An Introduction to the Special Issue: Modeling and Control of Integrated Bio-systems

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The special Issue "Modeling and Control of Integrated Bio-systems" appears in time of ubiquitous human connection by Internet technologies in popular social and professional nets, Google, Wikipedia, and many others. Their principles of function are connected with the terms like "collective or collaborative intelligence", "symbol intelligence", "quorum sensing", "quorum quenching ", "crowdsourcing". All these terms implies a cooperative behavior, or integrated systems concept, challenged by the evolutionary implication.

A "quorum sensing" is compared with stimulus and response, correlated to population density and can function as a decision-making process in any decentralized system, as long as individual components have a means of assessing the number of other components they interact with and a standard response once a threshold number of components is detected.

"Symbol intelligence" is connected with the formalization of the knowledge representation as an area of artificial intelligence research aimed at representing knowledge in symbols to facilitate inferencing from those knowledge elements, creating new elements of knowledge.

"Crowdsourcing" is related to human-based computation, which refers to the ways in which humans and computers can work together to solve problems. These two methods can be used together to accomplish tasks.

To take advantage of the possibilities these new systems represent, it is necessary to go beyond just seeing them as a collection of "cool" ideas. What is needed is a deeper understanding of how these systems work.

The genesis of the problem lies in the integrated bio-systems. Some of the best-known examples of "quorum sensing" come from studies of bacteria, which use it to coordinate certain behaviors, based on the local density of the bacterial population. Quorum sensing can regulate a host of different processes, serving as a simple communication network. Many species of bacteria use quorum sensing to coordinate gene expression according to the density of their local population. In biological systems, quorum sensing has several useful applications for computing and robotics.

Living matter is built by cells, which accept, conduct, transform, save and transfer information concerning the irritant (stimulus) from internal or external environment. All these actions realize many decision-making processes. In particular, the problem of synchronization of groups of neurons draws significant attention. In the special issue the problem of excitation of human neurons is considered in the first paper of Klaus Roebenack and Nicolas Dingeldey, entitled "Observer Based Current Estimation for Coupled Neurons". The studied object is a chain of mutually connected neurons and the processes in the cell membrane, where spring up neuronal impulses, which are reproduced as well as electrical current. The input current stimulating a neuron is not directly measurable without inference with the cell's activities. The standard technique to measure ionic currents across the cell's membrane is known as voltage clamping. Unfortunately, these approaches interfere with the cell's activity, limiting the applicability in vivo. In control theory, the problem of reconstruction of not directly measurable quantities using the dynamics of the underlying system is known as filter or observer design. Starting with linear time invariant systems, this research has been extended into several directions such as filter or observer design for time-varying and nonlinear systems. Two feedback control laws are proposed (one of them is adaptive) for asymptotic stabilization of the closed-loop system towards a previously chosen operating point.

For bio-systems, estimators based on observers or filters are also known as software sensors or software analyzers.

Observer and filter techniques can be used to reconstruct the input current into a single neuron using voltage measurement.

All living organisms are dependent on the living conditions of the nature and urban environment. In this connection bio-system integration studies the management of wastes and residues. The authors Neli Dimitrova and Mikhail Krastanov consider a nonlinear model of a biological wastewater treatment process, based on two microbial populations and two substrates in the paper entitled "On the Asymptotic Stabilization of an Anaerobic Digestion Model with Unknown Kinetics. Two approaches for global stabilization are presented, based on adaptive feedback law and state feedback control law. To prove the stabilizabilty of the control system, explicit Lyapunov-like functions are constructed and a recent extension of the LaSalle invariance principle is used. The robustness of the proposed feedback laws is demonstrated in a computer simulation process, assuming that the model parameters are uncertain but bounded within compact intervals.

Two examples of integrated biotechnological processes are shown in the paper "Advanced Fuzzy Modeling of Integrated Bio-systems" of Svetla Vassileva. The object of interest is the effect of the aerobe fermentation (aerobic growth of the starter culture) on the sparkling wine composition and quality in a multi-factorial integrated bio-system. The applied advanced modeling method by fuzzy networks for the Inferential Composition Model design shows that oxygen content and agitation speed influence the wine composition parameters as well as aldehydes, acetoin and diacetyl in both bio-subsystems – aerobic and anaerobic. The next example from microbial ecology studies the influence of poisoned environment at various cultivation conditions of a continuous microbial growth of yeast populations cultivated in mixed substrates consisting of wood hydrolyzates and whey. It is proved that new methods for modeling, simulation and control of integrated bio-systems, based on knowledge processing as well as fuzzy logic and neuro-fuzzy approaches, will help to discover the unknown mechanisms of bacteria "quorum sensing" for mutual coordination to grow or stop growing.

Human-based computation research has its origins in the early work on interactive evolutionary computation. The idea behind interactive evolutionary algorithms is due to Richard Dawkins. In the Biomorphs software accompanying his book The Blind Watchmaker (Dawkins, 1986) the preference of a human experimenter is used to guide the evolution of two-dimensional sets of line segments. In essence, this program asks a human to be the fitness function of an evolutionary algorithm, so that the algorithm can use human visual perception and aesthetic judgment to do something that a normal evolutionary algorithm cannot do. Victor Johnston and Karl Sims extended this concept by harnessing power of many people for fitness evaluation (Caldwell and Johnston, 1991; Sims, 1991). Human-based genetic algorithm (Kosorukoff, 1998) uses both human-based selection and three types of human-based innovation (contributing new content, mutation, and recombination). Thus, all operators of a typical genetic algorithm are outsourced to humans (hence the origin of human-based). This idea is extended to integrating crowds with genetic algorithm to study creativity in 2011 (Yu and Nickerson, 2011).

The last two papers in the special issue: "Application of Genetic Algorithm to Tuning a PID Controller for Glucose Concentration Control" by Tsonio Slavov and Olympia Roeva and "Modified Simple Genetic Algorithms Improving Convergence Time for the Purposes of Fermentation Process Parameter Identification" by Maria Angelova, Pedro Melo-Pinto and Tania Pencheva implement genetic algorithms in field of biotechnology, especially on integration between cultivation environment and its influence on the microbial population. In the first paper an equation for correction of the measured glucose based on Kalman filter estimates of biomass concentration and bacteria growth rate is suggested. To achieve good closed-loop system performance genetic algorithm tuning of the PID controller is used. Based on the proposed model correction, the estimations of the process parameters are brought closer to the real values. Tuning of the controller on the basis of a genetic algorithm leads to higher level of accuracy and efficiency of the system performance. In the second paper a comparison of two modifications of simple and standard GA towards algorithm convergence time and model accuracy is presented for parameter identification of *S. cerevisiae* fed-batch cultivation.

The special issue "Modeling and control of integrated bio-systems" is created from mathematicians and bio-engineers, which study living matter from biomedicine, biotechnology, microbial ecology and wastes treatment in a manner that could be useful to readers in their own work. We look forward to hearing reactions and learning from you, the reader, as you engage in your design struggles and successes as well. We hope also this special issue can support the field in designing for new communities and facilitating new groups of learners, and then we accomplished our goals.