



## Review:

# Recent advances in the artificial endocrine system\*

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**Abstract:** The artificial endocrine system (AES) is a new branch of natural computing which uses ideas and takes inspiration from the information processing mechanisms contained in the mammalian endocrine system. It is a fast growing research field in which a variety of new theoretical models and technical methods have been studied for dealing with complex and significant problems. An overview of some recent advances in AES modeling and its applications is provided in this paper, based on the major and latest works. This review covers theoretical modeling, combinations of algorithms, and typical application fields. A number of challenges that can be undertaken to help move the field forward are discussed according to the current state of the AES approach.

**Key words:** Artificial endocrine system (AES), Hormone, Endocrine cell, Artificial neural network (ANN), Artificial immune system (AIS)

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## 1 Introduction

Until recently, it was thought that the major regulation systems of the human body—the nervous system, the immune system, and the endocrine system—function independently. Now it is not only retained but reinforced by modern scientific research, that they are, in fact, all integrated into one single system of information communication. With cytokine, neurotransmitter, and hormone, bidirectional information transmission among these regulation systems is achieved, and these systems interact and cooperate with each other to organize a cubic and intelligent regulatory network. We believe that the structure of these regulatory systems may function in the regulation of metabolism, growth, development, reproduction, thinking, and motion of most mammals, in-

cluding humans. This subtle interaction is responsible for making adaptive overall response so as to maintain the long-term equilibrium of the organism and organization dynamically when internal and external environments are changing rapidly and physiological balance is disturbed.

The enormous achievements made in artificial neural networks (ANNs) (White *et al.*, 1992; El Sharkawi *et al.*, 2000; Rabunal and Dorrado, 2005; Graupe, 2007) and artificial immune systems (AISs) (Dasgupta, 1998; de Castro and Timmis, 2002; de Castro and von Zuben, 2004; Dasgupta and Nino, 2008) have shown a clear significance and value in both theory and application of intelligent computing and intelligent systems based on biological information processing mechanisms. These results have also inspired and guided the interest and enthusiasm in research on other biological information processing systems, including the endocrine system. Comparatively speaking, research on artificial endocrine systems (AESs) is just at the stage of discipline creation and preliminary exploration, and many challenges are yet to be discovered and overcome in theoretical models and engineering applications.

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It is well-known that the endocrine system is composed of various endocrine glands and histiocytes, widely distributed in different parts of the body, and the system plays a crucial role in cell growth, differentiation, and apoptosis, as well as in maintaining the stability of the internal environment in mammals. In recent years, revolutionary changes have taken place in modern endocrinology, through advances in molecular biology, cytobiology, immunology, genetics, ecology, psychology, and clinical medicine (Yang, 1996; Felig and Frohman, 2001; Liao and Mou, 2007). As a result, with improvements in the understanding of the information processing mechanisms of the endocrine system, a great variety of functional characteristics and action mechanisms have led to significant possibilities for industrial applications. Autonomous decentralized systems (ADSs) are perhaps the earliest attempt to provide a hormone-inspired methodology to construct functional distributed systems with the properties of on-line expansion, on-line maintenance, and also being robust and flexible (Ihara and Mori, 1984; Miyamoto *et al.*, 1984; Mori, 2001). In ADS, the content code communication protocol was established to connect distributed devices and communicate not by a conventional syntax-based system, but by a semantics-based system. ADS technology has been applied in various industrial systems to control trains, multi-stage dams, water supply, and production.

## 2 Theoretical model of artificial endocrine systems

Theoretical models of the biological endocrine system (BES) and AES, and their development, have similar important effects on AES research. Since the 1950s, a number of simulation models of biological hormone regulation have been put forward (Danziger and Elmergreen, 1957; Li *et al.*, 1995; Liu *et al.*, 1999; Farhy *et al.*, 2001; Keenan *et al.*, 2001; Farhy, 2004; Kyrylov *et al.*, 2005), but most of them have focused merely upon a particular physiological phenomenon observed within BESs. The results obtained from these models have been compared with those owned by biological organizations or experimental data of test tubes, so as to verify the correctness of the simulation models. Because differential equation

theory has been developed to a more systematic and mature extent, we have analytic solutions for some simplified differential equations. However, this approach is not very suitable for the endocrine system because: (1) Only the endocrinology theory involved with a few variables can be modeled and analyzed; (2) It is difficult for differential equations to describe features of complex systems such as diversity, randomness, uncertainty, and sensitivity to initial values; (3) Relationships among different endocrine phenomena cannot readily be expressed by differential equations, so it is extremely difficult to combine and realize all theories of different endocrine phenomena within the same model; (4) Differential equations are usually simplified from the mathematical perspective, so there are great differences between the differential equations and the actual endocrine system; (5) Usually, the differential equations approach cannot visually reproduce the microscopic and dynamic evolutionary characteristics of a BES, so it is impossible to demonstrate a visual simulation of the microscopic evolutionary process of the dynamic system; and, (6) Differential equations are determined mainly by relationships among known variables. On the contrary, artificial intelligence is focused mainly on unknown relationships.

### 2.1 Digital hormone model

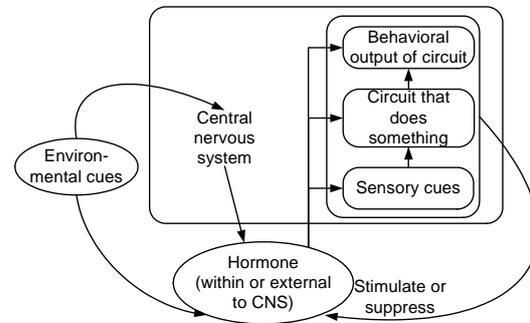
Shen *et al.* proposed the digital hormone model (DHM) as a bio-inspired, distributed control method for robot swarms self-organization and self-repair (Shen *et al.*, 2002a; 2002b; Heylighen *et al.*, 2003). The model integrated the advantages of Turing's reaction-diffusion model, topological stochastic action selection, dynamic network reconfiguration, distributed control, self-organization, and active learning techniques. Mathematically speaking, DHM has three components: a dynamic network, a specification of a probabilistic function for individual robot behavior, and a set of equations for hormone reaction, diffusion, and dissipation. The basic idea of DHM is that a self-reconfigurable system is a network of autonomous entities or agents that can dynamically change their physical or logical links in the network. Through the links in the network, entities use hormone-like messages to communicate, collaborate, and accomplish global behaviors. The hormone-like messages are similar, but not identical, to content-based

messages. They do not have addresses, but propagate through the links in the organization. All entities run the same decision-making protocol, but they will react to hormones according to their local topology and state information. Thus, a single hormone might cause different robots or agents in the network to perform different actions. As can be seen from the basic idea and mathematical definition, DHM has the advantages of simple structure, complete mathematical description, and extensive application areas, and will quite likely be a general theoretical model of AES (Jiang *et al.*, 2004; Shen *et al.*, 2004; Zhu and Yang, 2006; Peng *et al.*, 2008; Li *et al.*, 2010; Xu *et al.*, 2010). However, it lacks coordinative and cooperative mechanisms among endocrine cells, which may result in a difficult-to-overcome interference of the complicated external environment, such as multi-target cells and barriers.

## 2.2 Computational model of hormones

The computational model of hormones (CMH) is another AES theoretical model with obvious biological significance. As a basis for CMH, the principle of mutual interaction among hormones, neuro-hormones, and the nervous system to control lobsters behavior was first proposed by Kravitz (1988) (Fig. 1). Inspired by this principle, Brooks (1991) presented a CMH, an approach to the integration of the low level behaviors necessary for basic survival and navigation. In this model, a two-stage mechanism is used so that the summation of hormone quantities can be centralized. Any computational process can excite a condition with any increment to its own excitation level. Following Kravitz (1988), each behavior can be active or inactive, and the behavior becomes active when it passes the activation level. The original idea of activation was that it should be spread from behavior to behavior as a behavior attempts to have certain preconditions met by activating other behaviors. Based on CMH, swarm robots can exhibit perfect survival capacity and high efficiency, and avoid collision within the behavior selection process, but they are open to improvement and enhancement in terms of learning capacity and flexibility. In addition, based on the identical principles of biology systems, the regulation model of hormones (RMH) was developed by Avila-Garcia and Canamero (2004; 2005). They took into full consideration the affective sig-

nificance in behavior decision, and provided an ideal solution to deal with internal and external stimuli for selecting an appropriate behavior.



**Fig. 1** Diagrammatic representation of hormonal sensitization of the response of sets of neurons

## 2.3 Artificial hormone system

Currently, with the great progress and evolution of the Internet and software systems, a large amount of equipments and sensors are distributed extensively around us, which enhances the complexity of computers and calls urgently for a self-organizing system with the features of 'self-x'. Brinkschulte *et al.* put forward an artificial hormone system (AHoS) to resolve task allocation, coordination, and management of heterogeneous units (Brinkschulte *et al.*, 2007; 2008; von Renteln *et al.*, 2008; Brinkschulte and von Renteln, 2009). The system works in a fully decentralized way; that is to say, the suitable tasks are chosen at the discretion of each processing cell, and interact with the others via hormone information. This system consists of three hormones: eager value (to determine the quality of the heterogeneous unit to execute a particular task), suppressor hormone (to repress the heterogeneous unit to execute a particular task), and accelerator hormone (to activate the heterogeneous unit to execute a particular task). The time cost was analyzed for self-reconstruction, self-optimization, and self-regeneration in the worst situation, and a communications load was introduced due to AHoS. For each scenario, Brinkschulte *et al.* found upper and lower bounds for the number of tasks that will be allocated by the systems.

Another model of AHoS was proposed by Trumler *et al.* (2006) to establish a self-organizing system. The basic idea of AHoS is to define the resources such as CPU, memory, communication

bandwidth, or any other resource suitable to be used for the optimization of an application, and a corresponding digital hormone value which can describe the consumption of a resource. In contrast, this AHoS is grounded on an asynchronous processing mechanism; thus, over-loading is apt to be vulnerable at the node of request sending (Streichert, 2007).

#### 2.4 More discussions about the theoretical model

We refine and highlight some common features of most theoretical models of AES, as mentioned above: (1) From the micro level of AES, the behavior of a single cell is simple and is described clearly with some tools such as probability and feedback. The models may emerge and show some unexpected features such as self-organization and self-repair from the macro-level. (2) The bidirectional information transmission among AES, ANN, and AIS is necessary for a well-controlled system. With the help of this process, AES implements an effective combination of internal and external stimuli to choose the appropriate

behavior. As a result, AES can serve as an efficient action selection mechanism in dynamic and unpredictable scenarios. (3) Another common feature is quantifiable hormone concentration. Although the implications, sources, expressive forms, and intentions of hormones may differ in thousands of ways in all models, it is convenient and useful to compare and evaluate the primary instantiation by quantifiable hormone concentration.

A detailed comparison of the different models is shown in Table 1, in terms of inspiration sources, features, and application examples.

### 3 Computing with other natural computation methods

With a large amount of biology and medical experimental results and case analyses as the basis for argument, medical scientists have revealed the action mechanisms of various chemical messengers and

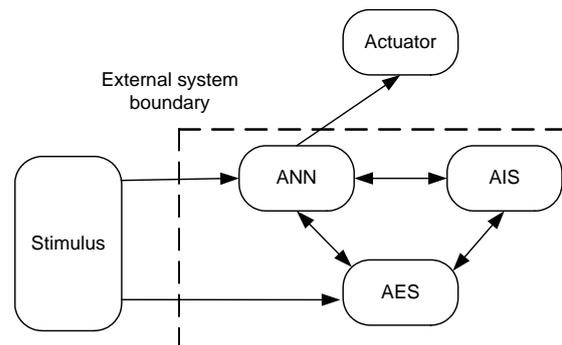
**Table 1 Comparison of the different artificial endocrine system (AES) models**

Model	Reference	Inspiration source	Feature	Application example
DHM	Shen <i>et al.</i> , 2002a	(1) Biological discoveries about how cells self-organize into global patterns; (2) existing self-organization models; (3) stochastic cellular automata; (4) distributed control systems for self-reconfigurable robots	Self-organization, self-repair	Robot swarms search and seize targets (1), spread and monitor a given area (2), self-repair unexpected damages (3), and surmount and detour in mission execution (4)
CMH	Brooks, 1991	Hormonal control of behavior in lobsters	General for the basic behaviors, versatile, reactive, efficient, no learning or explicit knowledge	Fully autonomous planetary exploration
RMH	Avila-Garcia and Canamero, 2004	Hormonal control of behavior in lobsters, especially hormonal feedback mechanisms	Adaptive, self-sufficient, combination of parallel and hierarchical structures	Dynamic competitive two-resource action selection problem
AHoS	Brinkschulte <i>et al.</i> , 2007	(1) Hormones are spread unspecifically over certain regions to cause some effects; (2) the reaction of a cell to a hormone depends on the cell itself; (3) the closed control loops are decentralized; (4) the hormone quantity is reduced by metabolism	So-called self-x, decentralized, real-time, low communication overload	Self-organizing real-time task allocation in middleware
AHoS	Trumler <i>et al.</i> , 2006	(1) Patterns of information transmission; (2) Relationship between a hormone and the corresponding receptors; (3) negative feedback loop	Self-organization, distributed, no communication mechanism, no explicit message	Distribution service in a networked system with limited resources

DHM: digital hormone model; CMH: computational model of hormones; RMH: regulation model of hormones; AHoS: artificial hormone system

numerous molecules, and have probed into cooperative relations among the immune, endocrine, and nervous systems (Besedovsky and Sorkin, 1977; Besedovsky et al., 1985; Weigent and Blalock, 1987; 1995; Savino and Dardenne, 1995; Wilder, 1995; Besedovsky and Del Rey, 1996). Based on mutual functioning and regulating mechanisms of bioactive molecules such as various neurotransmitters, neuropeptides, hormones, and cytokines, nerve-endocrine-immunity network theory proposed by Besedovsky et al. has the most profound effects. More details can be seen in Besedovsky and Del Rey (1996).

The findings of these studies not only help us to understand the diversity and mystery of nature, but also have laid solid biological foundations for current research on intelligent information processing. According to Neal and Timmis (2003; 2005) and Timmis et al. (2009), organism equilibrium is an outcome of interactions among the immune, endocrine, and nervous systems. Engineering and technical scientists were the first to elaborate mutual integration and functioning of ANN, AIS, and AES, and then put forward the concepts of artificial homeostatic systems (AHS), as shown in Fig. 2. AHS is composed of four parts: ANN, AIS, AES, and external system boundary. The ANN, connected with external sensors and actuators, is aimed to receive stimulation information from external surroundings. After processing with the intelligence computation method, the corresponding actuators are controlled to make correct responses. Resorting to the theory of antigen-antibody recognition, AIS can eliminate redundant or deleterious neurons, and stimulate reproduction and growth of useful neurons. Although AES cannot directly affect external behaviors or specific manifestation, the hormone concentration has a direct effect upon the functioning of B and T cells in the system, and can effectively adjust the characteristics of the system over a long period of time. External system boundary supplies an interface to external surroundings, so that external surroundings can receive information through the perception channel. However, self-adaptivity is not introduced into AHS. Therefore, once training in AHS is completed, the system cannot obtain new knowledge by itself, and it is difficult to make appropriate responses automatically to a new environment.



**Fig. 2 Overall system view of the artificial homeostatic system (AHS)**

AHS is composed of four parts: artificial neural network (ANN), artificial immunity system (AIS), artificial endocrine system (AES), and external system boundary

Neal and Timmis (2003; 2005) and Timmis et al. (2009) focused mainly on the theoretical framework and scientific strength of AHS. Vargas and Moioli applied Neal's theory into homeostatic control conflict behaviors of autonomous robots, and proposed an abstracted evolutionary artificial homeostatic system (EAHS) (Vargas et al., 2005; Moioli et al., 2008a; 2008b; 2009), which consists of one AES, three independent NSGasNets, and two sorts of hormonal sensors. In this model, AES is further divided into three parts: hormone level (HL), hormone producing controller (HPC), and endocrine glands (G). HL is responsible for recording hormone concentration within an organization; HPC controls the production of hormones by altering internal and external environments; and G receives signals from HPC, and, when necessary, produces hormones. Recently, a novel model, named EAHS-R (Vargas et al., 2009), which is derived from EAHS, but incorporates a hormone receptor, has been investigated. This hormone receptor proves vital for controlling the network's response to the signals promoted by the presence of the artificial hormone. The designed system is stochastically adaptable to violent fluctuation and unplanned disruptions in environments by making full use of its in-built homeostatic mechanisms. Recently, extracting useful homeostatic system principles, Laketic et al. (2009) presented a solution for adaptive man-made systems in dynamic and harsh environments such as space and deep sea exploration.

By referring to the control theory of biological systems, a multi-agent system was designed by

Huang *et al.* (2004), made up of genetic, neural, and endocrine control subsystems. After receiving internal and external information from the cerebral nervous system, an emotion learning model was applied to generate emotion factors, which, in turn, were applied to regulate memory and behavior decisions of the cerebral nervous system. Finally, the memory and behavior model of the cerebral nervous system was successfully inherited by the genetic system. This algorithm can effectively avoid intricate self-learning of the cerebral nervous system, and, meanwhile, can guarantee high capacity of self-organization and self-adaptation for behavior decisions of the system.

Chen and Zhao (2007) and Chen and Zou (2009) attempted to bring endocrine regulating mechanisms into particle swarm optimization. They took into overall consideration the cognitive property, social property, and affective property of particles in the renewal process of particle position, and then updated all hormones of the new particle swarm. We believe that this has opened up a new approach to combining AES and other natural computation methods.

## 4 Application of artificial endocrine systems

### 4.1 Robots

Perhaps the most extensive application of AES so far is in the robotics field. Researchers and engineers in Polymorphic Robotic Laboratory at the University of Southern California have conducted research in self-reconfigurable, autonomous, and adaptive robots, which adopted a hormone-inspired methodology. In general, these robots were assembled by numerous autonomous and mutually connected modules. The challenging task faced by most of these systems is that all positioning, prediction, and decision-making are done under the same decentralized circumstance, and the surrounding environment is altered all the time. What is more, we assume each single module to be simple to minimize the cost/complexity, so as to manufacture them in a large scale. Consequently, communications and control among multiple modules with limited resources become extremely complicated (Castano *et al.*, 2000; 2002; Yim *et al.*, 2007). Shen *et al.* (2000a; 2000b; 2002c), Salemi *et al.* (2001), and Krivokon *et al.* (2005) put forward a decentralized control mechanism based on

biological hormones. The key idea is to regard the hormone as a signal to trigger different modules and different behaviors which, in turn, once triggered, have their modules execute these behaviors in isolation. The authors hold the view that there are a variety of hormones in an organism which do not interfere with each other, but have an effect on particular receptors and cells, and can be disseminated in the entire network. Moreover, a self-reconfigurable system can be seen as a network. Each node (autonomous robot) in the network is equipped with an independent energy, flow, accelerator, sensor, and connector; the nodes contact and communicate with each other through hormone information. Hou and Shen (2006a; 2006b) proposed a general mathematical model for a self-reconfigurable robot system, based on hormone controlling. At the global level, the idea of virtual disconnection was developed to prevent information from being repeatedly disseminated in the circuit, and then into the communications protocol; at the module level, they provided an algorithm to construct the discrete state-space model to depict each module's internal state, input-output hormone transformation, and its action selection. Thus, as an example of the linear combination hormone-controlling idea and modern cybernetics, the new approach equips self-reconstruction robots with better characteristics, such as predictability and stability.

In the last few years, autonomous robots have become an important focus in robotics. Mendao (2007) used hormone signals to coordinate an individual autonomous robot to complete several tasks at one time. Each task was considered as a gland, which can release the hormone into a hormone pool with a fixed speed. Once the hormone quantity in the hormone pool was larger than a threshold, they were released as free hormones and disseminated everywhere in the whole network. Free hormones with maximum concentration motivate the behavior-controlling module to execute a corresponding task, during which the gland stops releasing hormones. Walker and Wilson (2007; 2008) expanded this scheme to the task assignment system for multiple autonomous robots. Without a central control strategy, each task was assigned dynamically to an autonomous robot with low complexity, and every robot can choose an appropriate response automatically to sustained changes of all robots and the external environment. Currently,

executed tasks are broadcasted among all robots. That is to say, when a robot receives the information, it prevents itself from releasing relevant hormones, and the hormone quantity in a hormone reservoir falls accordingly. However, this system may over-react to minor environmental changes and parameter adjustment. As a result, it may directly affect the overall system performance.

To solve emotion communication problems between humans and robots, an internal secretion system model was established by Sugano and Ogata to simulate the emotional state of human beings, and applied to WAMOEB-1R (Sugano and Ogata, 1996) and WAMOEB-2 (Ogata and Sugano, 1999). Based on emotional reaction mechanisms in BES, Huang (2003) modeled physiological and psychological activities of an organism in a dynamic environment at a bottom level, and then put forward the self-adaptive agent model. One of the prominent challenges in mobile robotics is to develop control methodologies that allow the adaptation to dynamic and unforeseen environments. The artificial homeostatic hormone system (AHHS), which allows the evolution of controllers with high evolving ability, was developed as a representation of robot controllers (Stradner *et al.*, 2009). Complex behaviors are performed by the controlled automata as they pursue homeostatic control of internal (virtual) hormone values, which are disturbed by external sensory stimuli. Recently, Liang *et al.* (2010) did similar work and used fuzzy logic to capture the inherent imprecision and uncertainties of emotions in the computation of new emotion intensity.

#### 4.2 Intelligent control system

With more and more intelligent controllers and algorithms, biological intelligent control has evolved into an important branch of modern cybernetics. Based on the principle of hormone regulation of neuroendocrine systems and a regulating loop model of hypothalamus-pituitary-epinephrine, a novel nonlinear intelligent controller was designed by Liu *et al.* with two levels of control system structure (Liu *et al.*, 2005b; 2006a; 2008; Liu and Ding, 2006). The master controller can dynamically regulate the control parameters of the secondary controller based on real-time control errors and the law of hormone secretion. In addition, according to the bidirectional

regulation principle of growth hormone, a complete decoupling controller and its decoupling algorithm have been presented (Liu *et al.*, 2005a; 2006b; Liu, 2006). This kind of decoupling controller is composed of two or more control cells, which control, communicate, and exchange the control information mutually. By this means, controllers dominate all actuators cooperatively to diminish or eliminate coupling between different loops. Based on the regulation mechanisms of the neuroendocrine-immune system, Liu *et al.* (2009) presented a bio-distributed network control system with several features, i.e., entirety harmony, bi-regulation, complicated feedback, no-delay field control, and remote network optimization.

Recently, a software model of the multiprocessors communication system was presented by Greensted and Tyrrell (2003; 2004; 2005). Communication among processors is similar to the endocrine system, which, through simulation of the feedback mechanisms dominated by hormone concentration, can control data cells and information packets of multiprocessor systems. This software model has been applied perfectly in terms of structure change, self-organization, self-adaptation to the environment, robustness, and fault-tolerance. Zhang *et al.* (2009) and Dong *et al.* (2010) presented a hormone based tracking and cluster selection strategy in wireless sensor networks, inspired from the communication mechanisms of the bio-endocrine system. With the help of different hormone messages, sensor nodes can choose to be asleep/awake or head/member nodes in order to achieve better tracking or clustering results with less energy consumption.

#### 4.3 Military use

It is a typical issue for multiple unmanned aerial vehicles (UAVs) to coordinate searches and mask potentially unknown targets in a wide operation area. Peng *et al.* (2008) combined DHM with the recent extended search map method to present a more effective method for multiple UAVs search. A single UAV can make local path decisions, and finally coordinate the search behavior with neighboring UAVs via digital hormones messages. As a result, multiple UAVs can search and locate potentially multiple targets without a central command or sophisticated control strategy.

With the rapid expansion of the scope and complexity of the Internet, modern warfare has been strengthened in terms of its explosiveness, randomness, globality, and quick decision capability. There is a severe challenge in terms of the survival and management of the network. Enlightened by biological concepts and principles such as glucose homeostasis, hormone information, chemotaxis, and the reaction-diffusion model, an automatic network management framework has been put forward by Balasubramaniam *et al.* (2007), offering the program of mutual combination of the system/network level and decentralized instrumentation level, which has an obvious effect on the rapid recovery of a route in an unexpected damaged circuit. Hormone-inspired node-detection mechanisms proposed by Zhang *et al.* (2007) also have reference value for military training under a virtual circumstance.

## 5 Further work

As a brand-new natural computation method and emerging field, there is a huge development potential for AES in the next decades. However, it is beyond question that the research on AES is still at a stage of disciplinary division, whereas interdisciplinary and disciplinary integrations in its true sense are still far from enough.

First of all, gaining from the latest theory achievements of BES, we will jump from theory discovery in the biological system to engineer applications in the near future. On the one hand, most studies on BES have been concentrated on model construction from a physiological and medical perspective, and have, in concert with various physiological experiment data, analyzed and interpreted important physiological phenomena of the endocrine system. However, this is insufficient and there has not been any recognized or unified endocrine system model for reference; thus, there is a need for further study on internal reaction and function (Danziger and Elmergreen, 1957; Li *et al.*, 1995; Liu *et al.*, 1999; Farhy *et al.*, 2001; Keenan *et al.*, 2001; Farhy, 2004; Kyrylov *et al.*, 2005). On the other hand, engineering researchers have not comprehensive and thorough understanding of BES. Many features of the endocrine system are applied merely in a metaphorical

form, but not actually realized within AES.

From the perspective of artificial intelligence, the priority problems of scientific research are whether BES is applicable to the field of artificial intelligence, and which properties and characteristics of the endocrine system are suitable or not suitable for resolving practical projects or scientific issues, and what kinds of endocrine mechanisms or theories will be applied in the future. As we all know, there exist complicated hormone regulation mechanisms within a BES, and it is a fundamental task to choose some beneficial features for artificial intelligence. However, it requires a long period and close cooperation among different disciplines, which, in turn, becomes the primary limitation on the development of AES. Therefore, it is necessary to extend from the traditional framework of hormone regulation and control, and to excavate information processing mechanisms for BES in a broader scope.

Second, we know from experience that interdisciplinary cooperation may improve current theoretical models, and present more efficient computation methods. At the very beginning, AES research has needed the mutual integration and promotion among different disciplines and scopes. Hence, in addition to endocrinology medicine knowledge, we should also resort to theories, methodologies, and technologies of relevant fields, especially engineering kingdoms, to improve existing achievements and enhance computation efficiency. (1) Modern medicine has shown that organism balance in the mammal, i.e., the ability to achieve a stable condition in a dynamic environment, requires mutual coordinate of numerous cells, organs, and tissues, especially in the nerve-endocrine-immunity system. So far, most studies on AES focus on theory, and even simplified models have provided only preliminary experimental results (Neal and Timmis, 2003; 2005; Timmis *et al.*, 2009). Through intensive studies on the three systems and their relationships, we may have the chance to completely understand how internal organisms attain an equilibrium state. According to the principle of dynamic organism equilibrium in the mammal (Besedovsky and Sorkin, 1977; Besedovsky *et al.*, 1985; Weigent and Blalock, 1987; 1995; Savino and Dardenne, 1995; Wilder, 1995; Besedovsky and Del Rey, 1996), we may present more novel and efficient artificial intelligence technology for engineering applications

(Timmis, 2007). (2) Cooperation with experts from relevant fields is also a shortcut to flexible and high-efficiency computation methods, and to some complex practical problems (Yao and Xu, 2006). The key is how to integrate knowledge in these fields into AES. (3) It is important to evaluate and compare the system performances of AES and other natural computation methods. Until now, there have not been any comparative experiments on AES and traditional computation methods or mature natural computation methods, let alone overall and efficient evaluation indicators and standard test issues for performance evaluation.

Third, one must maintain the balance between theoretical analysis and practical application. At present, most researchers lay particular stress on practical application, and most achievements are concentrated on simple metaphorical abstraction and direct application, and tend to ignore further study on the theoretical model and functioning mechanisms of AES. Further, we can say that fundamental theoretical research is the weakest aspect of these models. Therefore, we should strengthen theoretical analysis in AES, and work out an appropriate mathematical explanation for existing AES models. Only is the systematic and efficient theoretical analysis in terms of system stability, astringency, complexity, the emergent property (Ding *et al.*, 2007), vulnerability, and robustness established, will it be possible to construct a clear-cut theoretical framework. Guo (2009) and Zheng (2009) are elementary and profitable in the theoretical analysis of AES, and we are looking forward to more in-depth and valuable results. Numerical simulation or practical application has similar importance to AES. According to Fogel (2005), under normal circumstances, theoretical analysis can offer more information and knowledge than examples, and likewise, experimental verification is also persuasive. On some occasions, experimental results may derive theoretical sources, and deepen the understanding of some issues. Therefore, it is believed that theoretical analysis and practical application are two fundamental approaches and methodologies for a comprehensive grasp of the characteristics of AES. It is also totally necessary to make AES practical by means of appropriate numerical experiments and engineering applications.

Finally, developing new engineering applications for AES is a valuable and interesting task. At present, its most applications focus on traditional fields such as robots, intelligence control systems, and military systems. We can predict that combinatorial optimization, network security, and autonomic computation are optimal application directions. Possibly even endocrine computers based on the computation mechanisms of BES can be developed, just as in the case of DNA computers that have thoroughly broken through the limitations and constraints of von Neumann's computer structure. As a matter of fact, AES is not merely an intelligent controller; it should be seamlessly integrated into reality to process sustaining changes in internal and external environments.

In a word, it is the central focus and general direction of AES theory and application to analyze and extract its information processing mechanisms inspired from BES in the mammal, by adopting routine techniques with the integration of theoretical exploration and practical verification, to construct endocrine regulation mechanism-inspired AES models, and generate fresh artificial intelligence theory and technology to pursue for the resolution of many complex issues in reality.

## 6 Conclusions

Through review of the latest achievements in AES, we demonstrate that this is a dynamic open system constituted by a number of cells with different structures, properties, and functions, interacting effectively with the external environment in terms of information and energy, based on which the system can complete optimization and evolution in isolation. The so-called 'dynamic' not only refers to the steady state of the system viewed from the outside, and the fact that all components are still in a state of successive changes, but contains the concept of a time cycle—It is within a definite lifecycle in which various cells work, and there exists a life process of birth, growth, withering, and disappearance. According to our conceptualization, based upon environmental discretization, relying on cell intelligentization, connected by hormone information, and directed by target cells, AES can finally adapt to the continuous

volatility of the external environment and maintain the relevant stability of the internal dynamics of the system.

In this paper, theories and models of AES and its combination with other computation methods and relevant application fields are introduced. It is hoped that, through reading this paper, experts and scholars from different disciplines who are concerned about AES research can not only understand research progress in this field, but absorb inspiration from other fields to push forward their research. In this way, new momentum can be poured into AES in the process of sustaining debate and instructive speculation, which may initiate a new research stage.

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## JZUS (A/B/C) latest trends and developments

- In 2010, we opened a few active columns on the website <http://www.zju.edu.cn/jzus>
  - Top 10 cited papers in parts A, B, C
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  - Top 10 DOIs monthly
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- As mentioned in correspondence published in *Nature* Vol. 467: p.167; p.789; 2010, respectively:
 

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The publication, designated as a key academic journal by the National Natural Science Foundation of China, was the first in China to sign up for CrossRef's plagiarism screening service CrossCheck.
- *JZUS (A/B/C)* have developed rapidly in specialized scientific and technological areas.
  - *JZUS-A (Applied Physics & Engineering)* split from *JZUS* and launched in 2005, indexed by SCI-E, Ei, INSPEC, JST, etc. (>20 databases)
  - *JZUS-B (Biomedicine & Biotechnology)* split from *JZUS* and launched in 2005, indexed by SCI-E, MEDLINE, PMC, JST, BIOSIS, etc. (>20)
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