Biological Roots and Applications of P Systems. Further Suggestions

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1 Biological Roots

The History of Biology together with the history of ideas and theories comprises the history of imported methods from other sciences, mainly from physics, and chemistry. This is not the place to present, even briefly, the history of Biology, but the use of chemistry and physics to study the processes inside living organisms faced – at the beginning of experimental research in biology – the opinion that inside living cells there is no chemical reaction or physical processes. When the experimental biology significantly developed (in the first part of XIXth century), *it become evident for all scientist that chemistry and physics can be used to study living organisms because inside living mater chemical reactions and physical processes do occur.* However, some scientists, so called the vitalists, believed (and still believe) that these physical and chemical realities say nothing essential about the vital process called LIFE (and whose scientific definition is still missing, up to my best knowledge) (Ardelean, 2002).

The first major meeting between Biology and Mathematics was via Physics, caused by the debate concerning the usefulness of thermodynamics concepts and experiments in the study of biology. Thermodynamics introduced in the first half of XIXth century the key concept of energy, as the quantitative expression of the capacity of any system for doing work and overcome resistance (for more details see Ciures and Mărgineanu, 1970; Morowitz, 1972; Mărgineanu 2001). The usefulness of thermodynamics for biology was very doubtful until the emergence of so called thermodynamics of irreversible processes. However, both "types" of thermodynamics use continuous mathematics for reasons shortly shown below (vide infra). In conclusion, it become evident that living matter obeys the laws of thermodynamics.

The first direct and systematic meeting between Biology and Mathematics is, in my opinion, the birth of P systems in 1998–2000 (Păun, 2000; 2001; 2002). It was for the first time the biological realities occurring mainly across biological membrane, were used as raw material to abstract from it a calculus. *The ontological fundament of P systems* (apart from the inspiration of its initiator, the chance, etc. etc.) *seems to be the fact that the processes occurring across biological membranes are genuine natural calculi performed by living cells.*

The emergence and flourishing of cell biology with special emphasis on membrane biophysics, biochemistry and molecular biology generated knowledge concerning discontinuous processes occurring across, within and at biomembranes (Alberts et al., 1994), knowledge that sustained the emergence of membrane computing (= P systems).

Furthermore, any biological system, as a living bacterial cell for example, is an open system which exchanges mater, energy and information with its surrounding medium. As the infusion of chemistry and physics into biology mainly in the XXth century produced a wealth of knowledge concerning the fluxes of mater and energy within a living cell, the flux of information is illustrated, rather metaphorically than mathematically, by the flux of genetic information from DNA to polypeptides.

In the last decades it became evident that *not all functional proteins* within a cells are involved only in the flux of mater and energy, as is the case with energy conservation or the synthesis of cellular components (Bray, 1995). The most obvious example of biological process requiring/involving the flux of information is chemotaxis (Bray, 2002; Szurmant and Ordal, 2004; Martinez-Antonio et al., 2006)).

Chemotaxis, the movement of a bacterium (or other types of cells) toward a needed chemical (called attractant) or away a dangerous chemical (called repellent) is one example of cell behavior involving fluxes of matter, energy and information, a behavior which is essential for bacterial survival. Chemotaxis allows the bacterium to move towards the needed substance (or more precisely towards the increase in the gradient concentration of that substance); for example, oxygen respiring bacteria, which use molecular oxygen in respiration, move towards (optimal) oxygen concentrations. Chemotaxis also allows the bacterium to try to escape from a substance that is toxic for it.

The overall process of chemotaxis (e.g., aero taxis) involves the following four integrates stages: signal recognition and transduction, excitation adaptation and signal removal, the first three being clearly information-based processes.

2 Applications of P Systems

So far, the main application of P systems are in Biology, Computer sciences, Linguistics, and membrane software (Ciobanu et al., 2006).

3 Further Suggestions on P Systems

1) *The use of discrete mathematical P systems to model discrete, discontinuous processes in the living world.* In Biology it is obvious that matter and energy have a discontinuous nature; furthermore many (if not all) biological processes are discontinuous.

So far, the scientists used differential and integral calculus to describe continuous processes (for more discussions, see Bianco et al., 2006) as well as discrete, discontinuous processes in biology (or in other sciences). *The scientists know that they use a continuous mathematical tool to model a discontinuous process*; they claim for the validity of their approach taking into account the assumption that the system is composed of a great number of undistinguishable particles (for more discussion, see Mărgineanu, 2001). In my opinion, the so far success of differential and integral calculus in modelling discrete processes (e.g., the kinetic of enzymatic reactions, ionic processes at the neuron plasma membrane, etc.) was based – apart from the above heuristic argument – on the fact that no discrete Math has been used to model biological processes. Fortunately, since the birth of P systems several interesting approaches have been already published on the use of discrete mathematics to model discrete biological processes. However, even these approaches were done assuming a great number of (almost) undistinguishable particles, objects (e.g., enzymatic molecules, mechano-sensitive channels, etc.) a domain where the competition with continuous mathematics is very hard (mainly because the bioscientists are used with this type of approach!).

In my opinion, P systems should "attack" on the territory – just to use o common concept in military art and the game of GO (Păun, 2000) – where differential and integral calculus are not valid at all: the space of a single event, single occurrence of a catalyst (enzyme, mechano-sensitive channel etc.).

The chance is that in nowadays science there is a strong trend toward the study of single event or object (molecule, cell, etc.). To argue that, I will briefly focuss on Microbiology. Single cell Microbiology (SCM) is a trend in microbiological sciences which allows the study of an individual cell from a population (Brehm-Stecher and Johnson, 2004). The development of SCM roots in the technical advances in other sciences (mainly physics and biochemistry) where special tools were developed. The advances in SCM are already copious and even a first authoritative review has been written on this topic (Brehm-Stecher and Johnson, 2004). It is beyond the scope of this contribution to present the state of the art of SCM; I will show only a few achievements in SCM which, in my opinion, are very appropriate to be further modeled by P systems.

a) SCM allows the observation of discrete/discontinuous and dynamic processes within living (bacterial, yeast, etc.) cells with high spatial and/or temporal resolution. For example, the specific distribution at the cell surface of some receptors (receptor clustering) involved in chemotaxis. More precisely, it started to be shown that the protein acting as receptors in bacterial chemotaxis are not distributed uniformly at the surface of the *E. coli* cell, the main localization being at one pole of the cell (Bray, 2002) – it should be reminded that *E. coli* is an almost cylindrical cell (nothing is known so far about the specialized – if any – distribution of protein receptors at the surface of a spherical cell). This polarized distribution of receptors (objects) in space is a growing topic in Microbiology and it could be interesting for P systems at least as a new type of communication rules, in which the position, the density of the interacting "letters" is essential for the rule to occur. This could be a challenge for P systems to develop their application in those domains where spatial distribution of objects is very important: collective sports (football etc), military strategy, and games, such as chess, GO, etc.).

b) SCM allows the interplay between microscopic (in the sense of biology), mesoscopic and macroscopic properties of microbial population, with emphasis on the cellular origins of mesoscopic and macroscopic properties. For example, coordinated movement of (e.g., travelling waves, whirls, and jets) within population of myxobacteria or *Bacillus subtilis* have been studied at cellular level integrated in the population level (for more details, see Brehm-Stecher and Johnson, 2004). Similar movements have been described in magnetotactic bacteria whose study of movements of each individual cell still waits. So far, classical microbiology has traditionally been concerned with and focussed on the studies at the population level. Nowadays, with the emergence of SCM, Microbiology faced the same problem: the connection between macroscopic (= population) level (behavior) with microscopic (= cellular, in biology) level. Long time ago, Thermodynamics solved this problem by differential and integral calculus. The nowadays answer of microbiology can be based on the use of discrete Math P system based to describe discrete processes based either on single, small or huge (statistically relevant) number of cells. Furthermore, with the development of appropriate tools and techniques to study discrete realities, such as single individual microbial cell, there is the need for discrete models whose appropriate description seems naturally to be founded on discrete mathematics, with P systems appearing as a very powerful candidate.

c) The analytic progress of Microbiology toward the study of single individual cells raised new theoretical problems. Because an experiment and its control cannot be carried out on the same individual cell, it is impossible to be sure that the observation/measurements itself does not affect the cell. This statement is the biological equivalent of Heisenberg's "uncertainty principle" (for more details, see Brehm-Stecher and Johnson, 2004).

d) SCM has a large significance not only in basic science but also in applied science, mainly with respect to microbial heterogeneity related to antibiotic and biocide resistance, productivity and stability of industrial microbial based bio-tehnologies or the potential of pathogens to cause diseases (see more details in Brehm-Stecher and Johnson, 2004, and references herein).

Thus, it seems reasonable to conclude (and expect for the near future) that P systems could offer the appropriate software for the description of discrete biological processes (such as those related to SCM), and that it will be used to model the experimental data obtained on single cells (molecules, etc.) not only in basic science (e.g., mechano-sensitive channel behavior, enzymes, enzymatic cascade, etc.), but also in applied science such as the contribution of the sensibility of each individual cell from a population against a given substance, thus being useful for the development of biosensors.

In conclusion, *I suggest that P systems are most promising in describing discrete processes* performed by : i) single objects: catalitic molecule (= enzyme), supramolecular structures (MscL, porins, ionic channels, etc.), single cell, and ii) a small number of objects occurring in the sample, e.g., several mechano-sensitive channels occurring within a membrane patch. Furthermore, P systems could be valuable tools to describe discrete processes performed by a great number of undistinguishable particles.

Table 1. The main results on artificial membrane research (from Ottowa and Tien, 2001) with suggestion on their usefulness for the construction of a P-systems based PC.

Period	Main results	Significance for P systems
First decade (1961–1970)	Technique for BLM formation; excitability-inducing-material, discrete channel conductance, antigen-antibody, enzyme-substrate interactions photoelectric effects	The model of a single channel Kinetic model of enzymatic reaction based on P systems
Second decade (1971–1980)	Models for the plasma membrane of cells, the nerve membrane, the cristae membrane of mitochondria, the thylakoid membrane of the chloroplast, the visual receptor membrane of the eye, and many others, last but not least, a model for the purple membrane of *H. halobium*; ion channel reconstitution	The study of discontinuous bioenergetics processes based on electron transfer (respiration, photosynthesis etc.) to write a discrete model for them in order to
Third decade (1981–1990)	Molecular mechanisms of membrane processes: supported BLM's on metal substrates (s-BLMs); Mechanisms of photosymthesis, membrane bioenergetics; Solar energy utilization via semiconductor septum electrochemical photovoltaic cells; Electroporation	construct stable microdevices as hardware components of a P system-based PC
Fourth Decade (1991–2001)	Supported BLMs on hydrogels (sb-BLMs), tethered (t-BLMs); Supported BLM-based sensors and devices; Molecular mechanisms of membrane processes; BLM-based biotechnology and molecular electronics; DNA-BLM interactions	The construction of a P system-based PC having a P system-based software

2) *The use of P system to lead to a software able to manage the wealth of information obtained from different types of arrays: DNA-arrays; protein-, enzymes.* One requirement with these arrays is the rapid and correct process of information produced by these arrays. Again a reading tip leaded/controlled by a discrete program based on discrete mathematics would be more successful to monitor a discrete process (arrays function) than a classical program.

3) *Towards a P systems-based* in vitro *implementation of P systems.* The progress made in the last decades on the incorporating of different biological

molecules into artificial membranes (e.g., black lipid membrane – BLM) has lead to major progresses in understanding their *in vivo* function (Ottowa and Tien, 2001). In Table 1 there are presented some reconstituted systems within artificial membranes, with emphasis on original application for *in vitro* implementation of P systems.

This topic could let to the construction of P systems-based computers, and this kind of experiments could be for P systems what are DNA experiments for DNA computing: *in vitro* use of molecules to calculate. Moreover, there are the following advantages of *in vitro* membrane computing as compared with DNA computing:

i) The speed of these processes occurring at membranes (both artificial and natural) is much higher as compared with DNA computing experiments, thus a faster computation.
ii) The process will occur at a membrane which can function as a micro-device. Furthermore, planar BLMs can now be formed on various substrates with long-term stability, thereby opening the way for basic research and developments work in biotechnology (Ottowa and Tien, 2001).
iii) In many in vitro reconstituted systems at/within artificial membranes the output is an electric signal: either current or potential. That could facilitate the transfer of information from one *in vitro* structure to another one, as well as the building up of complex hierarchical structures, using the already acquired knowledge and skills used in the construction of to day computers.

In conclusion, nowadays status and the perspectives in BLM research allow the hope that they are appropriate tools for P systems-based experiments

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