



Bartłomiej Świątczak

University of Science and Technology of China, Hefei, China

ORCID: 0000-0001-6767-3064

e-mail: bart@ustc.edu.cn

## Francisco Varela's Vision of the Immune System

DOI: <http://dx.doi.org/10.12775/RF.2019.030>

### Introduction

Francisco Varela's contribution to cognitive science and neurobiology is well known.<sup>1</sup> Apart from introducing the concept of autopoiesis together with Maturana, he developed a doctrine of enactivism, which by portraying cognition as inseparable from action challenged representationist principles of classical cognitivism.<sup>2</sup> Varela applied his unique perspective on cognition and self also to immunology thereby advocating

---

<sup>1</sup> Evan Thompson, Antoine Lutz, and Diego Cosmelli, "Neurophenomenology: An Introduction for Neurophilosophers", in: *Cognition and the brain: The philosophy and neuroscience movement*, ed. Andrew Brook, Kathleen Akins (New York: Cambridge University Press, 2005), 40–97; David Rudrauf, Antoine Lutz, Diego Cosmelli, Jean-Philippe Lachaux, Michel Le Van Quyen, "From Autopoiesis to Neurophenomenology: Francisco Varela's Exploration of the Biophysics of Being", *Biological Research* 36, no. 1 (2003): 27–65; John Mingers, "The Cognitive Theories of Maturana and Varela", *Systems Practice*, 4, no. 4 (1991): 319–338; Adrián G. Palacios, Juan Bacigalupo, "Francisco Varela (1946–2001): Filling the Mind – Brain Gap: A Life Adventure", *Biological Research* 36, no. 1 (2003): 9–12.

<sup>2</sup> Francisco J. Varela, Eleanor Rosch, Evan Thompson, *The Embodied Mind* (Cambridge Mass.: MIT Press, 1993).

the universal character of these ideas.<sup>3</sup> In fact, despite recognizing fundamental differences between the immune system and the nervous system, Varela considered the immune system as a *bona fide* system of cognition and assumed that it shares many features with other cognitive systems including brain-based systems.<sup>4</sup>

The interest of Varela in immunology can be traced back as far as to the late 1970s and his semester-long collaboration with a Brazilian immunologist, Nelson Vaz.<sup>5</sup> The latter introduced Varela to immune network theory of Niels Jerne and participated in early development of the novel, radical view of the immune system as a system of circular cognition and self-identity constitution (a leitmotiv of most Varela's research studies). However, the Chilean initiated more systematic immunological studies only in the eighties when he became a member of Antonio Coutinho's research group in Paris.<sup>6</sup> While working in Paris he developed numerous mathematical models of the immune network function and elaborated a sophisticated, albeit somehow vague, conceptual framework to account for the immune system organization and structure.<sup>7</sup>

Here we discuss this conceptual framework by Varela and evaluate its current standing. In fact, since the immune network theory is no longer accepted there is a worry that Varela's original contribution might have been lost or condemned. In the final section of this paper we mention a few influential conceptual frameworks in the field to reveal that some ideas by Varela and other theoreticians of the immune network collective did enter into the mainstream immunology although being now present in an altered form, adapted to the present research context.

## Cognitive View of the Immune System

As mentioned above, Varela's vision of the immune system was deeply rooted in the immune network theory of Niels Jerne who believed that due to the enormous diversity of antibodies, which can recognize *any* antigen, they are not only able to bind to foreign substances (bacteria, viruses, nonself grafts etc.) but also to one another creating a complex,

---

<sup>3</sup> Nelson M. Vaz, "Francisco Varela and the Immunological Self", *Systems Research* 28, no. 6 (2011): 696–703.

<sup>4</sup> Francisco J. Varela, "A Cognitive View of the Immune System", *World Futures* 42, no. 1 (1994): 31–40.

<sup>5</sup> Vaz, "Francisco", 696–703.

<sup>6</sup> Antonio Coutinho, "A Walk with Francisco Varela from First- to Second-Generation Networks: in Search of the Structure, Dynamics and Metadynamics of an Organism-Centered Immune System", *Biological Research* 36, no. 1 (2003): 17–26.

<sup>7</sup> Coutinho, "A Walk", 17–26; Klaus Eichmann, *The Network Collective. Rise and Fall of a Scientific Paradigm* (Basel: Springer, 2008).

self-regulatory network of interactions.<sup>8</sup> Since anti-idiotypic antibodies (i.e. antibodies complementary to other antibodies in the network) are mirror images of the molecules they bind, they are structurally equivalent to the cognate antigens of the bound antibodies.<sup>9</sup> In fact, Jerne compared the immune network structure to an endless hall of mirrors and claimed that interacting antibodies collectively maintain an equilibrium state, which if disrupted by microbial invasion or other factors initiate an immune reaction to equilibrate the system while incidentally also helping to neutralize the invading agent.<sup>10</sup> He wrote: "the immune system (like the brain) reflects first ourselves, then produces a reflection of this reflection, and then subsequently it reflects the outside world: a hall of mirrors".<sup>11</sup> Overall, the immune network theory developed by Jerne and later expanded and modified by Varela represented the immune system as self-referential system made up of mutually interacting molecules, which respond to foreign materials only *accidentally*;<sup>12</sup> a cognitive vision quite at odds with the classical theory (the clonal selection theory), which emphasized importance of immune reactions against foreign bodies.

While the network theory was not a mainstream one, its associated, self-referential network was what attracted Varela to immunology in the first place. In fact, Varela was primarily a neurobiologist maintaining interest in the immune system only in so far as this system supported his overarching vision of life and cognition.<sup>13</sup> Postulating that the immune system is made up of interconnected components referring to one another, the network theory was offering him a solipsistic framework that fitted squarely into the ideas he derived from his long-term involvement in Buddhist theory and practice. In fact, Varela insisted that the immune system is a genuine cognitive system, which despite the probabilistic character of its intercellular connections can support processes like memory, learning, self and recognition.<sup>14</sup> Similarities between the immune

---

<sup>8</sup> Niels K. Jerne, "Towards a Network Theory of the Immune System", *Annales d'Immunologie* 125C, no. 1-2 (1974): 373-389.

<sup>9</sup> Niels K. Jerne, "The Generative Grammar of the Immune System. Nobel lecture, 8 December 1984", *Bioscience Reports* 5, no. 6 (1985): 439-451.

<sup>10</sup> Jerne, "Towards a Network", 373-389.

<sup>11</sup> Niels K. Jerne, "Idiotypic Networks and Other Preconceived Ideas", *Immunological Review* 79, no. 1 (1984): 19.

<sup>12</sup> Alfred I. Tauber, *Immunity. The Evolution of an Idea* (Oxford: Oxford University Press, 2017), 87.

<sup>13</sup> Varela, Rosch, Thompson, *The Embodied*; Palacios and Bacigalupo, "Francisco Varela", 9-12.

<sup>14</sup> Francisco J. Varela, Antonio Coutinho, Bruno Dupire, Nelson N. Vaz, "Cognitive Networks: Immune, Neural, and Otherwise", in: *Theoretical Immunology, Part 2*, ed. Alan S. Perelson (Reading, MA: Addison-Wesley, 1988), 359-375; Francisco J. Varela, Antonio Coutinho, "Immuknowledge: Learning Mechanisms of Somatic Indi-

system and the nervous system stemmed among other things from a distributed network character of underlying constituents, which according to Varela did not act as computational symbols of classical cognitivism.<sup>15</sup> Existence of an alternative system of cognition in the form of the immune system served for Varela as an evidence that cognitive systems are heterogeneous in nature and not limited to nervous systems.<sup>16</sup>

Assuming that the immune system is a true cognitive system, Varela focused on the apparent capacity of this system to define the limits of self.<sup>17</sup> As the network theory portrayed the immune system as a system of antibodies that bind to one another, Varela followed this idea to its logical conclusion suggesting that an immune network must be functionally *closed* and unable to interact with anything outside of its domain.<sup>18</sup> Assuming, unlike Jerne, that in addition to antibodies, an immune network also incorporates lymphocytes, their receptors and their antigens, he proposed together with Vaz, that the immune system is fundamentally insensitive to molecules, which are truly different from those that are already present in the body.<sup>19</sup> This was a major breach from the standard view of the immune system, which presupposed that outside the context of pathological autoimmunity the immune system ignores self-derived molecules.<sup>20</sup>

As emphasized by Varela, in a system whose components cannot recognize anything truly foreign, immune recognition becomes an act of "self-assertion".<sup>21</sup> Instead of distinguishing between self and nonself, such a system *enacts* or *brings forth* what it "sees".<sup>22</sup> This bringing-forth means that the immune system participates in defining which antigens are meaningful for its own perpetuation remaining insensitive to anything else. Thus the process of self-affirmation was for Varela not only cognitive but also creative, contributing to the construction and maintenance of organismal identity.<sup>23</sup> The process self-construction

---

viduation", in: *Doing Science*, ed. John Brockman (New York: Prentice-Hall, 1991), 237–256.

<sup>15</sup> Varela, Coutinho, Dupire, and Vaz, "Cognitive Networks", 360–361.

<sup>16</sup> Varela, "A Cognitive View", 31.

<sup>17</sup> Vaz, "Francisco", 696–703.

<sup>18</sup> Nelson M. Vaz and Francisco J. Varela, "Self and Non-sense: an Organism-Centered Approach to Immunology", *Medical Hypotheses* 4, no. 3 (1978): 231–267.

<sup>19</sup> Vaz, Varela, "Self and Non-sense", 231–67; Coutinho, "A Walk", 20.

<sup>20</sup> Macfarlane F. Burnet, *The Clonal Selection Theory of Acquired Immunity* (Nashville: Vanderbilt University Press, 1959).

<sup>21</sup> Varela and Coutinho, "Immuknowledge," 237–256.

<sup>22</sup> Francisco J. Varela, Antonio Coutinho, "Second-Generation Immune Networks", *Immunology Today* 12, no. 5 (1991): 165.

<sup>23</sup> Varela, Coutinho, "Second-Generation", 159; Francisco J. Varela, "The Emergent Self", in *The Third Culture: Beyond the Scientific Revolution*, ed. John Brockman (New York: Touchtone, 1995), 209–222.

was assumed by Varela to be dynamic as network identity was being continuously altered by chaotic changes in the concentration of natural antibodies and constituent lymphocytes.<sup>24</sup> These changes in the concentration of immune constituents, associated by Varela with immune learning,<sup>25</sup> were assumed by him to result among other things from variable turnover rate of lymphocytes in the network. To elucidate this process, Varela elaborated mathematical models of lymphocyte recruitment representing it as an autopoietic cycle of supplementation of lost lymphocytes with bone-marrow-derived ones (see below).<sup>26</sup> Overall, Varela believed that while being closed, an immune network was constantly changing, modifying the scope of its cognitive domain and shifting its identity.

While claiming, against the established paradigm, that the immune network is locked into itself, Varela still needed to account for defense capacities of the immune system.<sup>27</sup> Pointing out that the bone marrow constantly produces diverse lymphocytes, only some of which carrying receptors specific for self-antigens, he concluded that most of these newly produced immune cells never become part of the network.<sup>28</sup> In fact, as we have seen, he assumed that only those newly produced lymphocytes, which express receptors with specificity for antigens already present in the network can become activated and incorporated into it.<sup>29</sup> The remaining, resting lymphocytes (which make up estimated 90% of lymphocytes in the body) persist outside of the network. Varela and Coutinho suggested that since this pool of resting lymphocytes, disconnected from the network, consists of cells carrying receptors for nonself antigens, these cells were mediating defense reactions against bacteria, viruses, and other foreign targets.<sup>30</sup> Operating on principles defined by the clonal selection theory of immunity, the peripheral lymphocytes could become part of the immune network only after their activation when their increased concentration and the associated network perturbation could pave their way to the assimilation with the network (cf. Figure 1). In short, Varela assumed that the immune system operates on two distinct modes, a classical mode and a network mode, each of which being

---

<sup>24</sup> John Stewart, Francisco J. Varela, "Morphogenesis in Shape-space. Elementary Meta-dynamics in a Model of the Immune Network", *Journal of Theoretical Biology* 153, no. 4 (1991): 477–498.

<sup>25</sup> Varela, Coutinho, "Immuknowledge," 237–256.

<sup>26</sup> John Stewart, Antonio Coutinho "The Affirmation of Self: A New Perspective on the Immune System", *Artificial Life* 10, no. 3 (2004): 265.

<sup>27</sup> Coutinho, "A Walk", 22.

<sup>28</sup> Varela and Coutinho, "Second-Generation", 161–162.

<sup>29</sup> Coutinho, "A Walk", 20.

<sup>30</sup> Varela and Coutinho, "Second-Generation", 159–165.

mediated by dedicated compartment of the immune system: the central immune system and the peripheral immune system.<sup>31</sup>

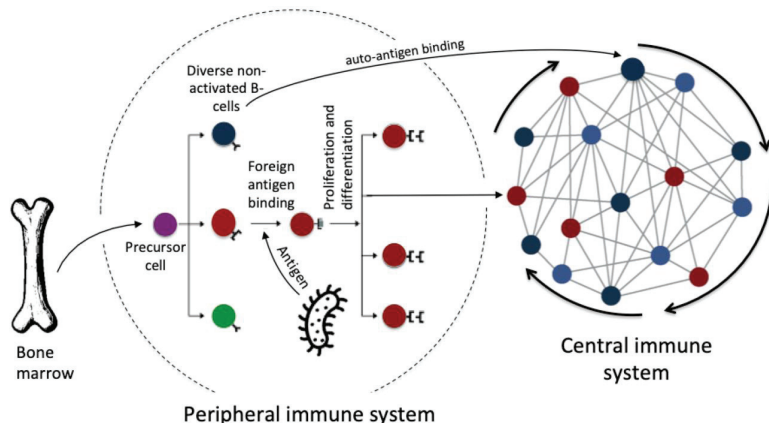


Figure 1. A two-component view of the immune system by Francisco Varela. Varela assumed that the immune system is divided into two parts: the peripheral immune system and the central immune system. He suggested that the peripheral system does not have a network character and is operating based on principles defined by the clonal selection theory. The central immune system, in turn, was assumed by Varela to have a network architecture consisting of natural autoreactive lymphocytes and antibodies. Lymphocytes and antibodies from the periphery periodically replaced autoreactive lymphocytes and antibodies in the central network thereby ensuring continued operation (and stable identity) of the network. In particular, newly produced lymphocytes with affinities to self-antigens and other lymphocytes in the network were readily becoming parts of the central immune system. In addition, B-cells activated by foreign antigens, which due to their clonal expansion were influencing changes in the central immune system could also become part of the network.

Even though Varela eventually allowed for nonself immune responses, the immune system remained for him primarily a system of organismal identity formation: “The emergent identity of this system is the identity of your body”, he claimed.<sup>32</sup> In fact, according to the Chilean, the chief function of the immune system was to define the organismal self in the process of autoantigen recognition and lymphocyte replacement.<sup>33</sup> He attributed the same function to the nervous system and claimed that the organism is in fact a meshwork of selfless selves

<sup>31</sup> Varela, “A Cognitive View”, 36–37.

<sup>32</sup> Varela, “The Emergent Self”, 209–222.

<sup>33</sup> Alfred I. Tauber, *The Immune Self: Theory or Metaphor?* (Cambridge: Cambridge University Press, 1994), 172–175; Tauber, *Immunity*, 237.

that these and other bodily systems constitute.<sup>34</sup> To give a hint of how an immune identity emerges as a global property of the network, he drew an analogy with Gaia: an interconnected system of living beings and their Earthly environment, whose emergent identity unfolds in self-regulating geophysical cycles.<sup>35</sup> Thus, the process of identity construction by the immune network was for Varela ecological in nature dependent on interactive exchanges between populations of immune cells and molecules that due to their network activity influence behavior of other bodily constituents and participate in autopoietic cycles of whole-organism construction.

## Theoretical Foundations of Varela's Immunology

Varela's idea of the immune network as a closed, self-organizing system was related to his and Maturana's concept of autopoiesis that is to an idea that a living being constructs its own identity by replacing its parts and allowing these parts to carry on the process of identity construction.<sup>36</sup> When viewed as a cognitive system, autopoietic system does not collect information about its environment to learn about the outside world but optimizes its coupling between perception and action to maintain itself in changing environmental conditions.<sup>37</sup> With these original ideas, Varela was trying to challenge the standard vision of a cognitive system as a stimulus/response system and establish a quasi-constructivist framework, in which organisms customize their cognitive states to what is relevant to these organisms' persistence.<sup>38</sup> A paradigmatic example of such cognitive adaptations was for Varela color vision, which involves perceptual states, having no direct equivalence in the outside world.<sup>39</sup> These and other aspects of cognitive functioning were used by Varela to argue against representationalism of modern cognitive science.

---

<sup>34</sup> Francisco J. Varela, "Organism: A Meshwork of Selfless Selves", in: *Organism and the Origin of Self*, ed. Alfred I. Tauber (Dordrecht: Kluwer, 1991), 79–107; Varela, "The Emergent Self", 209–222.

<sup>35</sup> James Lovelock, *Gaia: A New Look at Life on Earth* (Oxford: Oxford University Press, 1979); Varela, Coutinho, "Immunoknowledge," 237–256.

<sup>36</sup> Humberto R. Maturana, Francisco J. Varela, *The Tree of Knowledge: The Biological Roots of Human Understanding* (Boston and London: Shambhala Press, 1998).

<sup>37</sup> Francisco J. Varela, "Structural Coupling and the Origin of Meaning in a Simple Cellular Automaton", in: *The Semiotics of Cellular Communication in the Immune System*, ed. Eli E. Sercarz, et al. (Berlin: Springer-Verlag, 1988), 151–161; Humberto R. Maturana, Francisco J. Varela, *Autopoiesis and Cognition: the Realization of the Living* (Dordrecht: Reidel, 1980), 13.

<sup>38</sup> Vaz, "Francisco", 699.

<sup>39</sup> Varela, "Organism: A Meshwork", 79–107.

Varela's view of the immune system was an attempt to apply the above concepts that is the concepts of autopoiesis, enactivism and anti-representationalism, to a system whose basic mode of organization was different from that of the nervous system. As Varela rightly observed, immunology, like cognitive science, is also founded on a stimulus-response-regulation model, which postulates a consecutive sequence of activation steps from pattern recognition, through decision making to response.<sup>40</sup> With his novel vision of biological organization, Varela intended to overcome this reactive framework and establish one in which the immune system actively participates in creation of its recognition states bringing forth of what it "sees" as antigenic targets.<sup>41</sup> Consequently, he insisted that the immune system like the brain employs no representations in the classical sense but engages into action that helps to establish a meaningful coupling with the environment.<sup>42</sup> As we have seen, Varela referred to this form of cognition as enactive and considered it as inseparable from the processes of identity maintenance and construction.<sup>43</sup> Overall, Varela's view of the immune system can be traced to his basic idea of an autopoietic system, which constantly builds itself and interacts with the environment autonomously, that is in its own terms.

## Legacy

An elaborated critique of the Paris School (Varela-Vaz-Coutinho continuum) was provided by Tauber who considered the postulated closed character of an immune network as one of the principal problems of the Varela's theory.<sup>44</sup> In fact, even Coutinho who conducted empirical studies to test Varela's hypotheses rejected the idea that the immune system might be operationally closed.<sup>45</sup> More generally, the network theory of immunity, on which Varela's theory was based, is no longer accepted as a faithful depiction of the immune system structure and behavior.<sup>46</sup>

Despite the above problems, Varela's bold proposal that immune recognition might be pre-determined by what immune cells interact with in the network survived in various forms in modern science. In her

---

<sup>40</sup> Nelson N. Vaz, "The Specificity of Immunological Observations", *Constructivist Foundations* 6, no. 3 (2011): 337.

<sup>41</sup> Varela, Coutinho, "Immuknowledge," 237–256.

<sup>42</sup> Varela, Coutinho, Dupire, Vaz, "Cognitive Networks", 373.

<sup>43</sup> Varela, "The Emergent Self", 209–222.

<sup>44</sup> Tauber, *The Immune Self*; Alfred I. Tauber, "The Cognitivist Paradigm 20 Years Later. Commentary on Nelson Vaz", *Constructivist Foundations* 6, no. 3 (2011): 342–344.

<sup>45</sup> Coutinho, "A Walk", 17–26.

<sup>46</sup> Eichmann, *The Network*.



presentation of an influential "danger model", Polly Matzinger referred to the immune network theory to support her claim that innate immune cells evolved to react to endogenous danger signals rather than to invading microbes.<sup>47</sup> From the point of view of her theory, the capacity of innate immune receptors to bind to microbial molecules is contingent upon their phylogenetically more primitive capacity to recognize self-derived structures.

In fact, turning immune receptors to internal states of the organism makes sense on the supposition that the organism's ultimate interest lays in its self-preservation and perpetuation of its own existence.<sup>48</sup> This threat has been explored in the work of Cohen who developed the idea of homunculus that is of a system of self-reacting antibodies recognizing markers of pathological change in the organism.<sup>49</sup> The importance of immune interactions with inner molecules is also emphasized within the dynamic tuning theory of Grossman and Paul who suggested that the activation threshold of lymphocytes depends on the dynamics of their interactions with auto-antigens.<sup>50</sup> The greatest support for idea that the immune system shapes its own reactivity in the course of interaction with self-molecules comes from the studies of T-cell development showing that positive selection of these cells demands their weak reactivity with endogenous targets.<sup>51</sup> All these developments traceable to Varela and other researchers involved in the network paradigm still hardly fit into the dominant conceptual framework of immunology calling for a revision of the clonal selection paradigm.<sup>52</sup>

## Conclusion

Based on Jerne's immune network theory, Varela developed an original view of the immune system and its functions. The immune system was for him a system of mutually interacting elements, molecules and cells collectively engaged in organismal identity construction. This identity

---

<sup>47</sup> Polly Matzinger, "The Danger Model: A Renewed Sense of Self", *Science* 296, no. 5566 (2002): 301–305.

<sup>48</sup> Maturana, Varela, *The Tree of Knowledge*.

<sup>49</sup> Irun R. Cohen, "Biomarkers, Self-antigens and the Immunological Homunculus", *Journal of Autoimmunity* 29, no. 4 (2007): 246–249.

<sup>50</sup> Zvi Grossman, William E. Paul, "Dynamic Tuning of Lymphocytes: Physiological Basis, Mechanisms, and Function", *Annual Review of Immunology* 33, no. 1 (2015): 677–713.

<sup>51</sup> Timothy K. Starr, Stephen C. Jameson, Kristin A. Hogquist, "Positive and Negative Selection of T Cells", *Annual Review of Immunology* 21, no. 1 (2003): 139–176.

<sup>52</sup> Irun R. Cohen, *Tending Adam's Garden: Evolving the Cognitive Immune Self* (San Diego: Academic Press, 2000).

was emerging from local immune interactions of the network components very much like the identity of the neural network or Gaia network is also a product of local activities. Even though the network theory of immunity is no longer accepted in its original form, some key theoretical ideas of Varela and the network school persisted in immunology stimulating research on natural, spontaneous autoimmunity. In addition, Varela's attempt to relate immunological processes to most fundamental aspects of living beings, their identity and self-preservation remains an important source of inspiration for ongoing theoretical studies within the emerging field of philosophy of immunology.

## Bibliography

- Burnet Macfarlane F. 1959. *The Clonal Selection Theory of Acquired Immunity*. Nashville: Vanderbilt University Press.
- Cohen Irun R. 2000. *Tending Adam's Garden: Evolving the Cognitive Immune Self*. San Diego: Academic Press.
- Cohen Irun R. 2007. "Biomarkers, Self-antigens and the Immunological Homunculus". *Journal of Autoimmunity* 29, no. 4: 246–249.
- Coutinho Antonio. 2003. "A Walk with Francisco Varela from First- to Second-Generation Networks: in Search of the Structure, Dynamics and Metadynamics of an Organism-Centered Immune System". *Biological Research* 36, no. 1: 17–26.
- Eichmann Klaus. 2008. *The Network Collective. Rise and Fall of a Scientific Paradigm*. Basel: Springer.
- Grossman Zvi, William E. Paul. 2015. "Dynamic Tuning of Lymphocytes: Physiological Basis, Mechanisms, and Function". *Annual Review of Immunology* 33, no. 1: 677–713.
- Jerne Niels K. 1974. "Towards a Network Theory of the Immune System". *Annales d'Immunologie* 125C, no. 1–2: 373–389.
- Jerne Niels K. 1984. "Idiotypic Networks and Other Preconceived Ideas". *Immunological Review* 79, no. 1: 5–24.
- Jerne Niels K. 1985. "The Generative Grammar of the Immune System. Nobel lecture, 8 December 1984". *Bioscience Reports* 5, no. 6: 439–451.
- Lovelock James. 1979. *Gaia: A New Look at Life on Earth*. Oxford: Oxford University Press.
- Maturana Humberto R., Francisco J. Varela. 1980. *Autopoiesis and Cognition: the Realization of the Living*. Dordrecht: Reidel.
- Maturana Humberto R., Francisco J. Varela. 1998. *The Tree of Knowledge: The Biological Roots of Human Understanding*. Boston–London: Shambhala Press.
- Matzinger Polly. 2002. "The Danger Model: A Renewed Sense of Self". *Science* 296, no. 5566: 301–305.

- Mingers John. 1991. "The Cognitive Theories of Maturana and Varela". *Systems Practice*, 4, no. 4: 319–338.
- Palacios Adrián G., Juan Bacigalupo. 2003. "Francisco Varela (1946–2001): Filling the Mind-Brain Gap: A life adventure". *Biological Research* 36, no. 1: 9–12.
- Rudrauf David, Antoine Lutz, Diego Cosmelli, Jean-Philippe Lachaux, Michel Le Van Quyen. 2003. "From Autopoiesis to Neurophenomenology: Francisco Varela's Exploration of the Biophysics of Being". *Biological Research* 36, no. 1: 27–65.
- Starr Timothy K., Stephen C. Jameson, Kristin A. Hogquist. 2003. "Positive and Negative Selection of T Cells". *Annual Review of Immunology* 21, no. 1: 139–176.
- Stewart John, Antonio Coutinho. 2004. "The Affirmation of Self: A New Perspective on the Immune System". *Artificial Life* 10, no. 3: 261–276.
- Stewart John, Francisco J. Varela. 1991. "Morphogenesis in Shape-space. Elementary Meta-dynamics in a Model of the Immune Network". *Journal of Theoretical Biology* 153, no. 4: 477–498.
- Tauber Alfred I. 1994. *The Immune Self: Theory or Metaphor?* Cambridge: Cambridge University Press.
- Tauber Alfred I. 2011. "The Cognitivist Paradigm 20 Years Later. Commentary on Nelson Vaz". *Constructivist Foundations* 6, no. 3: 342–344.
- Tauber Alfred I. 2017. *Immunity. The Evolution of an Idea*. Oxford: Oxford University Press.
- Thompson Evan, Antoine Lutz, Diego Cosmelli. 2005. "Neurophenomenology: An Introduction for Neurophilosophers". In: *Cognition and the brain: The philosophy and neuroscience movement*. Ed. Andrew Brook, Kathleen Akins, 40–97. New York: Cambridge University Press.
- Varela Francisco J. 1988. "Structural Coupling and the Origin of Meaning in a Simple Cellular Automaton". In: *The Semiotics of Cellular Communication in the Immune System*. Ed. Eli E. Sercarz et al., 151–161. Berlin: Springer-Verlag.
- Varela Francisco J. 1991. "Organism: A Meshwork of Selfless Selves". In: *Organism and the Origin of Self*. Ed. Alfred I. Tauber, 79–107. Dordrecht: Kluwer.
- Varela Francisco J. 1994. "A Cognitive View of the Immune System". *World Futures* 42, no. 1: 31–40.
- Varela Francisco J. 1995. "The Emergent Self". in *The Third Culture: Beyond the Scientific Revolution*. Ed. John Brockman, 209–222. New York: Touchtone.
- Varela Francisco J., Antonio Coutinho. 1991. "Immuknowledge: Learning Mechanisms of Somatic Individuation". In: *Doing Science*. Ed. John Brockman, 237–256. New York: Prentice-Hall.
- Varela Francisco J., Antonio Coutinho. 1991. "Second-Generation Immune Networks". *Immunology Today* 12, no. 5: 159–165.
- Varela Francisco J., Antonio Coutinho, Bruno Dupire, Nelson N. Vaz. 1998. "Cognitive Networks: Immune, Neural, and Otherwise". In: *Theoretical*

- Immunology, Part 2*. Ed. Alan S. Perelson, 359–375. Reading, MA: Addison-Wesley.
- Varela Francisco J., Eleanor Rosch, Evan Thompson. 1993. *The Embodied Mind*. Cambridge Mass.: MIT Press.
- Vaz Nelson M. 2011. "Francisco Varela and the Immunological Self". *Systems Research* 28, no. 6: 696–703.
- Vaz Nelson M. 2011. "The Specificity of Immunological Observations". *Constructivist Foundations* 6, no. 3: 334–342.
- Vaz Nelson M., Francisco J. Varela. 1978. "Self and Non-sense: an Organism-Centered Approach to Immunology". *Medical Hypotheses* 4, no. 3: 231–267.

## Summary

The author of the method of neurophenomenology and an advocate of a novel understanding of biological organization, known as autopoiesis, Francisco Varela (1946–2001) conducted long-term theoretical studies of the immune system. Working within the framework of the immune network theory of Niels Jerne, the Chilean biologist turned conceptual foundations of immunology upside down and argued that instead of acting as a system of defense, the immune system is primarily involved in interactions with organism's own cells and molecules. Despite the immune network theory fell into disrepute, Varela left a lasting mark in the field's conceptual infrastructure instilling a thought that what the immune system interacts with is shaped by the spontaneous activity of this system.

**Keywords:** Francisco Varela, autopoiesis, immune system

## Streszczenie

### Francisca Vareli wizja systemu immunologicznego

Autor metody neurofenomenologicznej i zwolennik nowego rozumienia organizacji istot żywych, znanej jako autopoiesis, Francisco Varela (1946–2001) prowadził długoterminowe badania teoretyczne z zakresu immunologii. Działając w ramach teorii sieci immunologicznej Nielsa Jerne'a, chilijski biolog odwrócił koncepcyjne podstawy immunologii do góry nogami i argumentował, że zamiast działać jako system obrony, układ odpornościowy jest przede wszystkim zaangażowany w interakcje z własnymi komórkami i cząsteczkami organizmu. Pomimo że teoria sieci immunologicznej popadła w niełaskę, Varela pozostawił trwałe ślady w infrastrukturze koncepcyjnej immunologii, zaszczepiając idee, że to, z czym układ odpornościowy wchodzi w interakcję, jest kształtowane przez spontaniczną aktywność tego układu.

**Słowa kluczowe:** Francisco Varela, autopoiesis, układ odpornościowy