A multiplicity of statistical models for modeling the degeneracy of living communicating holons

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Abstract. Communicating living systems detect and process a multiplicity of events with degeneracy, to continuously cope with environmental aleatoric incertitude. The concept of holon, communicating at various scales of living organizations, is hereafter formalized through dynamical systems driven by the multiplicity of statistical models. Then, the stimulus-response of elementary biological holons can be modeled by memoryless Boolean automata with different signal processing methods, in presence of noise and stochastic interference. Detection of a specified signal, to update the automaton state, can be performed via multiple families of update functions, with differentiated balances between sensitivity and specificity in presence of interference: (i) Neyman-Pearson update functions provide the best possible sensitivity to detect the signal of interest in absence of interference, but cannot guarantee a desired specificity ; (ii) by detecting large amplitudes of any signal in noise, update functions based on Random Distortion Testing yield a suboptimal sensitivity to detect the signal in noise, but guarantee a wanted specificity even in presence of interference. Thus, statistical inference theories offer functional and structural redundancy and open prospects to model fractal-like holarchies, via networks of communicating degenerated automata, to feature properties of the immune system.

1 Introduction

Living systems, from cells to micro and macro-ecosystems, interact and adapt to their environment through permanent interactions and communications to perceive a multiplicity of events and detect signals of potential interest in noise and stochastic interference. Perception and detection occur within cell molecules, between cells, among and between multicellular organisms, to trigger biochemical reactions, molecular/cellular diversification, organism proliferation/selection and changes of state in living systems. Networked communication systems then occur at the level of the micro-ecosystems that are hosted in holobiont organisms, whose commensal microbiota is controlled by their immune systems. In turn, these micro-ecosystems are wired together to constitute macro-ecosystems connecting multicellular organisms in social-ecosystems. State transition models were presented in [1], [2] to account for the complex cell communications characterizing the immune ecosystems [3] and summarized in Figure 1. In these works, state transition models are state-machines whose state-diagram transitions are driven by rules.

In the present paper, we move from such a top-down approach, where state-machines are black boxes, to a bottom-up approach involving sensitive and reactive holons whose behavior is probabilistic according to random contextual changes. By so proceeding, we thus aim to improve modeling approaches by developing cognitive network models.

Understanding and modeling the balanced sensitivity and specificity of signal detection performed by living systems and required for these systems to communicate together is therefore of particular interest. This dynamic equilibrium is the consequence of the living system co-evolution with extremely high diversification and selection of structures and functions, including self-assembly and transmission of molecules and cells. The multiplicity of solutions induces resilience of dynamical living systems, but also potential disorders and failures.

We thus wonder whether a multiplicity of biological solutions generated by stochastic combinations and selection through evolution, could allow to consider a multiplicity of criteria for performance and/or optimality, each criterion being aimed to conciliate sensitivity and specificity. In this respect, we ask whether communication and resilience of a dynamical system could be attained through multiple statistical models, allowing for degeneracy of structure and functions. Indeed, biological dynamical systems as cells receive and perceive a multiplicity of physical or biological events and process them as a cascade of fluxes, through interacting molecules. These molecules act as adapted "sensors" issued from the long-term selection during species co-evolution to detect and transmit signals with various sensitivity and specificity. These sensors al-

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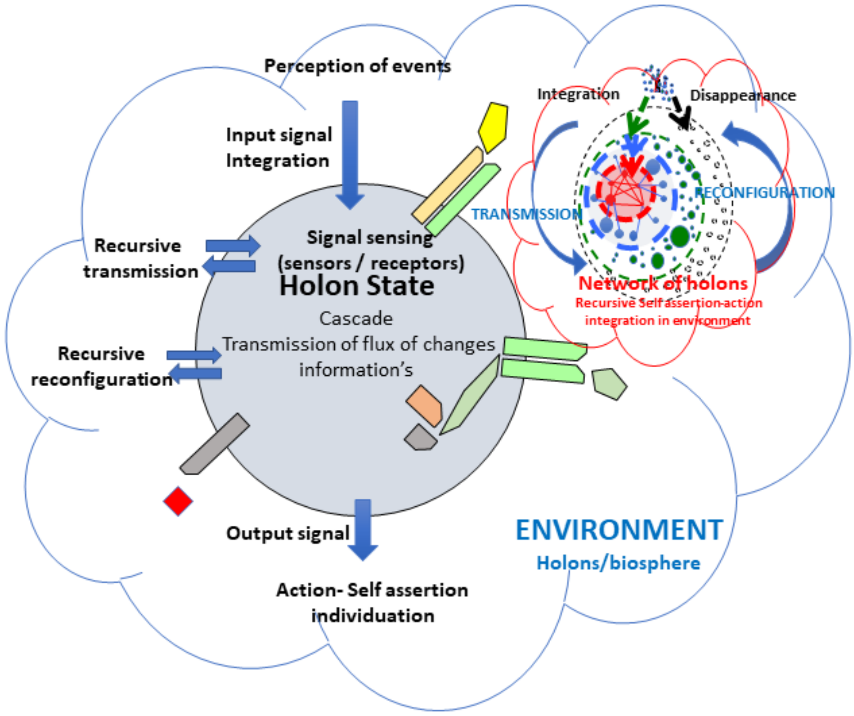

Figure 1: **Abstraction of biological communicating living holons, as dynamical systems perceiving fluxes of events, detecting signals and reacting in self-similar networks.** As an example (adapted from [3]), a cell is the smallest autonomous living dynamical system that can be modeled as a perceptive/reactive degenerate holon capable of perception, recursive transmission and reconfiguration of its state and functions. A cell is a local observer equipped with a network of thousands of internal and external holon-molecules that can combine together to make the cell integrate internal and external fluxes of changes. Holons can communicate by integrating input signals, transmitting flux of changes and generating output signals and actions.

low molecules to detect more or less expected signals, in presence of interference and noise, and to process such signals through a cascade of transmissions and reactions, to finally trigger a change of the system state. The immune system of high vertebrates moreover provides adaptive degenerated solutions, through stochastic receptors clonally expressed by lymphocytes and leading to adaptive capacities, regulations and self-organization.

A conceptual framework to model and simulate living systems as "*[...] self organizing open hierarchical systems*" [4] is provided by the concepts of holon and holarchy [5]. "*A holarchy is according to A. Koestler a tree-like hierarchy where the nodes of the tree — the components of the hierarchy — are autonomous intelligent acting I/0 systems*" [4]. The holons are the components of the holarchy. In Koestler's view, a holon is a whole, which is itself included in a vaster whole. A holon is autonomous in various senses: first, it can deal with events without "authorization" or "instruction" from any monitor; in addition, it communicates with other holons at the same level, but also between superordinate and subordinate structures. Mella extended this concept up to social holons and human artifacts [6].

A holon (also called a monad by Ehresmann [7]) preserves its identity while its internal components are continuously repaired or replaced. Then, the concept of holon appears as a suitable concept encapsulating the "fractal-like" structure of the living systems at any scale. By fractal-like structure, we do not mean that we retrieve the same pattern at every scale of the living system. We rather mean that the same type of communication processes, supported by agents with the same type of properties, are encountered at every scale of the living system and obey to self-similar cascades of signal processing.

The concept of holon was previously used in [3] to propose a model communication in the immune system through the notions of holon-cell, holon-lymphocyte and holon-organism. Such a model allowed to consider the recursive self-assertion and integration required for the dynamical individuation of the holon-lymphocytes in the communicating immune system evolving in the changing environment of vertebrate organisms. It accounts for the fact that, at each scale of the vertebrate organism and immune system organization (organism, cells, receptors), we face networks of biological agents whose patterns clearly differ from one scale to another, but that however interact and communicate via similar processes with similar properties and consequences. Cells equipped with a diversity of molecules displaying a diversity of molecular binding sites are typical examples of biological holons [3], as illustrated by Figure 1.

In the present paper, we follow Pichler who wrote that

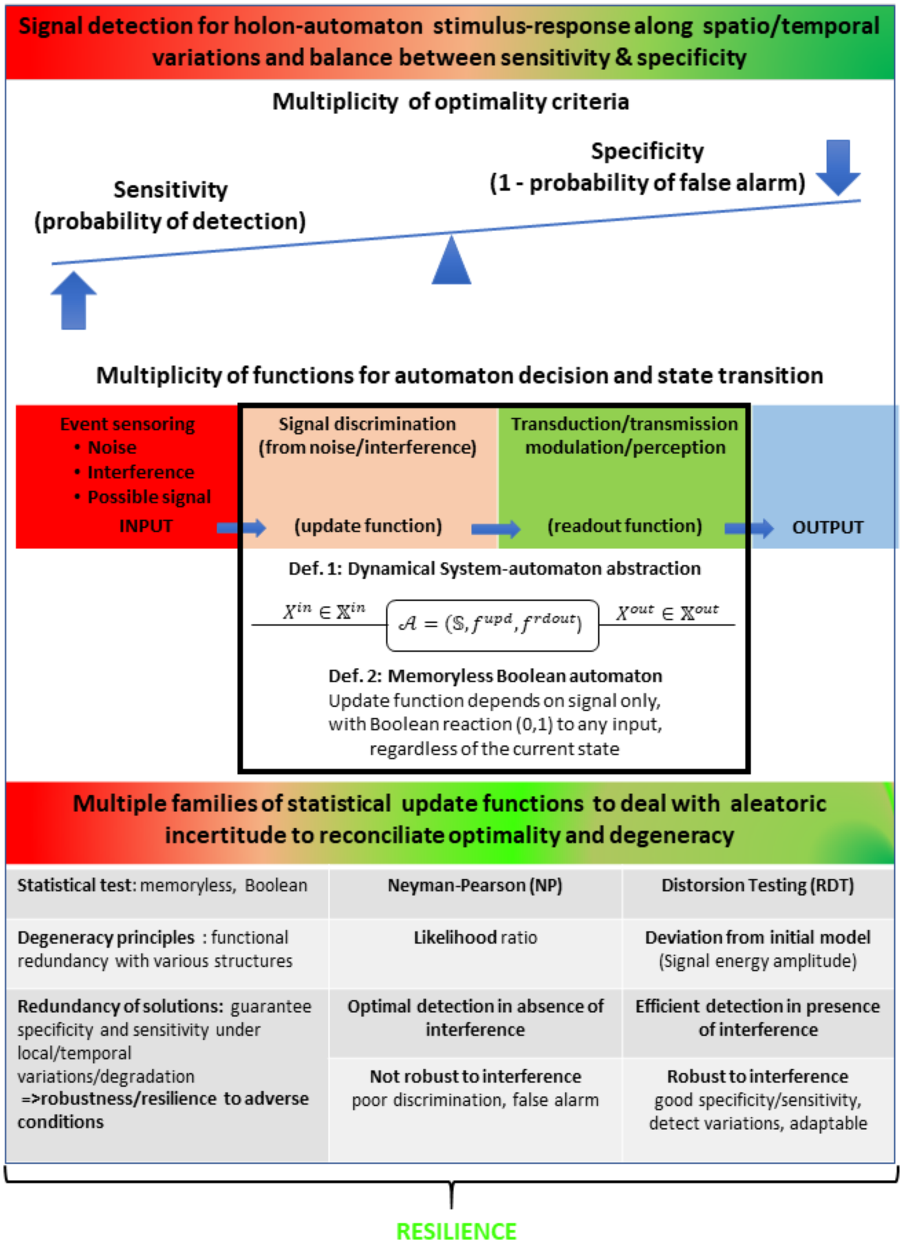

Figure 2: **Automaton communication based on a multipliticy of criteria for signal detection**. Facing a multiplicity of events and interference fluxes (schematized here by a superposition of colors), a discrete dynamical system (a biological holon, mathematically modeled as an automaton) should use a multiplicity of criteria to balance its performance and potential optimality, in terms of signal detection (sensitivity or $\mathbb{P}_{\text{DET}}$) vs. false alarm avoidance (specificity or $1 - \mathbb{P}_{\text{FA}}$), according to the changing environment and context of the signal detection. This balance can be sought by resorting to a multiplicity of statistical models, functions and structures. The signal detection on the basis of an input can be abstracted by an "update function" aimed at discriminating the signal from interference and noise. The outcome of the update function updates the holon state, which in turn triggers the transduction/transmission of a readout signal via a readout function. The automaton internal cascade of treatments thus allows for the holon action and the transmission of an external signal to other holons. The table at the bottom of the figure benchmarks the NP update functions and the RDT update functions by comparing the respective criteria they optimize.

"*[...] as seen from the systems-theoretical point of view, the most desirable formal model for a component of a holarchy is given by a dynamical system with input and output*" [8]. We thus seek models of living holons as dynamical systems that capture input signals, change state and output signals. Such a model is suggested by the typical holon-cell properties summarized by Figure 1. The same holds for antigen recognition molecules expressed by lymphocytes and that achieve interactions and perceptions of millions of antigens with various affinities. Collectively, this leads to a dynamic interactive network, where adaptive clonal selection of lymphocytes with degenerate repertoires can occur according to environmental changes.

On the other hand, degeneracy, in the scientific discourse, is a crucial feature of living systems at all scales [9]. In life science, degeneracy is not synonymous to degeneration and should therefore not be confused with deviance and decay of a system [10]. In fact, Edelman and Gally, considering the nervous and immune systems, define degeneracy as "*[...] the ability of elements that are structurally different to perform the same function or yield the same output*" [9]. Degenerate biological subsystems or organs, albeit structurally different, can thus substitute each other to perform a given task when one of them fails. The Jerne idiotypic network [11, 12] is a perfect example of degeneracy. Degeneracy also underlies the cross-reactivity of immunoreceptors expressed by lymphocytes [13] and that gives rise to novelty, evolvability, adaptiveness and functional integrity.

Since dynamical systems are generic models of living holons and degeneracy can mathematically be modeled through the Multiplicity Principle (MP) introduced in [14] and extensively studied in [15], the question addressed below is thus whether we can propose mathematical models of dynamical systems satisfying the MP. In the vein of Pichler, such mathematical models could prove helpful to model and simulate in multi-agent systems "*[...] the kind of complex biological or socio-economic systems which Koestler had in mind*" [4].

2 Summary of main results

The mathematical models exhibited in the sequel, as a first answer to the question above, are at the interface between theoretical biology, the theory of dynamical systems, category theory — from which the MP derives — and statistical inference. So, to ease the reading of this paper and convey the main concepts underlying the approach, this section summarizes our main results. In this section and throughout the paper, mathematical details will be omitted in favor of intuition. The interested reader can refer to papers cited herein for mathematical details.

To begin with, Figure 2 summarizes the multiplicity of aleatoric incertitudes and biological solutions selected by nature. This figure also features their abstractions considered in this paper to account for the capability of holons to perform detection, communication and achieve resilience in adverse conditions.

In Section 3, holons are abstracted as automata, also called Discrete Dynamical Systems in [16, 17]. Among all possible automata, memoryless Boolean automata are then our main focus because they can be interpreted as basic stimulus-response holons with the capacity to detect a signal in noise and possible interference. The detection of the signal by a given memoryless Boolean automaton is performed by the automaton update function f^{updt}, interpreted as a statistical test whose outcome triggers an update of the automaton state, regardless of the automaton previous state. Because the prior probabilities of presence and absence of the signal are unknown or even not defined, our approach is fundamentally non-Bayesian. The approach followed below thus aims to achieve a balance between $\mathbb{P}_{\text{DET}}$, the probability of detection, that is the probability of detecting the signal when this one is actually present, and $1 - \mathbb{P}_{\text{FA}}$, the probability of false alarm, that is the probability of erroneously detecting this signal — and thus triggering a spurious updating of the automaton state, when this signal is actually absent [1] This balance is illustrated in Figure 2 between the "sensitivity" and "specificity" used in biology and that are the empirical counterparts of $\mathbb{P}_{\text{DET}}$ and $1 - \mathbb{P}_{\text{FA}}$, respectively. Too many erroneous changes of states may significantly affect holons and the overall system they compose, especially in a biological context where such changes may trigger a system bolting. In the non-Bayesian framework, the balance is further controled by imposing a maximum value — or level — for $\mathbb{P}_{\text{FA}}$.

In Section 4, we propose a multiplicity of criteria to design update functions for signal detection according to the changing random context of the holon. The work hypothesis is that a system composed of memoryless Boolean automata should be resilient if the automata are equipped with detectors with different performance and potential optimality criteria that are "degenerate" in the mathematical sense specified by the MP. In this respect, we exhibit two distinct families of update functions for memoryless Boolean automata. Each update function of each family guarantees a sufficiently good and possibly optimal $\mathbb{P}_{\text{DET}}$, while maintaining the $\mathbb{P}_{\text{FA}}$ below a certain level. The first family is that of all Neyman-Pearson (NP) update functions based on the standard likelihood detection of a signal in noise (Neyman-Pearson theory). These update functions should be convenient to model germline encoded cell sensors and receptors. The second family is that of all RDT update functions that aim at detecting sufficiently large distortions of this same signal in noise (RDT theory). These RDT update functions are surrogates to NP update functions to detect the signal of interest in noise when some interference is present. Indeed, the effect of interference on the noisy signal can suitably be modeled as a distortion of the signal in noise, a situation to which RDT update functions are tailored. RDT update functions are expected to be suitable for modeling variable regions of immunoreceptors stochastically expressed by lymphocyte clones at the somatic level. In this respect, to the best of our knowledge, the present work is the first to exploit statistical inference as a theoretical tool to model holons as elementary components of leaving systems.

3 Memoryless Boolean automata

As highlighted in [4, 8], the theory of Dynamical Systems (DS) provides us with a suitable framework — summarized in Figure 2 — to model biological holons (Figure 1): a given holon captures an input signal; this signal and the current state of the DS induce a new state for the DS; according to its new state, the DS completes the transduction of the input signal by emitting an output signal. This output signal flags that the holon is still active and communicates to "the rest of the world" an information about

[1] In textbooks such as [23], the probability of false alarm is also called the size of the test. To alleviate the terminology, we will not use this terminology in the sequel.

its reaction to the input signal.

We can reasonably assume that processes evolve in discrete time at the holon scale. Therefore, we rather focus on automata and memoryless Boolean automata, particularly suitable for a direct implementation on a computer. Mathematically, we follow [16, 17] — where automata are called Discrete Dynamical Systems — and pose the following definition:

Definition 1 (Automaton) *Given two sets $\mathbb{X}^{in}$ and $\mathbb{X}^{out}$, an automaton, of which input (resp. output) signals are the elements of $\mathbb{X}^{in}$ (resp. $\mathbb{X}^{out}$), is a triple $\mathcal{A} = (\mathbb{S}, f^{updt}, f^{rdout})$ such that:*
***(i)** $\mathbb{S}$ is a set called the set of states of $\mathcal{A}$;*
***(ii)** $f^{updt} : \mathbb{X}^{in} \times \mathbb{S} \to \mathbb{S}$ is a function called the update function of $\mathcal{A}$;*
***(iii)** $f^{rdout} : \mathbb{S} \to \mathbb{X}^{out}$ is a function called the readout function of $\mathcal{A}$.*

With the notation used in the definition above, since an output signal $X^{\rm out} \in \mathbb{X}^{\rm out}$ of $\mathcal{A}$ is the outcome of the readout function $f^{\rm rdout}$, we will call $X^{\rm out}$ a readout signal. Note that the system does not issue a readout signal $X^{\rm out}$ according to a given input signal $X^{\rm in} \in \mathbb{X}^{\rm in}$ of $\mathcal{A}$, but to the current state of the automaton. It is also worth noticing that no specific condition is imposed to $f^{\rm updt}$ and $f^{\rm rdout}$. Note also that $\mathbb{S}$, $\mathbb{X}^{\rm in}$ and $\mathbb{X}^{\rm out}$ can be any sets. The definition given above for an automaton is thus very general. We restrict it now to the case of memoryless Boolean automata, which will be our focus throughout the rest of the paper. In what follows, we set $\mathbb{B} = \{0, 1\}$.

Definition 2 (Memoryless Boolean Automaton)
Given two sets $\mathbb{X}^{in}$ and $\mathbb{X}^{out}$, let $\mathcal{A} = (\mathbb{S}, f^{updt}, f^{rdout})$ be an automaton with input (resp. output) signals in $\mathbb{X}^{in}$ (resp. $\mathbb{X}^{out}$).
***(i)** $\mathcal{A}$ is said to be memoryless if $f^{updt} : \mathbb{X}^{in} \to \mathbb{S}$;*
***(ii)** $\mathcal{A}$ is said to be Boolean if $\mathbb{S} = \mathbb{B}$.*

The update function of a memoryless automaton depends on the input signal only. It is thus memoryless in the sense that it is essentially reactive, reacting to any input regardless of its current state (Figure 2). It is thus suited to model stimulus-response holons. In the sequel, we consider memoryless Boolean automata. Such an automaton is thus a triple $\mathcal{A} = (\mathbb{B}, f^{\rm updt}, f^{\rm rdout})$ such that $f^{\rm updt} : \mathbb{X}^{\rm in} \to \mathbb{B}$. It is then worth noticing that in the particular but practical case where $\mathbb{X}^{\rm in} = \mathbb{R}^n$ for some integer n and $\mathbb{R}$ is the standard set of real numbers, an update function $f^{\rm updt} : \mathbb{R}^n \to \mathbb{B}$ is nothing else but a test in the statistical sense[2].

4 Degeneracy of memoryless Boolean automata

4.1 Reconciliating optimality and degeneracy

The definitions proposed above for automata are very general. In the particular case of a memoryless Boolean automaton whose set of input signals is $\mathbb{X}^{\rm in} = \mathbb{R}^n$, we have further noticed that the update function $f^{\rm updt} : \mathbb{R}^n \to \mathbb{B}$ is a statistical test. There is a plethora of statistical tests and we can thus wonder whether there would not exist some "optimal" choices for $f^{\rm updt} : \mathbb{X}^{\rm in} \to \mathbb{B}$.

From the biological point of view, the sought for an optimal solution might seem of lesser importance than establishing that our models of holons satisfy a mathematical formalization of biological degeneracy. Since the MP is a mathematical formalization of degeneracy, the biologist might actually consider the MP as a far more relevant concept than optimality to seek models capable of accounting for the sustainability of living systems (see Figure 2).

Our approach reconciliates degeneracy and optimality by exploiting the fact that there is no unique and ultimate notion of optimal update function to detect the signal. As recalled in Section 2, when the prior probability of presence of the signal of interest is unknown or not defined, which is a reasonable assumption to model biological holons, optimality in the non-Bayesian sense is defined with respect to a certain criterion to achieve the best possible $\mathbb{P}_{\rm DET}$ with a $\mathbb{P}_{\rm FA}$ below a certain level (cf. Figure 2). In addition, optimality depends on the holon environment and can thus evolve according to the context. Therefore, different criteria tailored to different contexts may lead to different optimal solutions. If each of these criteria is relevant for a given problem, several optimal solutions can thus exist for the same problem. This multiplicity of criteria and solutions yields some functional and structural redundancy that can be exploited in case one of these solutions is unavailable at a given time because of degraded or adverse conditions.

Since we focus on the signal detection via the update function of an automaton, readout functions are not involved in what follows and will be considered in further work. Indeed, a readout signal can be regarded as a transduction of the input signal according to the outcome of the update function. A readout signal thus conveys the decision of the automaton as to the presence or the absence of the signal. Thus, it is rather at the update function level that we can actually expect to model degeneracy, as summarized by Figure 2.

4.2 A multiplicity of families of update functions for signal detection in interference and noise

A first attempt to embrace both the MP and the design of optimal tests within the same framework is provided in [18] from a pure statistical point of view. In what follows, we use arguments similar to those given in [18] to exhibit families of update functions that satisfy the MP. As a convenient shortcut, we hereafter say that these families of update functions are "degenerate" as compared to each other, as a reminder of the corresponding biological notion.

At this stage, we must introduce some additional material, mainly aimed at modeling the input signal to be treated by $f^{\rm updt}$. In this respect, we incorporate some randomness in our model, as a crucial feature. To cast the following in a probabilistic setting, we first assume that all the random variables and vectors encountered below are defined on the same probability space, the probability

[2] Strictly speaking, we should assume that $f^{\rm updt}$ is measurable. However, measurable functions exist in so great profusion that all tests of practical interest in statistical inference are measurable.

measure being hereafter denoted by $\mathbb{P}$.

Let $\mathcal{A} = (\mathbb{S}, f^{\text{updt}}, f^{\text{rdout}})$ be a memoryless Boolean automaton. The signal ξ to detect is hereafter modeled as an n-dimensional real vector $\xi = (\xi_1 \ldots, \xi_n) \in \mathbb{R}^n$ where $\xi_1, \xi_2, \ldots, \xi_n$ are n available samples in time of the input signal. Since this signal may be either captured or not by $\mathcal{A}$, we introduce a random variable ε to indicate whether ξ is randomly present or absent: if $\varepsilon = 0$, the signal is absent and if $\varepsilon = 1$, this signal is present.

Signals emitted by other holons can interfer with ξ at the input of $\mathcal{A}$. The resulting of all these possible interfering signals is denoted by Δ. We assume that it is an n-dimensional real random vector $\Delta = (\Delta_1, \ldots, \Delta_n)$, where $\Delta_1, \ldots, \Delta_n$ are n available random samples of Δ. These samples are supposed to be captured at the same times as those of ξ. When $\mathbb{P}[\Delta = 0] \neq 1$, since Δ is unknown to $\mathcal{A}$ and may result from highly variable signals emanating from a plethora of holons, we do not assume any known probability distribution for Δ. We assume that this interference is additive. Accordingly, the signal received by the automaton from its (external) environment is defined as

$$X^{\text{rx}} = \varepsilon\xi + \Delta \tag{1}$$

As any device that senses its environment, the memoryless Boolean automaton $\mathcal{A}$ introduces some corrupting noise when it receives X^{rx}. This noise is hereafter denoted by W. It is supposed to be an n-dimensional real random vector $W = (W_1, \ldots, W_n)$, where $W_1, \ldots, W_n$ are n noise samples captured at the same times as those of ξ and Δ. We further assume that W is independent of Δ. In contrast to the interference Δ, the noise W can reasonably be assumed to have a relatively stable probability distribution. In the sequel, we choose the standard Gaussian probability distribution $\mathcal{N}(0, I_n)$ for W, where $\mathcal{N}(0, I_n)$ is the centred Gaussian distribution whose covariance matrix is the $n \times n$ identity matrix I_n. Finally, we assume that the received signal X^{rx} is additively corrupted by W. Our model for the input signal X^{in} of $\mathcal{A}$ is therefore standard in time series analysis and statistical signal processing since it writes as:

$$X^{\text{in}} = X^{\text{rx}} + W = \varepsilon\xi + \Delta + W \tag{2}$$

Given X^{in} as defined by Eq. (2), the problem is to devise an appropriate update function f^{updt} to estimate the value of ε. We have already seen that such an update function is actually a statistical test. Therefore, to proceed further, we need additional probabilistic definitions.

First, we define the *probability of false alarm* $\mathbb{P}_{\text{FA}}\left[f^{\text{updt}}\left(X^{\text{in}}\right)\right]$ of a given update function f^{updt} for $\mathcal{A}$, as the probability that $f^{\text{updt}}(X^{\text{in}})$ is 1 when ξ is absent — that is, when $\varepsilon = 0$. With the assumptions above, we have:

$$\mathbb{P}_{\text{FA}}\left[f^{\text{updt}}\left(X^{\text{in}}\right)\right] = \mathbb{P}\left[f^{\text{updt}}(\Delta + W) = 1\right]$$

Second, we define the *probability of detection* of f^{updt} as the probability $\mathbb{P}_{\text{DET}}\left[f^{\text{updt}}\left(X^{\text{in}}\right)\right]$ that f^{updt} returns 1 when ξ is actually present — that is, when $\varepsilon = 1$. We thus have:

$$\mathbb{P}_{\text{DET}}\left[f^{\text{updt}}\left(X^{\text{in}}\right)\right] = \mathbb{P}\left[f^{\text{updt}}(\xi + \Delta + W) = 1\right]$$

We now consider two different families of optimal update functions and will explain why these two families are degenerate.

Neyman-Pearson (NP) update functions. Our first family is the family of optimal update functions that we can derive if $\Delta = 0$, in which case

$$X^{\text{in}} = \varepsilon\xi + W \tag{3}$$

This family is that of the NP update functions resulting from the Neyman-Pearson theory [19].

Given $\gamma \in (0, 1)$, the NP update function is hereafter defined by setting:

$$f^{\text{updt}}_{\text{NP}(\gamma)}(X^{\text{in}}) = \begin{cases} 1 & \text{if } \sum_{i=1}^{n} \xi_i X_i^{\text{in}} > \|\xi\|\Phi^{-1}(1-\gamma) \\ 0 & \text{otherwise} \end{cases} \tag{4}$$

with $X^{\text{in}} = (X_1^{\text{in}}, \ldots, X_n^{\text{in}})$ and where Φ is the cumulative distribution function (cdf) of $\mathcal{N}(0, I_n)$. This update function $f^{\text{updt}}_{\text{NP}(\gamma)}$ is optimal in the NP sense because it satisfies the following two properties. First,

$$\mathbb{P}_{\text{FA}}\left[f^{\text{updt}}_{\text{NP}(\gamma)}\left(X^{\text{in}}\right)\right] = \mathbb{P}\left[f^{\text{updt}}_{\text{NP}(\gamma)}(W) = 1\right] = \gamma \tag{5}$$

This property garantees that the memoryless Boolean automaton equipped with this update function controls the rate of false detections of ξ in absence of interference. Second, $f^{\text{updt}}_{\text{NP}(\gamma)}$ provides the highest possible probability of detection among all possible update functions whose probability of false alarm does not exceed γ. Thus, if f^{updt} is any update function such that $\mathbb{P}_{\text{FA}}\left[f^{\text{updt}}(\varepsilon\xi + W)\right] \leqslant \gamma$ then:

$$\mathbb{P}_{\text{DET}}\left[f^{\text{updt}}_{\text{NP}(\gamma)}\left(X^{\text{in}}\right)\right] \geqslant \mathbb{P}_{\text{DET}}\left[f^{\text{updt}}\left(X^{\text{in}}\right)\right]$$

After some algebra, we have:

$$\begin{aligned} \mathbb{P}_{\text{DET}}\left[f^{\text{updt}}_{\text{NP}(\gamma)}\left(X^{\text{in}}\right)\right] &= \mathbb{P}\left[f^{\text{updt}}_{\text{NP}(\gamma)}(\xi + W)\right] \\ &= 1 - \Phi\left(\Phi^{-1}(1-\gamma) - \|\xi\|\right) \end{aligned}$$

Unfortunately, when $\mathbb{P}[\Delta = 0] \neq 1$, $f^{\text{updt}}_{\text{NP}(\gamma)}$ is definitely hopeless because, as stated in [20, Appendix A], it incurs an unavoidable increase beyond γ of its probability of false alarms, whatever small the amplitude of Δ can be. In this sense, the NP update function is not robust to model mismatches and is thus not suitable to guarantee a specified probability of false alarm in presence of a non-null interference Δ.

Random Distortion Testing (RDT) update functions. In contrast, the RDT approach, introduced in [21] and extended in [22], aims to overcome the foregoing issue by addressing a different question from that tackled by the NP update function.

Although we do not assume a known distribution for the interference Δ, we bound our lack of prior knowledge about this distribution by assuming the existence of a tolerance $\tau \in (0, \|\xi\|/2)$ such that $\|\Delta\| < \tau$. It follows from this assumption and Eq. (1) that

$$\begin{cases} \varepsilon = 0 & \Leftrightarrow \quad \|X^{\text{rx}}\| \leqslant \tau \\ \varepsilon = 1 & \Leftrightarrow \quad \|X^{\text{rx}}\| > \tau \end{cases}$$

Therefore, for any interference Δ such that $\|\Delta\| < \tau$, deciding on the presence ($\varepsilon = 1$) or the absence ($\varepsilon = 0$) of ξ, when the input signal is X^{in} given by Eq. (2) and can be rewritten as $X^{\text{in}} = X^{\text{rx}} + W$, is equivalent to testing whether $\|X^{\text{rx}}\|$ exceeds τ or not. Such a problem is exactly a Random Distortion Testing (RDT) problem as defined in [21]. The RDT theory in [21] thus provides us with an optimal RDT update function given by:

$$\forall x \in \mathbb{R}^n, f^{\text{updt}}_{\text{RDT}(\gamma)}(x) = \begin{cases} 1 & \text{if} \quad \|x\| \leqslant \lambda_\gamma(\tau) \\ 0 & \text{otherwise} \end{cases}$$

where $\lambda_\gamma(\tau)$ is calculated according to [21, Lemma 2].

It is important to remark that the RDT update function harnesses the amplitude of the input signal. This is a key feature of the RDT theory: it basically aims at comparing some measure of the input signal amplitude to a suitable threshold. We write "some measure of the input signal amplitude" to convey the idea that we have many ways to measure this amplitude, depending on the environmental conditions. The interested reader can refer to [21] or [22] in this respect.

In the definition of $f^{\text{updt}}_{\text{RDT}(\gamma)}$ above, the parameter γ has exactly the same meaning as above: it is the maximum value specified for the probability of false alarm of the RDT update function. In fact, it can be proved that [21]:

$$\mathbb{P}_{\text{FA}}\left[f^{\text{updt}}_{\text{RDT}(\gamma)}(X^{\text{in}})\right] \leqslant \gamma \tag{6}$$

In addition, according to [21, Theorem 2, statement (ii)]

$$\mathbb{P}_{\text{DET}}\left[f^{\text{updt}}_{\text{RDT}(\gamma)}(X^{\text{in}})\right] \geqslant Q_{n/2}\left(\|\xi\|/2, \lambda_\gamma(\tau)\right) \tag{7}$$

where $Q_{n/2}$ is the generalized Marcum function [24]. Thus, in case of an interference, $f^{\text{updt}}_{\text{RDT}(\gamma)}$ keeps control of both its probability of false alarm and its probability of detection, whereas $f^{\text{updt}}_{\text{NP}(\gamma)}$ cannot guarantee its probability of false alarm anymore.

We will not describe further the criterion that an RDT update function optimizes. This criterion is slightly more difficult to discuss than that satisfied by $f^{\text{updt}}_{\text{NP}(\gamma)}$, because it requires introducing some material about the group invariance of the problem as well as some considerations on conditional probabilities. What actually matters with respect to our purpose is the following.

First, $f^{\text{updt}}_{\text{RDT}(\gamma)}$ is a surrogate of $f^{\text{updt}}_{\text{NP}(\gamma)}$ for testing whether ξ is present or not, even in presence of interference. Of course, when there is no interference, $f^{\text{updt}}_{\text{RDT}(\gamma)}$ is suboptimal. In contrast, in case of a non-null interference, $f^{\text{updt}}_{\text{RDT}(\gamma)}$ can still guarantee the same probability of false alarm as in absence of interference, whereas $f^{\text{updt}}_{\text{NP}(\gamma)}$ cannot. In addition, the NP update functions and the RDT update functions are based on different theories in statistics. It is worth elaborating further on this point.

The NP approach is based on likelihood theory in binary hypothesis testing [23], via the notion of likelihood ratio. In a few words, if $f_{\xi+W}$ and f_W are the probability density functions of $\xi + W$ and W, respectively, then the likelihood ratio between the two possible hypotheses — presence of ξ vs. absence of ξ — is $\mathcal{L} = f_{\xi+W}/f_W$ in absence of interference. Given $\gamma \in (0, 1)$, it turns out that comparing $\mathcal{L}(X^{\text{in}})$ to a threshold chosen to guarantee that $\mathbb{P}_{\text{FA}}\left[f^{\text{updt}}_{\text{NP}(\gamma)}(X^{\text{in}})\right] = \gamma$ amounts to comparing $\sum_{i=1}^{n} \xi_i X_i^{\text{in}}$ to $\|\xi\|\Phi^{-1}(1-\gamma)$ to another threshold, as specified in Eq. (4).

In contrast, the RDT approach resorts to criteria that do not involve likelihood ratio at all since, in this approach, the statistical properties of the input signal are not supposed to be known because the probability distribution of Δ is itself unknown. Moreover, the NP update function is optimal when there is no interference, whereas the RDT update function is optimal when this interference is not zero. For all these reasons, NP and RDT update functions are simply not comparable. Albeit simple, these remarks are decisive to explain, without getting the reader bogged down into mathematical details, why memoryless Boolean automata equipped with NP update functions and memoryless Boolean automata endowed with RDT update functions satisfy the MP.

More specifically, as conveyed by the term "Multiplicity Principle", we need multiple solutions to state that degeneracy is at work. These multiple solutions are simply the NP and RDT update functions.

The functional redundancy sustained by the different structures resulting from these multiple solutions is the ability to detect the presence or the absence of the signal ξ with a bounded probability of false alarm. Finally, the NP and RDT update functions are structurally different because, as explained above, these update functions cannot be compared together through the same preorder. For all these reasons summarized at the bottom of Figure 2, we can conclude that the family of NP tests and the family of RDT tests are degenerate in the MP sense. As such, these families should be convenient to model holons whose degenerative properties in signal detection and communication allow them to evolve with resilience in fluctuating contexts. A formal proof of this result can be achieved by mimicking the reasoning followed in [18]. It is not provided here because it would require a significant amount of additional material.

5 Conclusion

We have presented statistical models of elementary biological holons that detect signals in noise and presence of interference and satisfy the multiplicity principle, a mathematical formalization of biological degeneracy. These models are compatible with the degeneracy feature of living systems and, in particular, might explain the resilience of adaptive immune systems in vertebrates. They are based on the notion of memoryless Boolean automaton and the introduction of aleatoric incertitude to model input signals of such memoryless Boolean automata. To detect signals, these memoryless Boolean automata are equipped with update functions belonging to families verifying the multiplicity principle.

A key feature of the approach is that we can use various statistical update functions to detect signals even in adverse conditions. This might allow in future work to model the perception of the biological holon by combining different sensor types. Therefore, in our approach, statistical inference is not used to describe or analyze data but to model holons as elementary components of leaving and immune systems. Our theoretical approach also emphasizes that degeneracy allows to optimize the sensitivity ($\mathbb{P}_{\text{DET}}$) while maintaining the specificity ($1 - \mathbb{P}_{\text{FA}}$) within the same dynamical system.

We expect that this preliminary work along with our purely mathematical results in [18] can lay the groundwork to derive models of "fractal-like" holarchies, in the continuation of research works such as [3, 4, 8, 26] among others. We can also expect that our approach could be beneficial to theoretical biology in the sought for new models for real components of the immune system, at different scales, from the molecule to the organism scale [25]. In this respect, our on-going research involves a generalization of the theoretical material proposed in this paper to model such components.

However, to achieve such models via the holon-based approach proposed above, the issue is that the concept of holon is highly nonspecific. In particular, mentions of specific holons in biology are usually purely illustrative in references such as those cited in this paper. Further scientific efforts are thus needed to move from principles to models truly applicable in biology and capable of describing, explaining and predicting biological phenomena.

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