



# Theoretical Basis for Gene Expression Modeling Based on the IEEE 1906.1 Standard

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**Abstract.** Molecular communications essentially analyze the transmission of the information at the nano level in cells, the smart devices that constitute our bodies. This emerging field uses traditional communication systems elements and maps them to molecular signaling and communication found inside and outside the body. Hence, molecular communications' fundamental importance denotes the necessity to develop a new technology framework that provides a novel perspective to fight human diseases (the COVID-19 pandemic has highlighted this challenge). Thus, the architecture for molecular communications can be explored from the perspective of computer networks, i.e., the TCP/IP reference model and the basic model of MC can also be represented using Shannon's communication model (i.e., transmitter, communication channel, and receiver). In this field, IEEE impulses the 1906.1 and 1906.1.1 standards that establish definitions, terminology, and a conceptual model for ad hoc network communication at the nanoscale. With these ICT perspectives, we appropriately have analyzed gene expression in eukaryotes organisms as a layered stack (network, link, and physical layer) of a nano communication network. In this biological communication process, the cellular nucleus behaves as the DTE, the ribosomes, and Endoplasmic Reticulum represent the DCE, the Golgi Apparatus represents a border router. The proteins secreted by the cell move through the bloodstream (physical transmission medium) and reaching the receiver (DCE-DTE), which processes the information through ligands and their receptors.

**Keywords:** Genetic expression · Molecular communication · Stack network modeling · IEEE 1906.1 standard

# 1 Introduction

Molecular communications (MCs) essentially analyze the transmission information at the nano level; the cells, the “smart” devices that constitute our bodies, principally communicate fundamentally through molecules’ transport and binding. Despite their noisy world and often diffusive transport, nature has devised a way for all of these biomolecules to function in harmony so effectively and reliably, and this is a remarkable realization in robust communication. It’s a triumph that scientists must dissect in order to create devices that can communicate with nature in its own language [1].

MCs, in contrast to existing telecommunication paradigms, use molecules as information carriers; sender biological nanomachines (bio-nano machines) encode data on molecules (signal molecules) and release the molecules into the environment. The molecules then travel through the environment to reach the receiver bio-nano machines, where they biochemically react with the molecules to decipher information [2]. In biology, sender-receiver systems abound, with communication systems transmitting data in a variety of ways. Information and communication technology (ICT) offers a quantitative foundation for understanding natural and synthetic genetic processes.

Keeping the preceding ideas in mind, let us investigate a previously unimagined and unfortunate occurrence that has harmed humanity in the area of biological communications. Hundreds of millions of people are infected with viruses each year, but many of them do not have access to vaccines or adequate treatment during and after infection. The COVID-19 pandemic has brought this issue to light, demonstrating how rapidly viruses can spread and affect society as a whole. To fight viral infections and potential future pandemics, new approaches from various disciplines must arise. Over the last ten years, an interdisciplinary field known as molecular communications has emerged [3–5]; it involves bioengineering, nanotechnology, and ICT. This new area applies elements of traditional communication systems to molecular signaling and communication found both within and outside the body. The aim is to create new methods that will aid future medicine (the ICT system offers a novel approach to combating human diseases) [3, 6–9]). Characterizing the signaling pathways between cells and infectious disease locations at different levels of the human body is one of these methods [10].

Thus, MCs have been developing, and it bridges communication engineering and networking, molecular biology, and bioengineering areas [11, 12]. Much analysis, designs, and proposals in biological systems communications studies have been established from a typical layered network structures paradigm [13–25]. In this area, the Institute of Electrical and Electronics Engineers (IEEE) impulses the 1906.1 and 1906.1.1 standards [26–29]. In its first version, the IEEE 1906.1 standard recommended practice contains a conceptual model and standard terminology for ad hoc network communication at the nanoscale. The new version of the standard i.e., 1906.1.1 establishes a common YANG (Yet Another Next Generation) data model for IEEE 1906.1 nanoscale communication systems.

We introduced a stacked-layer network model to describe gene expression using the fundamentals of communication engineering and networking in MC as a guide, as well as the relevance of series IEEE 1906 standards [30]. The rest of the paper is organized as follows. Section 2 explains gene expression and protein delivery from an ICT paradigm; thus, Sect. 2.1 describes the transcription of DNA (DTE in the transmitter), Sect. 2.2 denotes translation of DNA (DCE in the transmitter), Sect. 2.3 describes Golgi apparatus (GA) as an internet (border) router, Sect. 2.4 establishes the protein delivery through a communication channel, Sect. 2.5 describes the use of information at the receiver (DCE-DTE). In Sect. 3 (application of the series standards IEEE 1906 to gene expression) is established our proposal, hence Sect. 3.1 indicates the IEEE Standard Data Model for Nanoscale Communication Systems, i.e., IEEE 1906.1 and 1906.1.1, Sect. 3.2 presents the proposal properly as a viewed digital communication networks through gene expression and protein delivery from the IEEE 1906.1 and 1906.1.1 paradigm. Conclusions enclose this paper in Sect. 4.

## 2 Gene Expression and Protein Delivery Analysis from a Network Layered Paradigm

### 2.1 DNA Transcription

The basic model of MCs may be described based on Shannon's model of communication (i.e., transmitter, communication channel, and receiver) [20] and as nanoscale communication network is a human-designed system for communicating at or with the nanoscale, using physical principles that are suited to nanoscale systems [26]. Then, from our previous work in [30], we suppose that the cellular nucleus represents the biological transmitter (or a biological Data Terminal Equipment (DTE) that contains the information source) composed of nucleotide blocks called genes (which must be processed intra-cellularly or extra-cellularly). We mainly focus on long-distance cellular communication (exhibited, for example, in the endocrine system, this type of MC is known as long nano range communication) [30–32]. In nature, a gene is a set of nucleotides that stores the information required for accomplishing a specific function (by a protein or RNA) [33] to be performed at a specific destination; Thus, we hypothesize that a gene's contents can be understood as addressing at the network layer. The transmission of information from the nucleus cell (i.e., from genes) to specific destinations begins with the transcription process in which DNA information is copied into RNA [30].

The DNA molecules are encoded by four distinct values, allowing them to contain digital information (i.e., four nucleotides, then a single nucleotide base will carry two bits of information  $[-\log_2(1/4)]$ ). Nucleotides are monomers of nucleic acids that contain one nitrogenous base, a five-carbon sugar (deoxyribose in DNA and ribose in RNA), and at least one phosphate group (DNA and RNA). Adenine (A), thymine (T), cytosine (C), guanine (G), and uracil (U) are nitrogenous bases (U). The DNA double helix is made up of nucleotides with

the bases A, T, C, and G [34], and it keeps its shape since the nitrogenous bases on each strand are complementary [35] (i.e., the affinity of adenine to thymine and that of cytosine to guanine [36]). Since biological information is divided into encapsulated data segments [19,30], the information in DNA is divided into blocks of nucleotides called genes [37,38] that have start and termination sequences. Digital information is split into packets in packet-switching networks to speed up transmission. As a result, a digital network packet may be thought of as a gene in a biological transmission network [19,30].

As transcription begins, the RNA polymerase II (RNAP II enzyme) molecular motor recognizes a region of the promoter region's DNA sequence [39]. When RNAP II starts adding nucleotides to create a complementary messenger RNA (mRNA) chain, it starts with the promoter. After that, RNAP II makes a single-stranded mRNA copy of one of the two DNA strands. The only difference between RNA and DNA is that in this step, RNAP II uses uracil (U) instead of thymine (T) [40,41].

The enhancer is another essential DNA strand component that controls the amount of protein produced in relation to the amount of mRNA (i.e., the amount of information sent to the receiver). As a consequence, this technique can be interpreted as a sender-side flow control [30]. Flow control is maintained at the data-link layer to ensure that a fast sender does not overwhelm a passive receiver with more messages than can be processed [42–44]. The transcription of one of the DNA strands from the 5'P to the 3'OH of the deoxyribose phosphate backbone was specifically unidirectional [39,40]. This precision is also present in computer networks, where the less significant bit must be signaled when information is transmitted using serial communication [43].

The halt of transcription is accomplished when an appropriate finalization sequence is recognized by RNAP II [29]. In the primary transcript molecule (i.e., pre-mRNA) occurs maturations such as: (i) Splicing, (ii) Capping, and (iii) Polyadenylation [45]. The information added during capping and polyadenylation may be equivalent to the delimiting data flags used in digital communication systems, for instance, headers and trailers that encapsulate the information (i.e., forms a molecular frame) in the data-link layer in protocol hierarchies in network software [20,30]. These flags are used for processing and error control [19,44,45]; mRNA molecules are stabilized (control and posterior processing) by the previously described maturations, which avoid mRNA degradation by enzymes in the cytosol (intracellular fluid), allowing them to progress to the next step of biological processing [30]. The data added during capping and polyadenylation could be compared to a header and trailer that encapsulates the data.

The mechanical transport of mRNA molecules through the cytosol may be analogous to the transmission of information in wired communications (physical layer task) [19,30,31,36].

## 2.2 DNA Translation

The transcription process permitted to copy the biological information from DNA to RNA; this is mandatory because DNA molecules cannot leave the

cellular nucleus. Hence, at this point, the biological DTE must transmit the information to biological Data Communication Equipment (DCE) through a physical interface (as in conventional communications systems). In our case, supported by [30], we assume that the cytosol may represent this physical interface.

The DCE (codec or modem) is the unit in a digital communication system that is responsible for properly formatting the data transmitted over a communication channel. According to [30], ribosomes and the ER (Endoplasmic Reticulum) serve the biological DCE since genetic information acquires a functional structure (or format when referring to data) through these organelles, which is then released into the biological communication channel and eventually reaches the biological recipient. The “right formatting” of biological data occurs during translation as the information is translated into amino acid chains in order to obtain functionality both within and outside the cell. Thus, the biological DCE processes (codifies) information through translation and provides a specific input sequence (mRNA data) that is associated with a specific output (amino acid sequence); this type of codification process corresponds to traditional codification in digital systems (i.e., a physical layer task) [30, 43, 44]. The natural world has created the opportune intermediate addressing at any point of transcription and translation; hence, the mRNA that leaves the nucleus has an implied contiguous address that is comparable to a data link layer address to enable communication within a direct communication range [19, 30, 43, 44]; as a result, cytosolic ribosomes or those associated with the rough ER (RER) bound the mRNA. The arrival and transfer of biological information through a biological communication medium, which is considered a task at the physical layer, is symbolized by the transmission (movement) of biological information from the nucleus to the ribosomes or ER through the cytosol [19, 30].

Ribosomes are the structures that function as molecular motors. They used a codon scheme (i.e., a triplet of nucleotides) to read the details found in the biological sequence [30, 46]. Transfer RNAs (tRNAs) identify the codons in the mRNA in the ribosome. They have an anticodon sequence that is complementary to a specific codon that is associated with a specific amino acid that attaches to the molecular structure of that tRNA [40].

The signaling of tRNAs triggers protein synthesis in the ribosome. To ensure proper biological information reading, they indicate the process’s start and stop codons to the ribosomes [46]. The study of amino acid interactions that shape proteins is critical for understanding evolutionary relationships among species, developing new drugs, and creating synthetic proteins from the perspective of digital communications systems [47]. The start and stop codons can correspond to synchronism signals in the digital communications systems paradigm. A start flag is used to execute synchronous transmissions between the source and destination. In this method of communication, the transmitter sends the data, which the receiver must then collect and process. The stop codon in biological signaling can be analogous to the stop flag used at the destination to signify the end of synchronous communications. Besides, synchronous transmissions are the focus of this investigation since synchronous communications allow for the transmission of large

amounts of data; for example, 455 EB of data can be encoded in 1 g of single-stranded DNA [48]. The signals that signal the start and stop of DNA translation enable biological clocks in cells to provide feedback during cellular processes [19,30].

As the processing of specific amino acids generates proteins, the quantity of information required to specify one amino acid from a set of 20 (the total number of amino acids) unambiguously is 4.3 bits  $[-\log_2(1/20)]$ ; then, using 6 bits to define an amino acid signifies an excess of information; nevertheless, this excess information capacity may explain the genetic code's redundancy [49].

In MCs, the modulation (a physical layer task) is a functionality at the transmitter to alter molecules' properties to represent the information that arrives as a concentration of molecules at the receiver [19]. One mechanism for this modulation is to choose one type of molecule from a set of molecule types, this type of modulation is known as MoSK (Molecular-Shift Keying) [50]. On the other side, as genetic code uses three nucleotides (codon) to represent a specific amino acid and as there are 20 amino acids, it is necessary to sort the four nucleotides into groups of at least 3 to encode all 20 amino acids in 64 possible combinations (i.e.,  $4^3 = 64$  because  $4^2 = 16$  is not sufficient to encode 20 amino acids) [51]. Hence, in our research, we assume that the biological DCE codifies a set of 6 inputs (3 nucleotides or 6 bits due each one is represented by 2 bits) with a set of 64 outputs (to encode the total of 20 amino acids) [30]. Then the DCE in our case may have a 64 MoSK (i.e., there exist 64 different cases to be considered, because, for the MoSK modulation scheme, the information is represented by using different types of molecules, for  $x$  bits information per symbol,  $2^x$  types of molecules are needed to transmit [52,53]).

The protein production processed in the ER (e.g., peptide hormones, such as insulin) is analyzed to achieve long nano-range communication; an addressing scheme similar to the network address in conventional computer networks is needed [19,30]. Note that many of these proteins have a function outside of the cell, where they enter the receiver in what is known as the long nano range. To obtain these proteins, they must be tagged (i.e., tagging to play a role outside the cell). As a result, the amino acid sequence is bound to a signal recognition particle (SRP), which provides an implicit adjacent address through molecular tagging [54]. This molecular tag functions similarly to a data link layer address in that it facilitates contact within a direct communication range [19,30].

The primary function of the SRP is to assist the nascent protein in reaching a channel protein in the ER that controls the protein's translocation. The SRP then separates from the protein and returns to the cytosol [30,54]. Similarly, after processing and control information have been used in automated communication systems, they are discarded [43,44]. The proteins are folded at this point and acquire the usable three-dimensional structure needed for them to perform their basic biological functions within the ER (equivalent to digital data after processing by the DCE, i.e., getting the necessary format [43,44]) [30,54].

In biological systems, information errors can occur during DNA transcription and translation, just as they can in traditional communication systems with

errors in the transmission media. Many medical conditions, such as autoimmunity, cancer, and diabetes, are caused by errors in cellular transmission and information exchange [55].

### 2.3 The Golgi Apparatus (GA) as an Internet (border) Router

The RER transfers to the GA the proteins when they are functional via molecular motors. Since each protein contains an implicit adjacent address (analogous to a data link layer address that aids communication within a direct communication range [19, 20, 30]), the proteins are routed to the proper inter-cellular destinations (i.e., in long nano range communications with addressing at the network layer); however, the GA decides whether the proteins remain inside the cell [56].

Proteins and their information content transfer from the RER to the GA during this phase. The data is then stored in vesicles that bind to the cis GA face. The protein information is then encoded in new vesicles, and other cellular components needed for protein processing are added. The contents of the new vesicles are deposited into the medial GA face, and new vesicles containing the protein and the elements required for further processing are produced. Finally, the vesicles enter the trans GA face, where they undergo the same process as previously mentioned; as a result, the proteins are incorporated into new vesicles but guided to the endoplasmic membrane, where they will be secreted outside the cell [54]; vesicles may naturally match a molecular frame at the molecular link-layer [19, 30].

As previously mentioned, the GA functions are identical to those of a network's boundary router. When encapsulating and unwrapping the information across layers, a router decides if the information stays within the network or leaves it. As a result, the behavior of depositing proteins, forming vesicles, and adding information to determine a protein destination are similar to the processing of protocol data units (PDUs) in a router's layers [30, 43, 44]. The layout of a layered model decomposes a large-scale system into a series of functionally independent smaller units (i.e. layers) and determines the interactions between the layers [19, 43, 44]. As a result, the benefits of using a stack of layers include using a data link layer to turn an unstable channel into a line free of transmission errors or reporting unresolved problems to the upper layer [30, 57]. As a result, by applying such a model to biological systems, high reliability can be achieved (e.g., in drug delivery) [13–25, 30].

### 2.4 Protein Delivery Through a Communication Channel

The mode of protein delivery depends on the body's destinations and the system's specific requirements (e.g., the endocrine system). Hence, cases in which the proteins secreted by the cell (e.g., hormones of a proteinaceous nature) move through the bloodstream, i.e., the physical transmission medium (active random with drift transport-diffusion with drift) to a target organ (with addressing destination at the network layer) are considered. This type of MC is referred to as intercellular communication (i.e., distances in the range of mm to m) [9, 30, 32].

Thus, the movement of the molecules in a fluid medium with drift (e.g., the bloodstream) is characterized as follows  $f(t) = \sqrt{\frac{\lambda}{2\pi t^3}} \exp\left(-\lambda \frac{(t-\mu)^2}{2\mu^2 t}\right)$ , for  $t > 0$ , where the mean is  $\mu = d/v$ , the shape parameter is  $\lambda = d^2/2D$ , the velocity of the fluid medium is  $v \geq 0$ , the diffusion coefficient is  $D$ , and the distance from the transmitter to the receiver is  $d$  [9, 19, 20].

As proteins move to a target destination through the bloodstream, the traffic of biological information from senders to receivers converts the blood into a shared media. This shared link requires media access control (MAC) to divide it among multiple senders and transmits molecular frames from multiple senders without causing interference between molecular frames. One mechanism for MAC is a time-division multiplexing (TDM), in which different senders transmit molecular frames at different times [19, 30].

During the transmission of information over communication networks, a number of issues can arise. Biochemical, thermal, and physical noise, interference (which can be regulated by an effective transmission rate), and attenuation are all problems in molecular communication (which depends on the distance traveled and the physical characteristics of the fluid medium) [20, 30]. The noise is any distortion that results in degradation of the signal at the receiver mainly due to stochastic nature; in MCs, the noise sources can be a) random propagation (diffusion) noise, b) transmitter emission noise, c) receiver counting/reception noise, d) environment noise such as degradation and/or reaction, e) multiple transmitters [14, 20, 58–60].

The resulting damage to the signal information can cause latency (i.e., movement delay) calculated as  $d/v$ , jitter (i.e., variation in latency) calculated as  $Dd/2v^3$ , and the loss rate (i.e., the probability that the intended biological receiver does not receive a molecule transmitted by a biological sender) can increase. The loss rate is calculated as  $1 - \int_0^T f(t)dt$ , assuming that the receiver waits for the time duration  $T$  [9, 30].

Based on the communicational parameters that denote the problems that can occur in a communication channel with noise, the Shannon theorem is used to determine the maximum biological information transfer speed (channel capacity) as  $C = \max\{I(X; Y)\}$  [20, 59, 61], where  $I(X; Y)$  represents the entropy of the mutual information (MI) of  $X$  and  $Y$ . The information signals at the transmission and reception ends are denoted as  $X$  and  $Y$ , respectively.

## 2.5 Use of Information at the Receiver

In the human body (considering Shannon's communication model [20]), the communication of biological information from a transmitter (DTE-DCE) to a receiver (DCE-DTE) is done through the bloodstream (i.e., the communication channel). A target cell, tissue, or organ performs a physiological function (due to a specific type of biological information comparable with network layer addressing [19, 30]); then, we focus on the type of receivers located in a long nano range. Therefore, the transmitter sends the information using the data stored in the DNA molecules and at the destination can recognize the target cell, tissue, or

organ. In terms of the type of proteinaceous hormone involved, the receiver processes the information received. Here, we briefly describe a case in which this processing is performed through ligands, and their receptors [62].

Signal molecules are received by receptors within the receiver in nature; the receiver is made up of a chemical detector that senses the concentration of molecules at a given sample time and demodulates the signal [20, 63, 64]. As a result, these protein structures can be thought of as antennas for receiving signals. Receptors are protein structures that have the ability to bind to complex ligand structures. Intermolecular forces such as ionic bonds, hydrogen bonds, and van der Waals forces are used to tie molecules together. In most cases, docking (association) is reversible (dissociation). The chemical conformation of a receptor is altered when a ligand binds to it, and the propensity to bind is known as affinity. This method of communication resembles a lock and key system in which only the “key” receiver can detect, read, and interpret the information; other receivers can detect but not process the information, implying process specificity [30]. A receptor’s functional state is determined by its conformational state. During the detection process, almost all ligand structures in nature catch and remove the propagation environment’s information particles [14, 20].

The membrane protein acts as a transducer in the biological process, decoding the received signal (i.e., performing typical DCE tasks at the receiver) and causing multiple reactions within the target cell, tissue, or body organ (i.e., accomplishing the typical DTE tasks at the receiver) [65]. This activity is similar to the work performed at the receiver end of digital communication systems to process data that will be useful at the destination [66, 67]. The biological data is transmitted to other organelles after the target cell receives it, using an implicit adjacent address similar to the data link layer address used to enable communication within a direct communication range [19, 30]. The biological message that has been received is physically transmitted to the target cell.

### **3 Application of the Series Standards IEEE 1906 to Gene Expression and Protein Delivery**

#### **3.1 IEEE Standard Data Model for Nanoscale Communication Systems IEEE 1906.1 and 1906.1.1**

In its first version, the IEEE 1906.1 standard recommended practice (approved in 2015 [27]) contains a conceptual model and standard terminology for ad hoc network communication at the nanoscale. More specifically, this recommended practice contains: a) the definition of nanoscale communication networking; b) the conceptual model for ad hoc nanoscale communication networking; c) the common terminology for nanoscale communication networking, including 1) the definition of a nanoscale communication channel highlighting the fundamental differences from a macroscale channel; 2) abstract nanoscale communication

channel interfaces with nanoscale systems; 3) performance metrics common to ad hoc nanoscale communication networks; 4) the mapping between nanoscale and traditional communication networks, including necessary high-level components such as a map of significant components: coding and packets, addressing, routing, localization, layering, and reliability.

According to [27], a common abstract model enables theoretical progress to proceed from different disciplines with a common language. As the industry becomes more interested in the commercial integration of the technology, this structure serves as a recommended practice for additional nanoscale communication networking standards. The biomedical industry needs nanoscale communication standards to create breakthrough diagnostic and treatment methods. Technical discussions and establishing standards in nanoscale communications are impaired by lacking a common conceptual model and standard nomenclature.

In [28], a new version of the standard was developed, i.e., 1906.1.1 (approved in 2020 by Internet Engineering Task Force, Request for Comment 7950) in which IEEE establishes a common YANG (Yet Another Next Generation) data model for IEEE 1906.1 nanoscale communication systems.

In accordance with IEEE Std 1906.1-2015, this data model consists of a series of YANG modules that describe nanoscale communication systems and their associated physical quantities (a common framework for all nanoscale communication technologies). The model depicts physics that are only found at the nanoscale. The physics are non-standard, as specified by IEEE Standard 1906.1-2015. For remote operation and study of nanoscale communication systems, the model specifies remote configuration and management. The model for datastores and repositories of nanoscale communication experimental data defines a self-describing data structure, allowing for a shared interpretation of data from a wide range of nanoscale communication media and technologies.

The YANG data model defines a standard network management and configuration data model for nanoscale communication systems. In doing so, it fulfills several purposes:

- Enforces requirements to conform to IEEE Std 1906.1(TM)-2015.
- Describes nanoscale communication systems.
- Represents the fundamental physics impacting IEEE 1906.1 systems.
- Defines configuration and management for simulation and analysis.
- Defines a self-describing data structure used in repositories of nanoscale communication experimental data.

IEEE 1906.1 systems and simulations can be easily understood and used thanks to a common network, management, and configuration data model. To ensure that systems and simulations comply with IEEE Std 1906.1-2015, a standard data model is required. IEEE 1906.1 systems need a standard data model to act as human and machine-readable documentation. Since nanoscale physics interacts directly with small-scale communication systems, a data model that represents fundamental physics is needed. To compare IEEE 1906.1

systems accurately and equally, a standard data model is needed. For experimental data from small-scale communication systems to be relevant, repositories need detailed and reliable documentation. This standard data model tackles this need by providing a self-describing data model.

### 3.2 Viewing Digital Communication Networks Through Gene Expression and Protein Delivery from the IEEE 1906.1 and 1906.1.1 Paradigm

The following Tables (1, 2, 3 and 4) provide an analogy of the IEEE Standards 1906.1 and 1906.1.1 for both Molecular Communications and Gene Expression and Protein Delivery. We do not apply specific metrics (defined in both standards 1906.1 and 1906.1.1) to characterize gene expression due we describe this biological process from a general perspective without particularizing the specific case of a particular type of protein.

It is worth noting that nanoscale communication networks shall describe their physical layer by denoting: transmitter, receiver, message, medium, components that have a dimension from 1 nm to 100 nm, the communication physics suited to the nanoscale, message carrier, motion, field, perturbation, and specificity (this is a definition from Sections 3 and 4 in IEEE 1906.1 and Section 3 in IEEE 1906.1.1). On the other hand, Gene expression and protein delivery as nano communication networks seem inertial described (as seen in the whole document) in the standard IEEE 1906.1 and IEEE 1906.1.1 as indicated previously.

**Table 1.** Introduction section (in IEEE 1906.1)

Molecular communications	Gene expression and protein delivery
(a) In the molecular nanoscale communication embodiment, it is assumed that molecules move into the medium following the omni-directional Fick's law (molecular concentration as a function of distance and time)	(a) $f(t) = \sqrt{\frac{\lambda}{2\pi t^3}} \exp\left(-\lambda \frac{(t-\mu)^2}{2\mu^2 t}\right)$ , $t > 0$ , where the mean is $\mu = d/v$ , the shape parameter is $\lambda = d^2/2D$ , the velocity of the fluid medium is $v \geq 0$ , the diffusion coefficient is $D$ , and the distance from the transmitter to the receiver is $d$ [9,19,20]
(b) Knowing the number of molecules released for each pulse	(b) 64 MoSK [30,51–53]
(c) Evaluation of the propagation delay	(c) latency = $d/v$ , jitter = $D d/2 v^3$ [9,30]
(d) Estimation of the maximum channel capacity when a concentration-based receiver is used	(d) $C = \max\{I(X; Y)\}$ , where $I(X; Y)$ represents the entropy of the mutual information (MI) of $X$ and $Y$ . The information signals at the transmission and reception ends are denoted as $X$ and $Y$ , respectively

**Table 2.** Definition section (Sections 3 and 4 in IEEE 1906.1 and Section 3 in IEEE 1906.1.1)

Molecular communications	Gene expression and protein delivery
a) A nanoscale communication network is a human-designed system for communicating at or with the nanoscale, using physical principles suited to nanoscale systems	a), b) The architecture for MC may be discussed from a computer networks perspective, i.e., the TCP/IP reference model and the basic model of MC may be described based on Shannon's model of communication (i.e., transmitter, communication channel, and receiver) [13, 16, 25].
b) Communication is the act of conveying a message from a transmitting party to a receiving party. This includes the components (a required element of the framework that provides a communication service in a network) of message, transmitter, receiver, medium, and message carriers. At least one of these components must have nanoscale dimensions. The standard has been defined as nanoscale dimensions between 1 nm to 100 nm	Thus, we have analyzed gene expression in eukaryotes organisms (which dimensions are in nanoscale range) from this ICT perspective. In this biological communication process, the cellular nucleus behaves as the DTE, the ribosomes and ER represent the DCE, the GA represents a border router. The proteins secreted by the cell move through the bloodstream (physical transmission medium) and reaching the receiver (DCE-DTE), which processes the information through ligands and their receptors [30, 62].
c) Active network: A network composed of packets flowing through a telecommunications pathway that dynamically modifies its operation. A packet of information encapsulated to be transported through a communication network	c) Supported by [30] is possible to hypothesize that a packet in a digital network may be analogous to a gene in a biological communication network. These genes are "encapsulated and unencapsulated" through their codification (64 MoSK) and with structures (as start and termination sequences and with capping, and polyadenylation, in transcription); additionally, the genes processing and subsequent transporting through GA to the appropriate destinations correspond to operation encapsulating and unencapsulated of this biological information [19, 20, 43, 44, 56]
d) Message: The information to be conveyed is known to the transmitting party, interfacing with a receiver and unknown but recognizable to the receiving party. The message relates approximately to a classical frame, packet, or protocol data unit (PDU)	d), e), f), g), h), i), j) To perform a biological role, proteins are formed in the cell and excreted. The biological information source (signal molecules) in eukaryotic cells is the nucleus, which must be changed through intracellular communication to reach an appropriate cellular or extracellular destination. This procedure entails the transmission of information through a biological pathway, followed by the performance of a biological function. The Golgi apparatus is involved in the transmission of proteins (specifically peptide hormones) to a target organ via the bloodstream, which is analogous to the digital communication mechanism in which a transmitter in one network sends data to a destination system in another network through a router (relay component) [30]. Hence, having in mind Shannon's model of communication [20], the communication of biological information from a transmitter (DTE-DCE) to receptors in the receiver (DCE-DTE) is done through the bloodstream (i.e., the communication channel) and in this way, a target cell, tissue or organ performs a physiological function (due to a specific type of biological information which is comparable with network layer addressing [19, 30]); then, we focus in the type of receivers that are located in a long nanorange (in which GA determines whether the information remains or leaves the cell, processing biological information as a conventional PDU). Therefore, the transmitter sends the information by using the data stored in the DNA molecules and at destination can recognize the target cell, tissue or organ [62]. In every stage of gene expression and delivery protein, mother nature has established the opportune intermediate addressing (data link layer addressing to facilitate communication within a direct range of communication) and physical layer functions also are executed to transport physically the information in this end-to-end communications nanonetwork [19, 30, 43, 44]
e) Message carrier: A physical entity that conveys a message across the medium. Message Carrier relates to a wave (the characteristic of a wave that encodes information)	
f) Transmitter: A device used to convey a message to a receiver	
g) Receiver: A device used to collect messages from a transmitter	
h) Receptor: A component that receives signals	
i) Relay: A component that facilitates communication between a transmitter and the receiver. This network element's motivation is to enable messages to travel longer distances and increase the likelihood of message deliverability. This might be thought of as a form of signal amplification (Section 5.3.2 IEEE 1906.1)	
j) Medium: The environment connecting the transmitter and receiver, which can include gas, gel, or liquid	
k) Specificity (sometimes called the actual negative rate) measures the proportion of negatives that are correctly identified (e.g., the percentage of Message Carriers not addressed to an intended target node that is not accepted by the intended target node)	k) MCs systems and typical communication systems can encounter problems during the transmission of information via communication channels. Specifically, in MCs, these problems include biochemical, thermal and physical noise, interference, and attenuation [20, 30]
l) Sensitivity (also called the true positive rate: the correct classification of a signal, or the recall rate in some fields) measures the proportion of true positives which are correctly identified (e.g., the percentage of Message Carriers addressed to an intended target node that are recognized and accepted by the correct intended target node). Specificity and Sensitivity are widely defined in Section 6.12 in IEEE 1906.1	l), m) Signal molecules are received by receptors within the receiver in nature; the receiver is made up of a chemical detector that detects the concentration of molecules at a given sample time and demodulates the signal [20, 63, 64]. As a result, these protein structures can be thought of as antennas for receiving signals. Receptors are protein structures that have the ability to bind to various ligand structures. Intermolecular forces such as ionic bonds, hydrogen bonds, and van der Waals forces are used to tie molecules together. In most cases, docking (association) is reversible (dissociation). The chemical conformation of a receptor is altered when a ligand binds to it, and the propensity to bind is referred to as affinity. A receptor's functional state is determined by its conformational state. During the detection process, almost all ligand structures in nature catch and extract information particles from the propagation area [14, 20]
m) The signaling molecules and cell surface receptor, acting as a message and receiver respectively	

**Table 3.** Framework section (Section 5.2 in IEEE 1906.1 and Section 3.1 in IEEE 1906.1.1)

Molecular communications	Gene expression and protein delivery
<p>a) Component 0: Message Carrier. The Message Carrier provides the service of transporting the message. The message carrier may be either particle or wave. Like quantum mechanics, the message carrier may also be a simultaneous combination of both particle and wave. A molecular structure may encode information transported by the Message Carrier from a transmitter to a receiver. Wave-like changes in message concentration may also encode information. In IEEE 1906.1.1 (Section 5.3.3.3.2) is defined some core message carrier specifications (with a label name) which include molecular motors</p> <p>b) Component 1: Motion. Defines the movement capability for Component 0 (Message Carrier). The Motion Component provides the service of movement for the Message Carrier (in any direction) caused by force or thrust applied to the Message Carrier. Motion provides the necessary potential to transport information through a communication channel. Message Carriers can be active, generating their motion, or passive, being propagated by the Media. Examples include Molecules diffusing through fluids, Brownian motion, self-propelled motion. Motion (Component 1) relates approximately to the classical physical layer (wave propagation). In IEEE 1906.1.1 (Section 5.3.3.3.2) are defined some motion specifications (with a label name) which include movement through diffusion in this component</p> <p>c) Component 2: Field. Defines organized movement of Component 1 (Motion). The Field Component provides the service of an organized motion for Message Carriers. It can be thought of as a virtual waveguide in communications. The Field may be implemented internally or externally relative to the medium. Examples include an internal implementation includes swarm motion or flocking behavior; external implementations are non-turbulent fluid flow, EM field, chemical gradient released to guide movement of bacteria, molecular motors guided by microtubules. Field (Component 2) relates approximately to the classical data link and network layers (ensuring node-to-node information flow). In IEEE 1906.1.1 (Section 5.3.3.3.2) are defined some field specifications (with a label name) which include concentration-gradient in this component</p> <p>d) Component 3: Perturbation Defines the signal transported by Component 0 (Message Carrier). The Perturbation Component provides the service of varying Message Carriers as needed to represent a signal. This may be thought of as modulation (signal impression). Examples include signals based on the number of received message carriers, controlled dense versus-sparse concentrations of molecules, simple on-versus-off flow of signal molecules, using different types of message carriers, modifying the conformation of molecules (e.g., deoxyribonucleic acid [DNA]) to represent multiple states. In IEEE 1906.1.1 (Section 5.3.3.3.2) are defined some perturbation specifications (with a label name) which include molecular-structure in this component. Perturbation (Component 3) relates approximately to classical modulation at the physical layer</p> <p>e) Component 4: Specificity Defines targeted reception of Component 3 (Perturbation). The Specificity Component provides the service of sensing or reception of a message carrier by a target. This can be mapped to addressing in classical communication systems. Examples include the shape or affinity of a molecule to a particular target, complementary DNA for hybridization. In IEEE 1906.1.1 (Section 5.3.3.3.2) are defined some specificity specifications (with a label name) which include receptor-sensitivity in this component. Specificity (Component 4) relates approximately to classical addressing at the data link layer</p>	<p>a) Gene expression (transcription and translation of DNA) is how information carried by deoxyribonucleic acid (DNA) is transformed into proteins. The transmission of information from the nucleus cell (i.e., from genes) to specific destinations begins with the transcription process in which DNA information is copied into RNA [30]. The DNA molecules contain digital information due it is encoded by four discrete values (four nucleotides, the quantity of information carried by a single nucleotide base is 2 bits <math>[-\log_2(1/4)]</math>). To begin transcription, the molecular motor RNA polymerase II (the RNAP II enzyme) recognizes a region of the DNA sequence called the promoter region [39]. The halt of transcription is accomplished when an appropriate finalization sequence is recognized by RNAP II [29]. In translation, fundamentally, ribosomes, which serve as molecular motors, read the information in the biological sequence using a codon system [30, 46]. In the ribosome, the codons in the mRNA are recognized by transfer RNAs (tRNAs) that possess an anticodon associated with a unique amino acid that binds specifically to the molecular structure of that tRNA [40]</p> <p>b) We focus on the protein delivery to destinations in the endocrine system (e.g., hormones of a proteinaceous nature) that move through the bloodstream (physical transmission or diffusion medium) [9, 30, 32]</p> <p>c) In a random walk with drift, information molecules may undergo a directional drift that continuously propagates molecules in the drift's direction (concentration-gradient). An example of this class of MCs is found in our body; cells in the body secrete hormonal substances that circulate with the bloodstream flow and propagate to distant target cells distributed throughout the body. This type of communication also represents the active mode of MC [9, 30, 68]</p> <p>d) We consider that the ribosomes and ER represent the biological DCE because, through these organelles, the genetic information acquires a functional structure (or format when referring to data). This biological DCE processes (codifies) information via translation and provides a specific input sequence (data in mRNA) that is associated with a specific output (sequence of amino acids). Hence, in our research, the biological DCE codifies a set of 6 inputs (3 nucleotides or 6 bits due each one is represented by 2 bits) with a set of 64 outputs (to encode the total of 20 amino acids) [30]. Then the DCE in our case may have a 64 MoSK (i.e., there exist 64 different cases to be considered, because, for the MoSK modulation scheme, the information is represented by using different types of molecules (molecular structure), for <math>x</math> bits information per symbol, <math>2^x</math> types of molecules are needed to transmit [52, 53])</p> <p>e) Signal molecules are received through protein structures called receptors within the receiver in nature (in the long nano range, an addressing network layer addressing [19, 30] is required); the receiver consists of a chemical detector, which will sense the concentration of molecules at a particular sample time and demodulate the signal [20, 63, 64]. As a result, these protein structures can be thought of as antennas for receiving signals. Receptors are protein structures that have the ability to bind to various ligand structures. Intermolecular forces such as ionic bonds, hydrogen bonds, and van der Waals forces are used to tie molecules together. In most cases, docking (association) is reversible (dissociation). The chemical conformation of a receptor is altered when a ligand binds to it, and the propensity to bind is referred to as affinity. This method of communication is similar to a lock and key system, in which the information is detected, read, and interpreted by a receiver with the "key"; other receivers can detect the information, but they are unable to process it, indicating the process's uniqueness [30]</p> <p>A receptor's functional state is determined by its conformational state. During the detection process, almost all ligand structures in nature catch and extract information particles from the propagation area [14, 20]. The membrane protein acts as a transducer in the biological process mentioned, decoding the obtained signal (i.e. performing standard DCE tasks at the receiver) and causing multiple reactions within the target cell, tissue, or organ of the body (i.e. accomplishing the typical DTE tasks at receiver) [65]. This activity is similar to the work performed at the receiver end of digital communication systems to process data that will be useful at the destination [66, 67]. When the biological data is received by the target cell, it is transmitted to other organelles through an implicit adjacent address, which is similar to the data link layer address used to enable contact within a direct range of communication [19, 30]. The biological message that has been received is physically transmitted to the target cell</p>

**Table 4.** Framework components section (Section 5.3.5 in IEEE 1906.1 also supported in IEEE 1906.1.1)

Molecular communications	Gene expression and protein delivery
a) Message-to-Message Carrier (encoding)	a), b), c), d), e), f), g)
b) Message Carrier-to-Motion (range of motion)	Having in mind that the intracellular distance is in the range <100 nm and that a typical long nano range is in the range of mm to m [20, 31, 32, 69], and that the functions of biological DTEs and DCEs have been described in this document
c) Motion-to-Field (controlled motion)	
d) Field-to-Perturbation (rapid control of field)	
e) Perturbation-to-Specificity (ability to dynamically change Specificity to encode a message)	
f) Specificity-to-Message Carrier (Message Carrier and binding capability)	
g) Message Carrier-to-Receiver (decoding)	

## 4 Conclusions

Molecular communications essentially analyze the transmission of the information at the nano-level in cells, the “smart” devices that constitute our bodies. This new emerging area uses classical communication systems elements and maps it to molecular signaling and communication found inside and outside the body. Hence, molecular communications’ fundamental importance denotes the necessity to develop a new technology framework that provides a novel perspective to fight human diseases (the COVID-19 pandemic has highlighted this challenge). As a result, the architecture for molecular communications can be explored from the perspective of computer networks, i.e., the TCP/IP reference model and the basic model of MC can also be represented using Shannon’s communication model (i.e., transmitter, communication channel, and receiver). In this area, IEEE impulses the 1906.1 and 1906.1.1 standards that establish definitions, terminology, and a conceptual model for nano communication networks. With these ICT perspectives, we have analyzed gene expression and protein delivery as nanoscale communications networks that describe functions at the physical layer (real communication through a physical medium), link layer (to facilitate communication within a direct range of communication), and network layer (the contents of a gene can be understood as addressing that performs a physiological function at target destination in a long nano communication) by denoting: transmitter, receiver, message, medium, and communication components (i.e., message carrier, motion, field, perturbation, and specificity) from the mentioned standards perspective.

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