# Simulating Metabolic Processes Using an Architecture Based on Networks of Bio-inspired Processors

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In this work, we propose the Networks of Evolutionary Processors (NEP) [2] as a computational model to solve problems related with biological phenomena. In our first approximation, we simulate biological processes related with cellular signaling and their implications in the metabolism, by using an architecture based on NEP (NEP architecture) and their specializations: Networks of Polarized Evolutionary Processors (NPEP) [1] and NEP Transducers (NEPT) [3]. In particular, we use this architecture to simulate the interplay between cellular processes related with the metabolism as the Krebs cycle and the malate-aspartate shuttle pathway (MAS) both being altered by signaling by calcium.

NEP is complete and efficient from the computational point of view (i.e. is able to solve hard problems NP complete given linear time solutions). This model consists of several processors, each of one is placed in a node of a virtual graph. Each processor acts on local data in accordance with some predefined rules (evolutionary operations simulating point mutations of nucleotides over DNA sequences) and communicates the results using a filtering strategy. This strategy may require satisfy some conditions that are imposed by processors, when sending, receiving or both. The processors can communicate the resulting data with the rest of the processors connected with it. A processor node can be viewed as a cell that carries out only one specific evolutionary operation (substitution, elimination or insertion). NEPT uses these operations in order to generate recursively enumerable languages recognized by other NEP (without filtering strategy). On the other hand, NPEP uses these operations together with a valuation mapping (from strings to integers) to generate strings labeled with an electrical polarization. Each node has their own polarization, then the filtering strategy consists in let pass those strings with their same polarization.

NEP architecture sees a biological process like a web, that is, a network of several NEP working in a collaborative way. This architecture consist in three layers each one representing one block of computing: *selection layer* (implemented by a NEPT), represents the reception of an extracellular signal molecule arriving at the cellular membrane, and its alteration (transduction); *control layer* (implemented by a NPEP), realizes the monitoring functionality of signaling pathway, either activates or inactivates the target proteins (effectors); and finally the *processing layer* (implemented by one or several NEP), represents the target activity which alters the metabolism.

A very well known metabolic process is the *Krebs cycle* that is critical in cellular respiration. Signaling by calcium helps to activate metabolic pathways, such as the *malate-aspartate shuttle* pathway (MAS). Krebs cycle and MAS are linked through shared substrates as the $\alpha$-ketoglutarate ($\alpha$KG). The interplay between these processes, sharing and competing for $\alpha$KG, as well as being altered by calcium is an important study of the brain stimulation *in vivo*. In order to model the interplay between these biological processes, we define a NEPT in the selection layer, which is able to translate strings representing chemical compounds into new specific strings representing some receptor proteins, enzymes and metabolites (i.e. piruvate, malate, aspartate, calcium, etc). These strings are collected in the output node and are sent to the input node of NPEP in the control layer. NPEP recognizes these strings and generates new polarized strings that are collected in their output node: a negative charge means an inhibitor substance for MAS, a neutral charge represents a promoter for MAS and positive charge represents a promoter for Krebs cycle. Resulting polarized strings with a negative or neutral polarization are sent to the input node of the NEP representing the MAS shuttle and the string with a positive charge are sent to the NEP for Krebs cycle. Finally in the NEPs, each node receive only the necessaries substances (filtered by the input strategy), transforming them (using substitution, elimination or insertion rules representing the corresponding chemical transformation) and only the necessaries substances for the linked nodes (filtered by the output strategy) are sent as can be seen in Fig. 1 and 2.

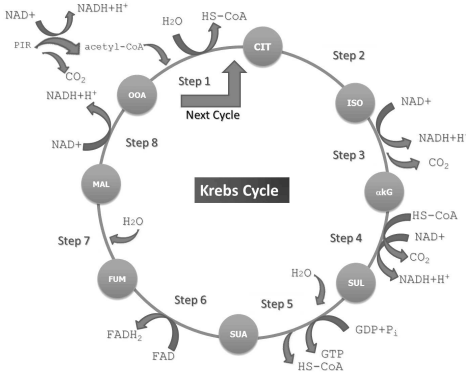


**Fig. 1.** Krebs cycle

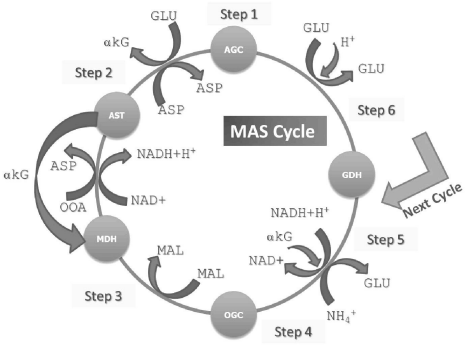


**Fig. 2.** MAS shuttle pathway

## References


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