_i(p, w) = 1$, it is not activated if $e_i(p, w) = 0$, it is not known that w is activated if $e_i(p, w) = 1/2$. So, for evaluation V we have the set of points of $\bigcup_{i=1}^{n} W_i$ such that part of them is activated, part of them is not activated and part of them is unknown they are activated or not activated.

A function $Es : \bigcup_{i=1}^{n} W_i \to S_2^c$ is named *an epistemic state* if for every $w, w' \in W_i$ it is hold

$$(w, w') \in R_i \Rightarrow (Es(w) = 1 \Rightarrow Es(w') = 1).$$

Let $e_i : Var \times W_i \to S_2^c$ be an evaluation for agent i, $i = 1, ..., n$. Let $e : Var \times \bigcup_{i=1}^{n} W_i \to S_2^c$ be an evaluation of $\bigcup_{i=1}^{n} W_i$ $(= W)$ such that $e(p, w) = e_i(p, w)$ if $w \in W_i$. A formula φ defines a function $S_\varphi^e(w) : \bigcup_{i=1}^{n} W_i \to S_2^c$ such that $S_\varphi^e(w) = e_i(\varphi, w)$ for $w \in W_i$. We say that a formula φ is *labelled by the evaluation*

e if $S^e_\varphi(w)$ is an epistemic function and denote such kind of function by ES^e_φ. The process of transformation Act of one epistemic function Es_1 to an another epistemic function Es_2 we name "$\varphi - activation$". So, for a formula φ a transferring of the epistemic state function ES^e_φ to the epistemic state function $ES^{e'}_\varphi$ is a φ-activation of points of $\bigcup_{i=1}^n W_i$ $(= W)$.

We described an immune system as a Kripke Frame. It means that by Kripke frame we capture just the relational structure of an immune system.

This representation of immune system neglects the epistemic information about the immune system, that is some knowledge on the points w are not represented. So to recover such an information we give the notion of *Epistemic State function* of an immune system. This is done by a function Es defined on all possible worlds to S^c_2. Of course Es satisfies some suitable conditions, which are essentially compatibility conditions with respect the relational structure of the immune system. In this way we have a more faithful representation of the knowledge about the given immune system. It is reasonable to think that to get the value $Es(w)$ it is needed some laboratory job. We plan mathematically to study the set of all epistemic states. Our aim is to help the immunologist to have a formal and canonical way to explore the possible Epistemic State (function) of an immune system. Since to an immune system, as defined in the paper, can be associated a logic which is complete with respect to certain Kripke frames, and since immune system representation gives us as Kripke Frame, we use formulas of the logic of our Kripke Frame immune system, to define some Epistemic States of the immune system. Actually we use a formula φ and an evaluation e of φ, in the following way: $ES^e_\varphi(w) = e(\varphi, w)$.

It is worth to note that a single formula φ essentially represents a set of Epistemic States, actually all such states defined by ES^e_φ when e varies in the set of all evaluations. In this way a given formula represents a collection of Epistemic States of the immune system. It could be of interest to explore the possibility to check whether given a collection of Epistemic States we can found a formula representing such a collection.

We defined the Activation function Act as a functions defined on the set of all Epistemic States with value in the same set. This is a way to represent how changes the epistemic information after, say an experiment, that produces new information about the epistemic values of all points w. To know facts about the function Act means to know facts about possible variations of the epistemic state of the system, and to check whether these variations can be described by formulas.

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1.5 Conclusion and Perspectives

We have introduced the new logic - three valued multi-modal epistemic Łukasiewicz logic $E\text{Ł}^c_3(n)$ adequate semantic of which are special relational systems named 3-valued descriptive Kripke frames. In other words we have proven completeness theorem, i. e. a formula α of $E\text{Ł}^c_3(n)$ which is a theorem of $E\text{Ł}^c_3(n)$ iff it is (globally)

modally valid. So we have shown that some immunological systems, described as relational systems, are Kripke Models of the logic we have presented. This means that theorems in our logic describe true properties in the model of immune system - the network of T lymphocytes' subpopulations and that we can set some conjecture on the model, which at the moment is not clear to medical and life sciences, and try to prove it as a theorem, or disprove it.

The principal role of the immune system is thought to be host defense against invasion by pathogenic agents. For this reason, the study of the immunology of infection offers important insight concerning effector functions and regulatory interactions fundamental to the immune response. In reacting to infectious agents, the immune system can generate to varying degrees unwanted immunopathologic side effects in the form of fever, tissue damage and immune complex lesions. The balance between resistance and pathology is delicate and determined both by the virulence of the pathogen and the immunoregulatory state of the host. It has become increasingly clear that cytokines, and in particular those associated with the Th1/Th2 CD4+ T cell subsets, are key determinants of the beneficial vs disease consequence of the host response.

So, if we have a theorem φ (which is a proposition) of multimodal epistemic 3-valued Łukasiewicz logic with constant $E\text{Ł}_3^c(n)$, then any evaluation in any immune system, represented as a 3-valued Kripke model, is equal to 1.

We have represented an immune system ImS as a relational system with epistemic information. This epistemic information is expressed by epistemic state function Es. Moreover, having some formula φ we define a collection of epistemic states which determined by the epistemic function ES^e_φ. In the perspective it will be interesting to find a corresponding formula for some epistemic state which is very important for immune systems.

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