Natural computing in biochemistry: stochastic (bio)-logic gates

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In the last years several scientists involved in the disordered-systems route to decode biological complexity (from the group of Mheran Kardar at MIT or those of Curtis Callan and William Bialek at Princeton, to our ones between Sapienza and King's College, with Ton Coolen and Peter Sollich) highlighted several emergent properties of lymphocyte's networks, such as their multitasking capabilities, the clonal selection at ontogenesis for shaping their repertoires and the correct balance between clonal expansion and lymphocytosis, just to cite a few (and in [1,2,3] I report some of our works on this study). Not as a minor point, in decoding the collective behavior of these cells (via this approach, that is a large and massive use of statistical mechanics and graph theory), researchers have largely borrowed concepts from an already developed branch of statistical mechanics, that is "spin glasses & neural networks", as the extreme value statistics, the Hebbian kernel for a distributed memory (playing for vaccination in the present context) or the whole fingerprint of "frustration", with the related package of physical characteristics.
This shift of concepts to a structurally-similar but operationally very different network (namely from neural to lymphocyte networks) however demands the by far non-trivial extension of information processing pathways from electrical networks (i.e. brains or computers, the original framework where those ideas were originated) to chemical ones. Indeed, while neurons in biological neural networks, or operational amplifiers in artificial neural networks, dialogue via electric currents and the basic bit of information (1,0) is coded by the difference between high and low voltages on their membrane (for neurons from -65mV -state 0- to a few mV -state 1-), the latter, chemical networks. dialogue with variations of relative concentrations as dictated by their coupled reaction dynamics (chemical kinetics) and store a bit of information (1,0) in the difference between high and low concentrations of ligands effectively bound to reactants: in order for the analogy between these networks to hold, these information processing pathways must be safetly compared and overall coherence should be demanded.
In this report we first present a streamlined introduction to the genesis of the problem, that is immune information processing; in particular we consider the main paradigm for clonal expansion of lymphocytes, namely the "two-signal model" (within the Burnet's clonal selection theory, see Fig.1): the latter states that a clone, in order to start expansion, needs two signals to be integrated (within a short timescale) on its membrane and these signals are the presence of the antigen (signal one) and the "consensus" by a T-helper encoded by diffusing cytokines, as interleukins or interferons (signal two), and we show that this scenario can be naturally described as a stochastic AND gate.
Then, summarizing our results presented in [4,5], we build a solid bridge between electric information processing and chemical information processing, showing how single-input/output chemical systems naturally play for logic YES and NOT (stochastic) gates and how double-inputs/outputs chemical systems naturally play for AND, NAND, OR, XOR (stochastic) gates: the adjective stochastic is to remark that, at difference with standard information processing with electronic gates (for instance inside a computer), where information flow is deterministic, these systems operate at high level of noise, thus the correct theoretical reference framework is no longer mathematical logic (that remains as an ideal setting), while, we propose, that statistical mechanics can successfully accomplish this role.
Our findings quantify the scenario where chemical computing uses molecular systems to perform logical operations, mimicking processes typical of electronic devices and allow for a comparison between these machineries: advantages and disadvantages appear when comparing these two approaches to computation. Chemical computing requires (for a single operation) a smaller size (Angstroms versus microns) and a lower energy consumption (10^(-19) Joule versus , 10^(-9) Joule), yet it is slower than electronic computing (from kilohertz to megaherz versus gigahertz). Further, biochemical information processing performs at relatively large levels of noise (and this happens at different scales, ranging from enzyme-based logic gates to nucleic acid logic circuits: noise propagates in the system as thermal disorder or in form of cross-talk among system's constituents).
Such investigation suggests that much of the already known information processing mechanisms, learned in neurobiology and robotics disciplines, are also widely shared among several, possibly really different, chemical networks, made of by several elementary elements (binding sites and substrates) that, crucially, must be non-linearly interacting, frustrated and allowed to receive feed back signals.

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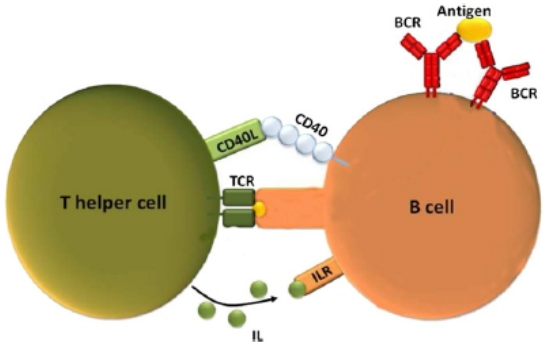

Figure 1: this picture represents the "two signal model" in action: the B-cell (large orange ball on the right) has already encountered the antigen (in yellow, top right), that is the first signal, and is exposing antigenic peptides (i.e. epitopes) to the T-helper cell receptor (TCR, center). The latter (large green ball on the left) performs pattern recognition on the shown peptides and releases interleukins (IL, small green spheres at bottom center) that play as the second signal: these are received by the interleukin receptor on the B cell that gets activated. Overall, in this framework, the B-cell behaves as a (stochastic) AND gate.

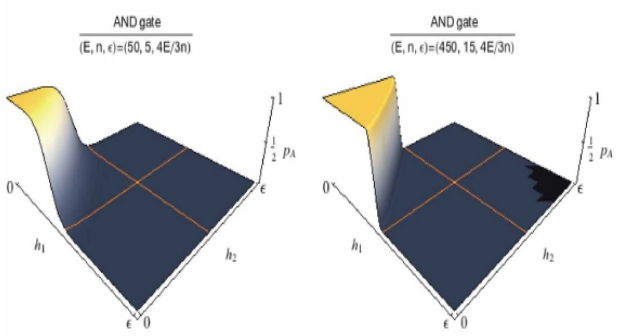

Figure 2: schematic representation of an AND gate where on the orizontal axes the amount of input signals is reported, while on the vertical one the response of the system is shown. The system gets active only when both the stimuli are present (thus only in one over four quadrants).

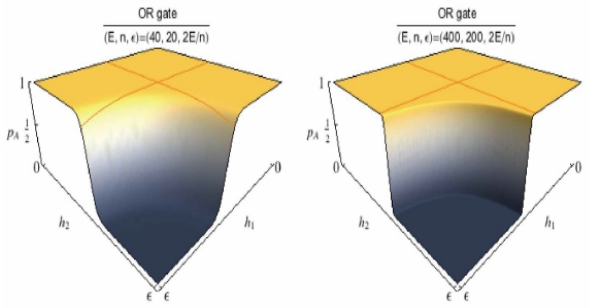

Figure 3: schematic representation of an OR gate where on the orizontal axes the amount of input signals is reported, while on the vertical one the response of the system is shown. The system gets active when at least one of the two stimuli is present (thus in three over four quadrants).

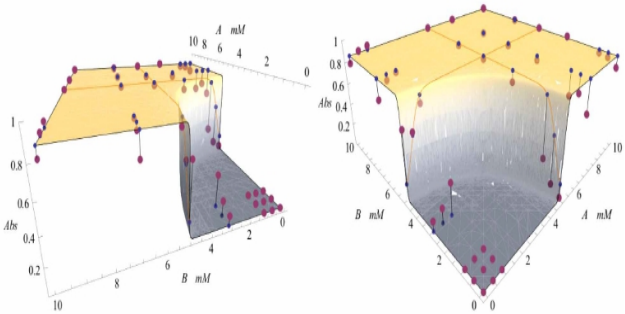

Figure 4: comparison among the theory of stochastic (bio)-logic gates obtained via statistical mechanics in [4] and data on enzyme allosteric kinetics, gave to us by Prof. Evugeny Kats from Clarcson University.