Chapter 20

A NeuroCognitive Approach to Decision Making for the Reconstruction of the Metabolic Insulin Profile of a Healthy Person

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Abstract. Human decision-making is defined as a cognitive process in which a preferred option or a course of action is chosen from among a set of alternatives, based on certain information or considerations. One important facet of decision-making is to facilitate an appropriate response to a dynamic and uncertain environment. Dynamic decision-making is inherently complex, and it is characterized by multiple, interdependent, and real-time decisions, which occur in an environment that may change independently as a function of a sequence of actions. In order to acquire a certain degree of proficiency in such a decision making process, the decision makers often have to be subjected to a lengthy practice. This subsequently implies that decision-making in a dynamic environment is based on experience, and further reinforces the notion of dynamic decision making as a cognitive skill that can be developed through practice. As with the acquisition of other cognitive skills, decision makers improve their decision-making skills through the accumulation, recognition and refinement of encountered decision episodes. Pivotal to the development of cognitive skills including dynamic decision-making are the abilities to acquire new knowledge (learning) and to retain such knowledge for future references (memory). The human procedural memory system is a facet of the brain's computational fabric that exhibits the capacity for learning and memory, and constitutes a vast array of meticulously calibrated knowledge bases for coordinated behaviors and skills that are manifested in everyday life. This chapter describes the use of a brain inspired, cerebellar-based learning memory model named PSECMAC to functionally model the process of autonomous

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decision-making in a dynamic, complex and uncertain environment. The PSECMAC network is primarily modeled after the cerebellar learning mechanism in which repeated trainings induce a greater fidelity and precision in the knowledge acquired. PSECMAC employs an experience-driven adaptive quantization scheme to construct its computing structure by allocating more memory cells to significant regions of the input stimuli feature space. The validity of this neurocognitive approach to decision making is subsequently evaluated by employing the PSECMAC learning memory model to dynamically model the autonomous decision making process of insulin regulation in the physiological control of the human glucose metabolic process. The objective of the study is to approximate the metabolic insulin dynamics of a healthy subject in response to food intakes. In this case, the physiological regulation of insulin can be perceived as a biological example of a dynamic decision making process in which the human body dynamically determines the amount of insulin necessary to maintain bodily homeostasis in response to food disturbances. The preliminary experimental results are encouraging.

Keywords: autonomous decision making, human cerebellum, procedural memory, PSECMAC, diabetes, insulin dynamics.

1 Introduction

Human decision making is defined as a cognitive process in which a preferred option or a course of actions is chosen from among a set of alternatives, based on certain information or considerations [1]. It forms a vital and integral component of our everyday life, and common examples range from trivial decisions such as what to eat or where to shop, to more elaborate decisions, such as deciding on the next most advantageous move in a chess play or thinking of how to exploit new business opportunities. The human decision making process involves the gathering and processing of current available choices of alternatives; integrating them with their expected outcomes based on the recall from previous encounters, as well as subsequent choice evaluation with respect to the intended goals [2,3]. Decision making is ubiquitous in everyday life and it is reflected through our behavioral responses. Since each of us behave differently and is varied in our responses to the myriad choices, it is therefore of great interest to study the cognitive mechanisms and faculties underlying the human decision making process, so as to identify the affective and differentiating factors behind the difference in performance of each decision maker.

An important facet of decision making is to facilitate an appropriate response to a dynamic and uncertain environment. Dynamic decision making is characterized by multiple, interdependent, and real-time decisions, which occur in an environment that changes independently as a function of a sequence of actions [4, 5]. Such a decision making process is dynamically complex, as it involves both time delays and decisions that can positively or negatively influence one another in complicated ways. In order to establish a certain degree of logical and reasonable causal and temporal relationships of decisions and outcomes under these dynamic circumstances, the decision makers often have to be subjected to a lengthy

practice [6]. This subsequently implies that decision making in a dynamic environment is based on experience, and further reinforces the notion of dynamic decision making as a cognitive skill that can be acquired through practice. Indeed, a recent research to understand how decision-making skills are developed in dynamic situations has revealed that, over the time, there is an increase in the usage of the accumulated prior knowledge and past experiences by the decision makers to facilitate their thinking process [7].

Cognitive skill, on the other hand, is defined as the ability to use one's knowledge effectively and readily in the execution of cognitive processes [8]. With reference to cognitive skill acquisition, learning from examples has been established as the primary cause driving the gradual transition from a novice's slow and laborious performance to an expert's rapid and accurate execution of a skilled behavior [9]. It is widely believed that any skill development process requires the individual to progress through a series of learning stages and involves some form of memory for the retention of the acquired knowledge [8–10]. Based on the well-established Fitts and Posner's three stage model of skill acquisition [11, 12], learning is hypothesized to proceed through three consecutive phases of development: the *cognitive* phase, the *associative* phase, and the *autonomous* phase. In this model, it is contemplated that the critical component of skill learning lies in the individual's ability to differentiate and to filter a subset of stimuli that is important for the performance of the skilled behavior.

Learning commences with the cognitive phase, in which the learner consciously attempts to form a general understanding of the task undertaken, and a set of information pertaining to the task is accumulated and retained in memory. This stored information forms the basic building block of the knowledge base to be acquired from the learning process. In this phase, the mental processing of information is slow and tedious, and it requires a lot of cognitive resources. In the associative phase, the individual learns to respond more efficiently by retaining effective actions and eliminating the ineffective ones. Experience and repeated exposures to the learning episodes serve to amplify the salient features of the skill, and as performance is repeated, the subject learns new patterns of responding by recognizing cues and stimuli that are more significant than others, thereby directing attention towards those cues. These patterns of associations form the knowledge base for the attention-direction of the learner. As the learner becomes competent at the task, the discrimination of exogenous stimuli and cues are performed more rapidly and involves a lesser degree of consciousness. The autonomous phase refers to the stage during which this discrimination process is performed subconsciously, allowing an expert of a task to very rapidly discriminate the many stimuli and to focus on the highly specific cues. An expert's profound knowledge, accumulated through repeated practice, allows for a recognition of interrelationships among problem elements that is simply not available to novices [9].

As with the acquisition of other cognitive skills, decision makers improve their decision making skills through the accumulation, recognition and refinement of encountered decision episodes [7, 8]. Such skills developed primarily through the recognition of salient features and an increased familiarity to each of the past episodes. The knowledge of previous decision episodes becomes the primary

differentiating factor between a novice and the expert decision makers. Novice decision makers follow decision-heuristics more closely, resulting in lower efficiency due to the exhaustive search for familiar features in their memories. Skilled decision makers, on the other hand, exploit their accumulated prior knowledge to conduct a very selective, attention and episodic-triggered guided search to achieve great computational efficiency. Dynamic decision making is a skill that develops via the learning and acquisition of domain-specific knowledge, and that the underlying mechanism of this knowledge-acquisition process involves the accumulation and retrieval of decision instances [7, 13–15]. Hence, the development of the human decision making process requires the ability to acquire new knowledge (learning) and to store such information for future use (memory). Learning and memory are cognitive faculties sub-served by the massive connectivity of the brain circuitry.

The human brain is undoubtedly still by far the most powerful computing machine available today, in which complex networks of neurons collaborated in a highly non-linear manner to create a massive information computing structure. As part of the efforts to understand the human decision making process, neurocognitive science is employed to study the underlying mechanisms of cognitive skill acquisition. That is, learning and memory. The primary objective is to study and develop functional models of the brain systems that exhibit the ability to learn and acquire knowledge from exogenous inputs and the capacity to store the acquired knowledge for subsequent usage. This subsequently leads to the construction of computational models of learning memory systems, which aim to provide a functional description of the mechanisms and processes involved in learning and memory formation. Such functional models, however, do not attempt to depict every physiological detail of the corresponding memory systems in the brain. Instead, they sought to emulate the higher level cognitive faculties responsible for learning and memory. Although it would be interesting to build more physiologically realistic models, this is clearly not possible given the limited knowledge one has of the inner workings of the human brain today.

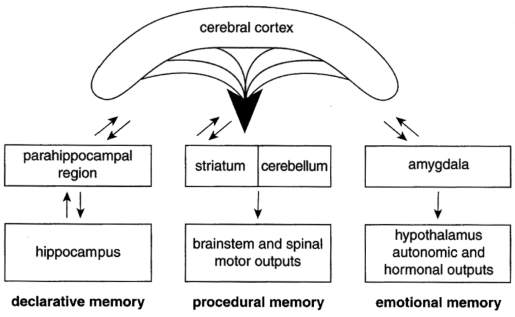


Fig. 1. Anatomically inspired framework of major human memory systems. Adapted from [16].

Neurophysiological studies on human and animal memory have established the existence of multiple brain systems responsible for memory formation, namely *declarative* (explicit), *procedural* (implicit) and *emotional* memories [16]. Anatomically, each of these memory processing tracts is different, and mediated by distinct functional systems in the brain (see Figure 1). Each of these information pathways is responsible for perceptual, motor, or cognitive processing respectively, and caters to memories of the same domain. Of particular interest to the study of decision making at the autonomous level is the procedural memory system, which consists of the striatum and the cerebellum [16]. The putative involvement of this information processing pathway in the acquisition of specific behavioral responses has led many researchers to consider this system as specialized for habit or skill memory [17]. The procedural memory pathway constitutes an endless array of meticulously calibrated knowledge bases for coordinated behaviors of habits and skills that are manifested in everyday life. There are two main characteristics of the procedural memory system. Firstly, knowledge retrieval from the procedural memory is performed unconsciously. Secondly, the procedural memory system is continuously being updated by experience and adapted by repeated exposures to learning episodes. These characteristics underlie the procedural memory system's capability to acquire a wide repertoire of habits and skills, resulting in the subsequent capacity of the individual to display a broad variety of stereotyped and unconscious behavioral manifestations.

This chapter proposes the use of a brain-inspired cerebellar-based learning memory model named Pseudo Self-Evolving Cerebellar Model Articulation Controller (PSECMAC) to functionally model the process of autonomous dynamic decision making. Drawing inspirations from the neurophysiological understandings of the human cerebellum, PSECMAC performs as a computational model of its biological counterpart and is useful for learning and knowledge acquisition in a dynamic, complex and ill-defined environment. In this chapter, the PSECMAC network is employed to model the insulin profile of the human glucose metabolic process when perturbed by food intakes. The human body has a well-regulated capacity to autonomously maintain the homeostasis of numerous biological and physiological processes without voluntary and conscious supervision. The regulation of the glucose metabolic process through the corresponding meticulous control of insulin is one of such processes. That is, the human body's natural insulin-glucose regulatory mechanism represents a meticulously and finely calibrated autonomic decision making process for a dynamic environment that is the glucose metabolic cycle. This provides reinforcing support to the notion that PSECMAC can be employed to model the inherent knowledge driving the autonomic decisions of the body's natural mechanisms in efficiently dispensing the appropriate amount of insulin to regulate the blood glucose level within tight physiological bounds. This constitutes the primary key component in the successful management of Type I diabetes, where PSECMAC can be employed to replicate the insulin profile responsible for maintaining long-term near-normoglycemia state of a diabetic patient. That is, in the effort towards developing an ideal treatment regime for Type I diabetic patients, the ability to compute appropriate decisions on the amount of insulin to dispense in response to the perturbations of the glucose

metabolic process by exogenous disturbances due to food ingestion is an initial but significant step.

The rest of this chapter is organized as follows. Section 2 briefly describes the neurophysiological aspects of memory and learning in the cerebellum that inspires the development of the PSECMAC learning memory model. Section 3 outlines the architecture of the proposed PSECMAC network and highlights the cerebellar-inspired memory formation and the experience-driven learning mechanisms of the network. Section 4 presents an overview of diabetes and the current treatment protocols available, as well as motivates the physiological regulation of insulin in the human glucose metabolism process as a biological example of autonomous decision making. Section 5 demonstrates the dynamic modeling capability of the proposed PSECMAC network by using it to model the blood insulin profile of a healthy subject. Section 6 concludes this chapter.

2 Cerebellum and the Human Procedural Memory System

The most profound and fascinating aspects of the human intelligence are the capacity for learning and memory. *Learning* is defined as a process that results in a consistent change in behavioral responses (due to the learned knowledge) through repeated exposure to the environmental stimuli [9] and *memory* is the storage of this acquired knowledge [18]. The human procedural memory system is a facet of the brain's information computing capacity, which represents a learning memory system for skills and procedures. Due to the nature of sub-conscious recall from this particular memory pathway, the procedural memory system is also often referred to as the "implicit knowledge" memory [19].

The human procedural memory system consists of the cerebellum and the striatum [16]. Due to its structural neuronal organization and anatomic simplicity, the cerebellum is perhaps one of the few constructs in the central nervous system where the patterns of intrinsic connections are known in considerable details [20]. The fact that the cerebellar cortex has the most regular anatomy of any brain region has enabled neuroscience researchers to derive a number of important neurophysiological relationships on the working mechanisms of the human cerebellum. These in turn offer a wealth of information on the functional and physiological aspects of the cerebellum. The cerebellum, which in Latin means *little brain*, is a brain region important for a number of motor and cognitive functions, including learning and memory [21, 22].

Although the cerebellum functions primarily as a movement regulator [23], there have been observations that suggested that the cerebellum also plays an active role in purely cognitive tasks [24]. Functional neuroimaging studies conducted by Desmond and his colleagues [25] have revealed traces of evidences for cerebellar involvements in the activation of the working memory, implicit and explicit learning and memory, as well as language processing. Further support for the existence of cognitive function associated with the cerebellum came from lesion studies, in which it is observed that patients with blocked posterior inferior cerebellar artery encountered difficulties in learning word association tasks [17]. In this section, the underlying anatomical and physiological properties that

facilitate and sub-serve the knowledge acquisition and information retention capabilities of the cerebellum are presented.

2.1 Mechanisms for Information Retention in the Cerebellum

The cerebellum is located at the bottom rear of the head (the hindbrain) directly above the brainstem and is highly recognizable for its structural regularity and the near-crystalline structure of its anatomical layout. However, despite its remarkably uniform anatomical structure, the cerebellum is divided into several distinct regions, each of which receives projections from different portions of the brain and spinal cord and projects to different motor systems. This feature suggests that the different regions of the cerebellum perform similar computational operations but on different inputs [17].

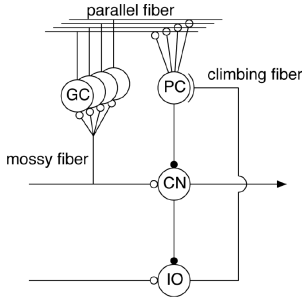


Fig. 2. A diagram of the cerebellar circuitry. GC - Granule Cell; PC - Purkinje Cell; CN - Deep Cerebellar Nuclei; IO - Inferior Olive. Adapted from [28].

In order to perform its motor regulatory functions effectively, the cerebellum is provided with extensive information about the objective (intentions), the action (motor commands) and the outcome (feedback signals) associated with a movement [26]. There are three sets of extra cerebellar afferents: the mossy fibers and the climbing fibers, both carrying sensory information from the periphery as well as sets of commands-related information from the cerebral cortex; and a set of mono-armigenic and cholinergic afferents, which is speculated to signal rewards [27]. The mossy fibers carry information originating from the spinal cord and brainstem, while the climbing fibers originate from the inferior olivary in the medulla oblongata.

The afferent inputs to the cerebellum flow into the granule cell layer, which is the input layer of the cerebellar cortex. The mossy fiber input, which carries both sensory afferent and cerebral efferent signals, is relayed by a massive number of granule cells. These granule cells work as expansion encoders of the mossy fiber input signals, combining the different mossy fiber inputs. Each of them extends an ascending axon that rises up to the molecular layer of the cerebellar cortex as parallel fiber, which in turn serves as the input to the Purkinje cells at the

cerebellar cortex. The Purkinje cells are the main computational units of the cerebellar cortex, whereby each of the cells draws input from the parallel fibers, the climbing fibers, as well as the inhibitory stellate and basket cells. The parallel fibers run perpendicularly to the flat fan-like dendritic arborization of the Purkinje cells, enabling the greatest possible number of parallel fibers and Purkinje cells contact per unit volume. The Purkinje cells perform linear combinations of the synaptic inputs, and their axons carry the outputs from the cerebellar cortex downward into the underlying white matter to the deep cerebellar nuclei. The output of the deep cerebellar nuclei forms the overall output of the cerebellum. Figure 2 depicts a diagram of the cerebellar circuitry.

Memory formation in the cerebellum is facilitated by the long term information recollection embedded in each of its synaptic connections. The cerebellum can be visualized as an associative memory system, which performs a nonlinear mapping between the mossy fiber inputs and the Purkinje cells' outputs. This mapping is depicted in Figure 3. The granule cell layer is essentially an association layer that generates a sparse and extended representation of the mossy fiber inputs. The synaptic connections between the parallel fibers and the dendrites of the Purkinje cells form an array of modifiable synaptic weights of the computing system. The Purkinje cell array subsequently forms the knowledge base of the cerebellum, and generates the output of the memory system by integrating its input synaptic connections.

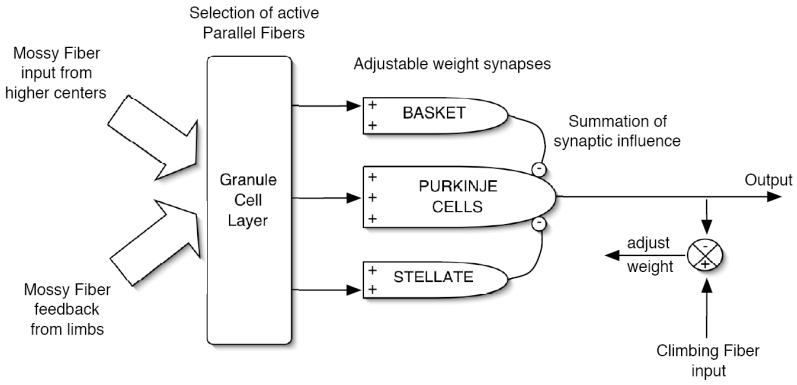


Fig. 3. Schematic Diagram of the Cerebellum. Adapted from [29].

2.2 Mechanisms of Learning in the Cerebellum

The cerebellum functions primarily as a movement regulator, and although it is not essential for motor control, it is crucial for precise, rapid and smooth coordination of movements. It achieves its role in influencing the motor system coordination by evaluating the disparities between intention and action and subsequently adjusting the operation of the motor centers to affect and regulate the particular movement currently progressing. Neuroscience has established that the cerebellum

serves its functions by performing an associative mapping from the input sensory afferent and cerebral efferent signals to the output of the cerebellum, which is subsequently transmitted back to the cerebral cortex and spinal cords through the thalamus [29–33]. This physiological process of constructing an associative pattern map constitutes the underlying neuronal mechanism of learning in the cerebellum. The fact that the cerebellum is provided with extensive information about the goals, commands and feedback signals associated with a particular movement, signifies that the cerebellum adopts an error-correction-driven supervised learning paradigm. This also implies that learning in the cerebellum requires extended trials with repeated exposures to similar sequence of movements in order to achieve a finely calibrated mapping with high fidelity to error corrections between the intended and actual execution of motor movements.

The cerebellum constitutes part of the human procedural memory system for habits and skills, which is subjected to continuous adaptation throughout the life span of an individual. In the cerebellum, the cerebellar learning mechanism is facilitated by the modifiable synaptic transmissions (cerebellar synaptic plasticity) and synaptic re-organization (cerebellar structural plasticity) of its neuronal connections.

Research into the physiology of the cerebellum have sufficiently demonstrated that the Long Term Depression (LTD) of the likelihood of the Purkinje cell firing action potentials in response to synaptic inputs from the parallel fibers by altering the chemical properties of the neuro-receptors, is the underlying cellular mechanism responsible for cerebellar learning [17,27,30,33–35]. The parallel fiber inputs to the Purkinje cells provide large vectors of sensory information, transmitting a diverse array of signals. The climbing fibers, meanwhile, function as training signals, which teach the Purkinje cells to respond to specific patterns, by adjusting the synaptic weights of their parallel fiber synapses. The climbing fibers alter cerebellar output by selectively modulating the synaptic effect of the parallel fiber inputs to the Purkinje cells through the mechanisms of LTD. The effect of the LTD can vary from minutes to hours, depending on the degree of depolarization and the quantity of calcium produced by the climbing fibers in the Purkinje cell dendrites [17].

However, clinical evidences suggest that synaptic depression may not be the sole mechanism underlying learning in the cerebellum [33]. In particular, the cellular mechanism of LTD may not be adequate for forming permanent, long term memories of motor programs. Some studies provide the evidences of Long Term Potentiation (LTP) in addition to LTD of the cerebellar synapses [36–38]. Yet other studies have shown that cerebellar learning also involves the alteration of the morphology of the cerebellar cortex. Cerebellar structural plasticity studies conducted by Greenough and his colleagues have demonstrated that complex motor skill learning actually leads to an increase in the number of synapses within the cerebellar cortex [39–42].

In such studies, rats were given acrobatic training by challenging them to acquire complex motor skills necessary to traverse a series of obstacles. It is discovered that rats with such training developed an increased density of the parallel fibers to Purkinje cells synapses per unit volume. The increased synaptic density was accomplished by increased dendritic aborization and increased dendritic spine

densities along the Purkinje cell's spiny branchlets [40]. Several conclusions can be derived from such observations: (1) that cerebellar learning leads to an enduring functional and structural adaptation of the cerebellar cortex; and (2) acquiring experiences can alter the neuronal connectionist structure of the cerebellum. Such experience-driven plasticity may constitute part of the neurobiological substrates underlying the formation of long term procedural memory at the cerebellum.

The experience-driven cerebellar structural plasticity phenomenon suggests that the cerebellum organizes its learned knowledge in an adaptive manner, where repeated training (exposures to a particular input-output mapping association tuple) yields an increase in the synaptic connections as well as finer calibrations in the neural circuitry of the Purkinje cells. This results in the biological formation of a more precise knowledge representation scheme.

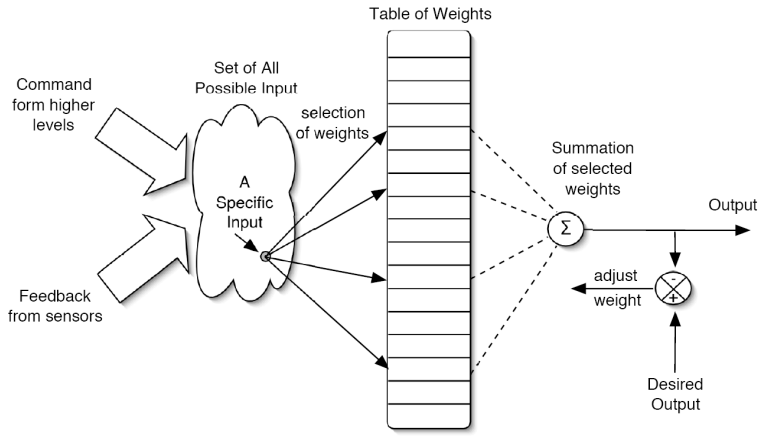


Fig. 4. Schematic Diagram of the CMAC Neural Network. Adapted from [29].

3 The PSECMAC: A Brain-Inspired Multi-resolution Cerebellar Learning Memory Model

The Cerebellar Model Arithmetic (or Articulation) Controller (CMAC) neural network is a well-established computational model of the human cerebellum [43, 44]. The schematic of the working mechanisms of the CMAC network is depicted in Figure 4. From the neurophysiological perspective, the CMAC structure is a synthetic model of the cerebellum and employs error correction signals to drive learning and knowledge acquisition to emulate the learning mechanism and function approximating capabilities of its biological counterpart. In essence, CMAC functions as a static associative memory that facilitates local generalization and epitomizes the nonlinear mapping between the mossy fiber inputs and the Purkinje cell outputs. The computing (memory) cells of the CMAC model are analogous to

the Purkinje cells in the human cerebellum and the grid-like organization of these computing cells is inspired by the anatomy of the biological interconnections of the Purkinje cells and the parallel fibers, which originate from the granule cell layer and are the signal paths for the information projecting into the cerebellum from other functional brain parts.

From an engineering point of view, CMAC is an associative memory based neural network that performs mapping of multi-dimensional input-output data tuples. The CMAC memory can be visualized as a hypercube array of storage cells. These cells are employed to store sets of weight values, which constitute the knowledge base of the CMAC network. The elements in the input vector to the CMAC network are used as indices to activate a particular set of storage cells, and the aggregation of the stored values in these activated cells forms the computed output of the CMAC model. In the CMAC network, the computing cells are organized as a multi-dimensional memory array, and the resolution (receptive field) of these cells are defined through an even quantization of the input space along each of the input dimensions. Each of the computing cells thus covers a region of similar size in the input surface.

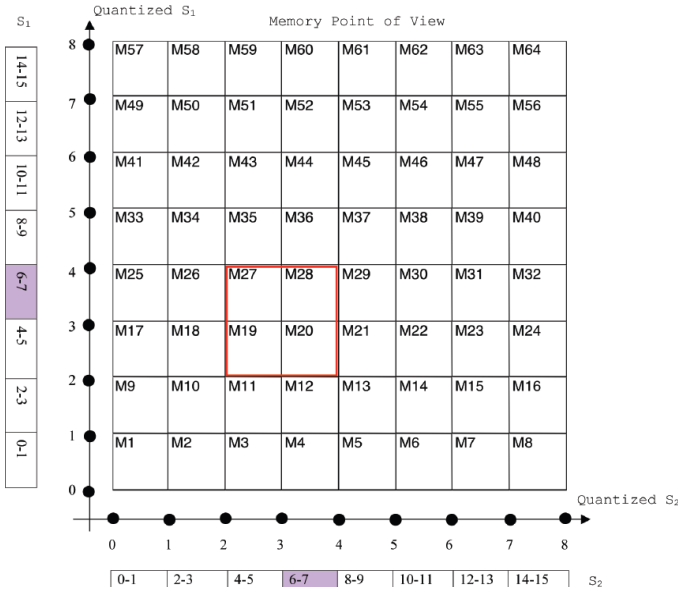


Fig. 5. An example of 2D CMAC memory cells

Figure 5 illustrates a two-dimensional input CMAC network with 64 quantized memory cells, which is employed to store the associative mapping for 256 (16 S_1 by 16 S_2) input training patterns. In this example, both input dimension is quantized into 8 segments, and each two-dimensional input vector to the CMAC

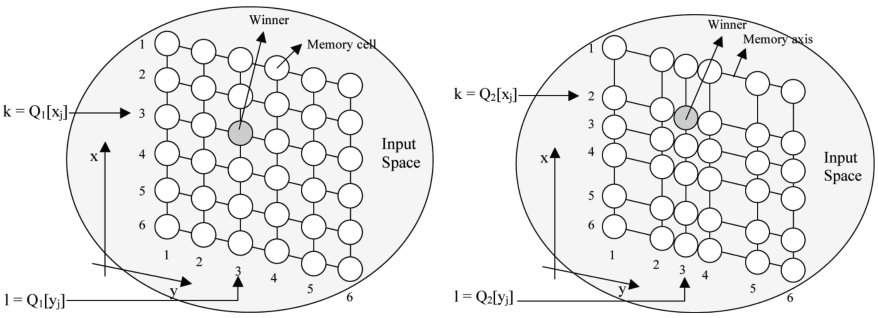
network activates a region of four neighboring memory cells. There are two immediate consequences following this rigid CMAC memory allocation scheme. Firstly, the resolution of the CMAC network output is solely dependent on the size of the network; that is, the larger the network size, the finer is the output resolution. Secondly, the resolution of the CMAC output remains constant over the entire memory surface of the CMAC network, regardless of the variability in the complexity and information content of the training data used to construct the output responses.

However, in many real-life skill acquisition episodes, behavioral proficiency is driven by the learner's sensitivity towards a selective group of salient stimuli, which constitute only a relatively small proportion of the entire set of input sensory cues. Depending on the underlying dynamics and characteristics of the skill to be learned, some regions of the stimuli feature space will contain more skill-related information than the rest. Furthermore, with repeated exposures to the learning phenomena, an effective skill-acquisition mechanism is expected to develop a higher fidelity towards frequently encountered sequences. Thus, by drawing inspirations from the notion of experience-driven cerebellar structural plasticity, as well as the honing effects of repeated training to the development of cognitive skills, a cerebellum-inspired computational-model is proposed to synthesize dynamic decision making in complex and ill-defined problems. The proposed architecture, named Pseudo Self-Evolving CMAC (PSECMAC), employs an adaptive resolution scheme for knowledge representation via a variable quantization of the input training vectors. The proposed PSECMAC network enhances the knowledge-acquisition capability of the basic CMAC by utilizing an experience-driven memory management scheme, which subsequently produces a finer output resolution in the significant regions of the stimuli feature space.

3.1 PSECMAC Network Architecture

Neurophysiological studies have established that the precise wiring of the adult human brain is not fully developed at birth [17]. Instead, there are two overlapping stages in the development of the human's central nervous system. The first stage of this process encompasses the formation of the basic architecture of the nervous system, in which coarse connection pattern emerges as a result of the genesis of the brain cells during prenatal development. Subsequently, in the second stage, the initial architecture is refined and extraneous synaptic connections are pruned throughout an individual's life-span by repeated exposures to various activity-dependent experiences. Such experience-driven plasticity is also observed in the cerebellum (refer to Section 2), suggesting that it may constitute as one of the neurobiological substrates underlying the formation of the human procedural memory system. The cerebellum organizes its learned knowledge through an adaptive and non-trivial mechanism, where repeated training (exposures to particular input-output association tuples) yields a higher fidelity in the associative mapping between the input stimuli and the output actuations, thus resulting in a more precise behavioral response. These observed cerebellar learning principles are dutifully incorporated into the proposed PSECMAC network in order to construct a cerebellar-based learning memory model.

Figure 6 illustrates the fundamental architectural distinction in the organization of the memory structure of the proposed PSECMAC model in comparison with the basic CMAC model. While the basic CMAC memory cell structure is evenly distributed over the entire associative mapping space, the computing cells in the PSECMAC network are selectively allocated to achieve an efficient overall feature space representation. This selective allocation scheme is facilitated via the identification of salient stimuli features that are significant for performance from the input training tuples, resulting in an adaptively granularized associative mapping function of the PSECMAC network.



(a) 2D CMAC Memory Cells (b) 2D PSECMAC Memory Cells

Fig. 6. Comparison of CMAC and PSECMAC Memory Surface for 2-inputs problem

The initial step towards the creation of an adaptive-resolution associative mapping of the PSECMAC network is to identify key areas of the stimuli feature space that contains more information pertaining to the task as compared to the rest, and subsequently assigning a finer granularity (i.e. more memory cells) to these significant regions of the feature space. Analogical to the repeated exposures of learning episodes and skill-training, these key areas correspond to the densely populated information regions in which a large amount of data points existed within close proximity. Figure 7 depicts a 2D illustration of this principle of density-based adaptive computing granularity in the proposed PSECMAC network.

In PSECMAC, memory assignment and adaptive quantization are performed on a per-dimension basis and consisted of several steps: (1) computing the density clusters; (2) performing memory cells allocation based on the computed density profile; and (3) determining the quantization points within each of the allocated memory cells. The Pseudo Self Evolving Cerebellar (PSEC) clustering algorithm [45] is employed to compute the centers of the density clusters in the input training space. The PSEC algorithm is a density-based clustering algorithm which

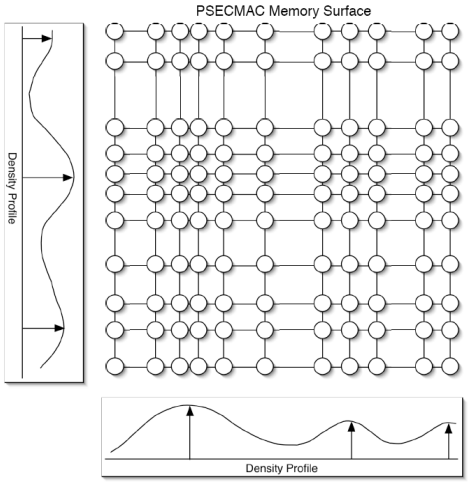


Fig. 7. An example of 2D PSECMAC Memory Surface

synergizes the merits of the incremental learning procedure of the Learning Vector Quantization (LVQ) [46] technique with the effectiveness of the density-based partitioning method of the DBSCAN algorithm [47]. PSEC is inspired by the biological development of the human's central nervous system, whereby neural cell death plays an integral part in the refinement process of the brain's neuronal organization [45].

The operations of the PSEC algorithm are performed individually for each component dimension of a given training data set. Significant data clusters supporting the inherent organization of the data set are identified by the PSEC algorithm through an analysis of the density distribution of the data points along each of the component dimensions. The PSEC algorithm is briefly outlined as follows:

Step 1 Initialize the density threshold β prior the search for the significant data clusters (structures) along an arbitrary dimension d of the data set.

Step 2 Construct a linear cerebellar structure with m regularly spaced neurons that span the input space of dimension d. This step models the first-stage development process of the human central nervous system.

Step 3 PSEC performs structural learning by executing a one-pass pseudo weight learning process to obtain a density distribution of the training data along dimension d.

Step 4 The linear cerebellar structure is evolved by identifying the surviving neurons with high tropic factors (using the density threshold β) whose pseudo weights (aggregated densities) form prominent convex density peaks in the computed density distribution of Step 3.

The remaining neurons are pruned. This is analogous to the activity-dependent refinement process of the human brain's neuronal organization and synaptic connectivity.

Step 5 The surviving neurons subsequently provide the initial weights for further refinements by the LVQ algorithm to identify the eventual positions of the centers of the density-induced data clusters along dimension d.

Figure 8 illustrates the end result of the operations of the PSEC clustering algorithm. In essence, PSEC computes a set of density-induced clusters, whose centers denote the highest density point in each of the corresponding clusters. The PSEC clustering algorithm autonomously assigns the cluster centers to the equilibrium density points such that the density of the left-sided region of a cluster center is equivalent to that of its right sided counterpart. The computed data clusters are arbitrarily-shaped, and the boundary between any two neighboring clusters is conveniently assumed to be at the bisection of the two respective cluster centers.

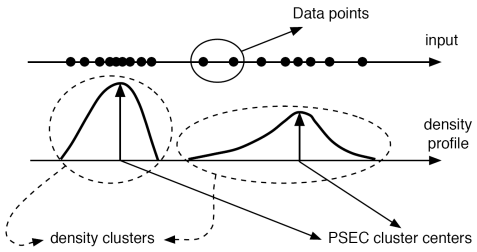


Fig. 8. A sample clustering output of the PSEC clustering technique

In the PSECMAC model, the number of memory cells allocated to each of the clusters is proportional to the normalized density of the corresponding cluster center in relation to the overall cluster densities. Let the total number of memory cells per input dimension be M, and the memory allocation process of PSECMAC is formulated as

$$M_i = \left\lfloor \frac{P_i}{\sum_{j \in S} P_j} \right\rfloor \times M \tag{1}$$

where M_i is the total number of memory cells allocated for the i^{th} cluster, M is the total number of memory cells available per input dimension, P_i denotes the density of the cluster center of the i^{th} cluster, and S refers to the set of clusters in the entire input feature's space.

In order to obtain a gradually-refined granularity for areas of the input space with high densities, a non-linear assignment scheme is introduced to the memory cell allocation process of the PSECMAC network by varying the quantization step sizes of the memory cells inside the clusters. In PSECMAC, the memory cells allocated to an arbitrary cluster is equally distributed to the left (left subregion) and right (right subregion) side of the corresponding cluster center. In each of the subregions, the quantization point of each of the memory cells is logarithmically assigned with respect to the cluster center. The result of this computation is illustrated in Figure 9, which depicts the variable quantized memory cells inside the region of an arbitrary cluster. The center of each density-induced cluster constitutes the finest granularity within the region of the cluster. Consequently, the further is an allocated memory cell from its cluster center, the coarser is the granularity of its quantization step size. The degree of non-linear progression in the granularity of the quantization step sizes of the memory cells in a cluster is governed by a parameter μ. A logarithmic quantization (commonly referred to as the μ-law quantization technique [48]) is subsequently employed to vary the distribution of the memory cells in the cluster.

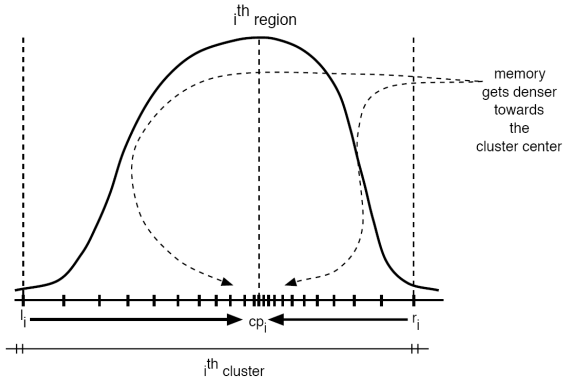


Fig. 9. Variable memory cell distribution in a cluster

Assuming that an arbitrary cluster i as depicted in Figure 9 is assigned M_i number of memory cells by the PSECMAC memory allocation process, the quantization point of the j^{th} memory cell (denoted as Q_{ij}) in the cluster is computed as:

- If $j \leq \left\lfloor M_i / 2 \right\rfloor$:

$$stepsize = \frac{cp_i - l_i}{\left\lfloor M_i / 2 \right\rfloor} \tag{2}$$

$$pt_j = l_i + (j - 0.5) \cdot stepsize \tag{3}$$

$$Q_j = cp_i - \left\lfloor \frac{(cp_i - l_i) \cdot \log\left(1 + \frac{\mu \cdot |cp_i - x|}{(cp_i - l_i)}\right)}{\log(1+\mu)} \right\rfloor \tag{4}$$

- Else if M is odd and $\left\lfloor M_i / 2 \right\rfloor < j < \left\lceil M_i / 2 \right\rceil + 1$:

$$Q_j = cp_i \tag{5}$$

- Else if $j > \left\lceil M_i / 2 \right\rceil$:

$$stepsize = \frac{r_i - cp_i}{\left\lfloor M_i / 2 \right\rfloor} \tag{6}$$

$$pt_j = cp_i + (j - \left\lfloor M_i / 2 \right\rfloor - 0.5) \cdot stepsize \tag{7}$$

$$Q_j = r_i - \left\lfloor \frac{(r_i - cp_i) \cdot \log\left(1 + \frac{\mu \cdot |x - r_i|}{(r_i - cp_i)}\right)}{\log(1+\mu)} \right\rfloor \tag{8}$$

where j is the index of an allocated memory cell in an arbitrary cluster i, cp_i is the center of cluster i, l_i and r_i denote the left and right borders of cluster i respectively, M_i is the number of memory cells allocated to cluster i, μ denotes the degree of nonlinear progression, pt_j is the pseudo quantization point of the $j^{th}\psi$memory cell in cluster i, and Q_j the resultant μ-law based PSECMAC quantization point of the j^{th} memory cell in cluster i.

The computed quantization decision points of each input dimension of the training data set subsequently form the memory axes of the PSECMAC network to define its overall computing structure. The intersections of these memory axes at the input space denote the computing cells of the proposed PSECMAC network (see Figure 7). This adaptively computed organization of the memory cells represents the eventual structure of the PSECMAC model employed to learn the characteristics of the training data set. The following subsection describes how this computing structure of the PSECMAC network is utilized as a memory store for knowledge acquisition.

3.2 PSECMAC Working Principles

The proposed PSECMAC model employs a Weighted Gaussian Neighborhood Output (WGNO) computation process, where a set of neighborhood-bounded computing cells is simultaneously activated, to derive an output response to each set of input stimulus. In this computation process, each of the neighborhood cells has a varied degree of activation that is inversely proportional to the distance from the input stimuli. The purpose of implementing this neighborhood retrieval scheme in the PSECMAC model is to minimize the effects of quantization errors on the computed output of the network. In addition, the WGNO process also introduces a topological generalization capability into the proposed PSECMAC model. Given an input stimulus $\boldsymbol{X} = [x_1, x_2, ...x_d]$ to the PSECMAC network, the computed output of the network is derived as follows:

Step 1: Determine the Region of Activation
The PSECMAC network employs a neighborhood-based output retrieval process in which the computed output of the network corresponding to an input stimulus is derived from a weighted combination of the memory values of the neighborhood cells in the vicinity of the input stimuli as observed in the multi-dimensional feature space. The size of this neighborhood is defined by a neighborhood constant *N*, which determines the relative size of the neighborhood with respect to the overall feature space. To simplify the network computations, the neighborhood boundary is defined on a per dimension basis. For an input stimulus $\boldsymbol{X}$, its activation neighborhood is defined as:

$$l_i = x_i - 0.5 \cdot N \cdot range_i \tag{9}$$

$$r_i = x_i + 0.5 \cdot N \cdot range_i \tag{10}$$

$$i \in \{1, 2, \ldots, d\} \tag{11}$$

where i is the dimension index, d is the number of input dimensions, N denotes the neighborhood constant, $range_i$ is the input range for the i^{th} dimension, and l_i and r_i are the left and right boundaries of the neighborhood in the i^{th} dimension corresponding to stimulus X. Consequently, the memory axes encapsulated inside the defined boundaries are activated, and the memory cells denoted by their intersections contribute to the set of activated PSECMAC computing cells for the input stimuli $\boldsymbol{X}$.

Step 2: Compute the Gaussian weighting function
The WGNO retrieval process of the proposed PSECMAC model is illustrated as Figure 10. The degree of contribution of each of the activated cells to the output of the PSECMAC network corresponding to the input stimuli $\boldsymbol{X}$ is inversely proportional to the distance between the quantization points of the memory cells and $\boldsymbol{X}$. A Gaussian weighting factor (g_k) is employed to attenuate the synaptic weight contributed by each of the cells in the activated neighborhood with respect to the Euclidean distances of the computing cells to the actual point of activation $\boldsymbol{X}$ in the PSECMAC memory space. The Gaussian weighting function is defined as:

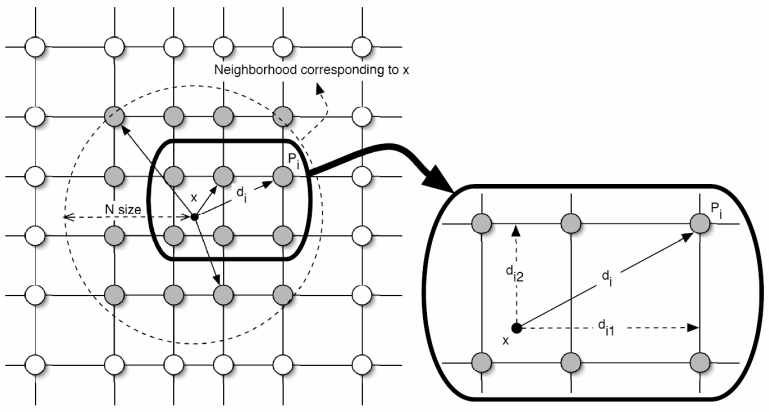


Fig. 10. An example of 2D PSECMAC Neighborhood

$$g_k = (1 - d_k)\, e^{-d_k^2 / 2\gamma^2} \tag{12}$$

where k denotes the index of an arbitrary activated cell, d_k is the Euclidean distance between the quantization point of the cell and the input stimulus $\boldsymbol{X}$, g_k is the Gaussian weighting factor for the k^{th} activated cell, and γ refers to the Gaussian width constant.

Step 3: Retrieve the PSECMAC output
The output of the proposed PSECMAC model is computed as a weighted linear combination of the memory contents of the activated cells:

$$Z_X = \frac{\sum_{k \in K} (g_k \cdot W_k)}{\sum_{k \in K} g_k} \tag{13}$$

where K denotes the set of activated neighborhood cells, W_k denotes the weight value(s) of the k^{th} activated cell, g_k is the Gaussian weighting factor for the k^{th} activated cell, and Z_X is the output of PSECMAC corresponding to the input stimulus $\boldsymbol{X}$.

3.3 PSECMAC Learning Paradigm

The proposed PSECMAC network employs a two-phase training algorithm, namely: *structural learning* and *memory learning*. The objective of the first (structural learning) phase is to construct the underlying memory structure of the PSECMAC network using the adaptive memory allocation scheme as described in Section 3.1. The second (memory learning) phase is the network training phase in which patterns of association between the input and the output of the training data tuple are incrementally mapped into the network structure. The objective of the

memory learning phase is to adaptively tune the PSECMAC network to associatively respond to the presented input stimuli with increasing accuracy. In order to emulate the neighborhood learning phenomenon observed in the human cerebellum [17, 28, 49], the proposed PSECMAC network adopts a modified form of the Widrow-Hoff learning rule [50] to implement a *Weighted Gaussian Neighborhood Update* (WGNU) process.

Under this learning scheme, PSECMAC does not only update the winning neuron to an input-output association pattern of the input stimulus. Instead, a neighborhood of cells centered at the input stimulus is activated, and the degree of learning or adaptation for each of the activated cell varies with respect to the distance between that cell and the input stimulus. Essentially, WGNU combines the Widrow-Hoff training algorithm with a Gaussian weighting function, which is defined as in Equation (12). The objective of this neighborhood update scheme is to distribute the effect of learning so as to increase the fidelity and the generalization capability of the PSECMAC network, as well as to improve the network training time. WGNU also partially epitomizes the human learning behavior, where it is observed that the learning of an associated task will enhance the subsequent learning process of a related task.

The PSECMAC memory learning process is mathematically described by the following equations:

$$Z_{X_j}^{i} = \frac{\sum_{k \in K_{X_j}} \left(g_k \cdot W_k \right)}{\sum_{k \in K_{X_j}} g_k} \tag{14}$$

$$W_{k \in K_{X_j}}^{i+1} = W_{k \in K_{X_j}}^{i} + \Delta W_{k \in K_{X_j}}^{i+1} \tag{15}$$

$$\Delta W_{k \in K_{X_j}}^{i+1} = \alpha \frac{g_{k \in K_{X_j}} \left(Z_{X_j}^{i+1} - D_{X_j} \right)}{\sum_{k \in K_{X_j}} g_k} \tag{16}$$

where I is the training iteration number, $\boldsymbol{X}_j$ denotes the j^{th} input vector (stimulus) to the network, $\boldsymbol{K}_{\boldsymbol{X}j}$ is the set of activated computing cells corresponding to the input $\boldsymbol{X}_j$, g_k is the Gaussian weighting factor of the k^{th} activated memory (computing) cell, $Z_{\boldsymbol{X}j}$ is the output of the network to the input $\boldsymbol{X}_j$, $D_{\boldsymbol{X}j}$ is the expected output of the network in response to the input $\boldsymbol{X}_j$, $\boldsymbol{W}_k$ denotes the content of the k^{th} activated memory cell, and α is the learning constant.

The PSECMAC memory learning phase commences with the computation of the network output corresponding to the input stimuli $\boldsymbol{X}_j$. A learning error is computed based on the derived PSECMAC output and the desired response to $\boldsymbol{X}_j$. This error is subsequently distributed to all the activated computing (memory) cells based on the computed Gaussian weighting functions of these cells. The respective local errors, adjusted by the learning constant, are then used to update the memory contents of each of the activated cells. In addition, a theoretical proof of WGNU update convergence has been undertaken and is reported in [51].

4 Diabetes as a Disease

Diabetes Mellitus, commonly known as diabetes, is a chronic disease where the body is unable to properly down-regulate glucose concentrations in the blood, resulting in elevated blood glucose (hyperglycemia), passage of excessive glucose-concentrated urine (osmotic diuresis) and thirst. Correspondingly, the treatment of diabetes is focused on glucose lowering therapy using oral hypoglycemic agents and insulin. Sub-optimal therapy results in persistent hyperglycemia while excessive treatment may cause hypoglycemia (reduced blood glucose).

Chronic hyperglycemia causes damage to the eyes, kidneys, nerves, heart and blood vessels [52]; and there is unequivocal evidence that intensive glucose control further reduces risk of end-organ damage compared to conventional therapy [53, 54] as well as provides a legacy effect [55]. Yet intensive glucose lowering therapy may result in severe hypoglycemia that deprives the body of energy and causes confusion resulting in loss of consciousness or death [56].

The medical profession has classified diabetes into two main subtypes based on their pathogenesis – (1) Type-1 diabetes, also known as juvenile or insulin-dependent diabetes mellitus (IDDM) occurs as a result of death or destruction of pancreatic beta-cells [57], while (2) Type 2 diabetes, also known as adult-onset or non-insulin-dependent diabetes mellitus (NIDDM), occurs as a result of reduced cellular insulin sensitivity causing initial elevated insulin levels (to compensate for reduced insulin sensitivity) followed by progressive beta-cell insufficiency and eventual relative insulin deficiency [58].

In recent years, there has been an urgency to address the treatment efficiency of diabetes, driven mainly by concerns regarding the rising social and economic cost of the disease. Due to its chronic nature, as well as the severity of complications related to the ailment, diabetes is a costly disease that exacts heavy financial burden on both patients and society. As the numbers of diabetic patients increases worldwide [59, 60], the proportion of national health care budgets allocated for diabetes treatment is further expected to balloon. A report from the American Diabetes Association [60] listed diabetes as the fifth leading cause of death in the U.S. with an annual direct and indirect medical expenditure of approximately $132 billion. This amount is projected to increase to $156 billion by 2010 and to $192 billion by 2020 for the U.S. alone.

Successful management of diabetes requires long term maintenance of near-normal glucose levels. To achieve this, all diabetics are required to maintain a disciplined dietary plan in addition to prescribed diabetic medications. The type of diabetic medication needed depends on the nature of the diabetic condition and the ability of the beta-cells to produce insulin – all type 1 diabetics will require insulin replacement; most type 2 diabetics early in the course of the illness will only require oral medications while type 2 diabetics of long standing duration will increasingly face the need for insulin therapy.

Insulin replacement therapy plays a critical role in the management of both type 1 and type 2 diabetes. The ideal insulin regimen is the physiological mimicry and recreation of non-diabetic insulin response to glucose in a diabetic patient; so as to regulate the blood glucose level within tight physiological limits

(typically 60-110 mg/dl or 4-7 mmol/l) [61]. Insulin can be administered subcutaneously, intravenously or through a trans-peritoneal route, and it can take the form of discrete insulin injections or continuous insulin delivery via an insulin pump. Extensive studies on the advantages, disadvantages and peripheral issues regarding these insulin delivery approaches have been performed and reported in the literature [62, 63].

Because of its open-looped nature, the therapeutic effect of discrete insulin injections is not ideal for the treatment of diabetes. Continuous insulin infusion through an insulin pump, on the other hand, offers a more viable approach due to its controllable infusion rate [64]. The workings of such insulin pumps are algorithmically driven, with a host of techniques proposed, investigated and reported in the literature [65,66]. Classical control methods and advanced algorithms using implicit knowledge or explicit models (empirical, fundamental, or graybox) of the diabetic patient have been studied and examined in [67–69]. These proposed methods all require some form of modeling of the glucose metabolic process of the diabetic patient before a suitable control regime can be devised. However, the use of classical modeling techniques (data fitting, compartmentalized differential / difference equations, statistical or machine learning approaches etc) [70, 71] to describe the dynamics of the impaired diabetic metabolism process generally results in a rigid regulatory system. These are unable to dynamically evolve and respond to the inter- and intra-day glucose variability [72, 73] and represent a critical limitation of classical control algorithms.

From a biological perspective, insulin serves as the principal regulatory hormone that ensures homeostasis of the human blood glucose level [74]. Much progress has been made in the last three decades to characterize the metabolic pathways that are involved in the physiological process of insulin secretion. Of all the pathways identified so far, the mechanism of glucose metabolism in triggering insulin secretion from the pancreatic β-cells has been the most extensively studied [75]. Blood glucose is the most effective physiological nutrient stimulus of insulin secretion [76]. This homeostatic function depends on the glucose uptake in the pancreatic β-cells and the subsequent signaling pathways that influence the rate of insulin secretion [77]. The pancreatic β-cells are physiologically designed to measure the level of glucose in the blood on a moment to-moment basis, in order to secrete insulin at rates that are exactly appropriate to ensure an optimal level of circulating glucose in the blood [75]. When the blood glucose level increases, insulin secretion is enhanced with a characteristic dependency. Therefore, the human body is naturally endowed with a vigorous and robust regulatory mediation to the secretion of insulin.

The central nervous system participates in maintaining energy equilibrium and an important function of the CNS is to ensure a steady supply of energy substrates. To accomplish this task, widely divergent afferent signals are integrated within the brain and transduced into signals that facilitate homeostatic adjustments of food intake and energy expenditure. The various afferent inputs that the brain employs to dynamically adjust food intake and energy metabolism can be broadly categorized into two subgroups: those that communicate information pertaining to body energy stores and signals that are generated in response to nutrient ingestion.

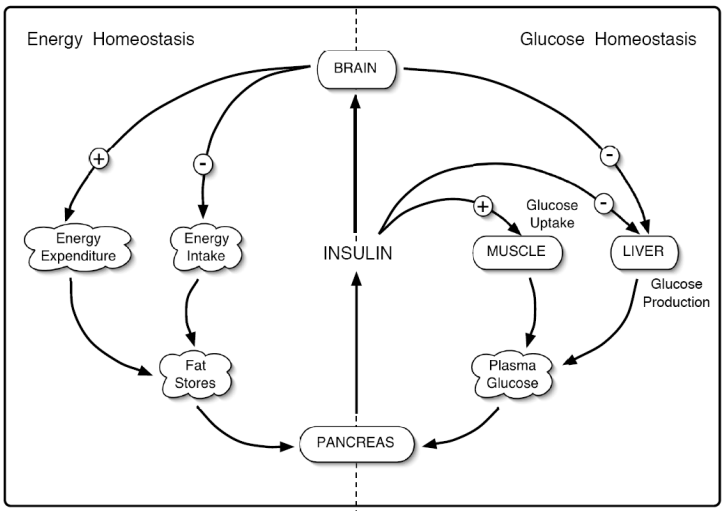


Fig. 11. Model of energy and glucose homeostasis in human. Adapted from [79].

Emerging evidence suggest that glucose metabolism throughout the body is coordinated by the brain and mediated by insulin [78]. This is supported by the finding of glucokinase receptors, the established glucose sensor of the pancreatic β-cells, in the central nervous system (CNS) [79]. There is common consensus that the liver plays a central role in the human glucose metabolism process by acting as a glucose buffer; that is, extracting glucose from the bloodstream in times of plenty and synthesizing glucose when needed by recognizing the different bodily energy states through the detection of changes in the blood insulin concentration [80]. Hitherto, insulin is known to target the liver directly. However, precise experiments have subsequently demonstrated that insulin, via its action on the hypothalamus (a sub-cortical brain structure central to the autonomic control of the human endocrine system), exerts a higher level of supervisory control on glucose production by the liver [81]. This observation suggests that insulin can in fact modulate liver glucose production through an unknown signaling pathway via the CNS [82, 83]. In addition, bio-physiological studies have established the presence of an inhibitory physiological response to food intake when the insulin hormone is directly administered to the CNS, particularly in the hypothalamus region [84, 85]. Hence, insulin appears to be required by the CNS to regulate food intake, body weight and the homeostasis of physiological processes [86]. These intertwined and complex relationships are depicted in Figure 11.

While many of the mechanisms and inter-dependent relationships between insulin, the central nervous system and the overall metabolic process remain under extensive research and has yet to be scientifically established, the facts presented above have sufficiently demonstrated that the human insulin regulatory mechanism is a complex dynamic decision process in a rapidly changing and uncertain environment, in which each of the participants influence one another in a highly

complex and nonlinear manner. The purpose of this chapter is therefore to support the use of the PSECMAC network, which is a cerebellar-inspired adaptive learning memory model, to dynamically model the insulin profile of the glucose metabolic process of a healthy person, so as to determine the insulin dynamics required to achieve homeostasis of the glucose metabolic process when perturbed by food intakes. The objective is to subsequently employ this PSECMAC-based insulin model as a reference to regulate insulin infusion by means of an insulin pump in order to achieve long-term near normoglycemia in patients with type I diabetes and those with type 2 diabetes and beta-cell deficiency, while avoiding hypoglycemia at all times.

5 Glucose Metabolisms: A Study of the Insulin Dynamics for Normoglycemia

The first step into constructing a model of the human glucose metabolic process is to determine the patient profile to be modeled. Due to the lack of real-life patient data and the logistical difficulties and ethical issues involving the collection of such data, a well-known web-based simulator known as *GlucoSim* [87] is employed to simulate a person subject to generate the blood glucose data that is needed for the construction of the patient model. The objective of the study is to apply PSECMAC, a neurophysiologically-inspired computational model of the human cerebellum, to the modeling of the glucose metabolism of a healthy subject. For this purpose, a human profile (Subject A) for the simulated healthy subject is created and outlined in Table 1.

Table 1. The profile of the simulated healthy Subject A

Attribute Name	Attribute Value
Sex	Male
Age	40 years old
Race	Asian
Weight	67 kg (147.71 lbs)
Height	1.70 m (5ft 7in)
BMI	23 (Recommended for Asian)
Lifestyle	Typical office worker with moderate physical activities such as walking briskly, leisure cycling and swimming.

The simulated healthy person, Subject A, is a typical middle-aged Asian male. His body mass index (BMI) is at 23.0, within the recommended range for Asian. Based on the person profile of Subject A, his recommended daily allowance (RDA) of carbohydrate intake from meals is computed using an applet from the website of the Health Promotion Board of Singapore [88]. According to his sex, age, weight and lifestyle, the recommended daily carbohydrate intake for subject A is approximately 346.9g per day. For the purpose of the study, a total of 100 days of glucose metabolic data for Subject A are to be collected.

GlucoSim requires 10 different inputs to be generated, which consists of the body weight, the simulation period, and both the time and carbohydrate content of each of the assumed daily four meals, namely: breakfast, lunch, afternoon snack, and dinner respectively. With the person profile of Subject A and the carbohydrate contents of his typical meals in compliance with his calculated RDA, 100 days of glucose data are to be generated from the simulator. The carbohydrate contents and the timings of the daily meals varied from day-to-day during the data collection phase. To account for the inter and intra-day variability of his eating habits and the contents of the meals he has, as well as the possible fluctuations of his body weight within the simulated period of 100 days, the computation listed in Table 2 were performed to generate 100 different sets of inputs, one for each day of the simulated period, to be used with the simulator to generate the glucose data. This ensures that the proposed PSECMAC is not being trained on a cyclical data set, but employed to discover the inherent relationships between food intakes and the glucose metabolic process of a healthy person.

Figure 12 illustrates a sample output from GlucoSim for Subject A. This output consists of six elements: blood glucose, blood insulin, intestinal glucose absorption rate, stomach glucose, total glucose uptake rate and liver glucose production rate of Subject A respectively over a simulated time period of 24 hours. The peaks in the stomach glucose subplot of Figure 12 coincide with the timings of the assumed daily four meals (i.e. breakfast, lunch, afternoon snack and dinner) while those peaks in the intestinal glucose absorption rate subplot reflect a delay effect (response) of food intake on the blood glucose level of Subject A. The subplots of blood glucose and blood insulin illustrate the insulin-glucose regulatory mechanism in a healthy person such as Subject A and depict the dynamics of the metabolic process when subjected to disturbances such as food intake.

Since the glucose metabolic process depends on its own current (and internal) states as well as exogenous inputs (or disturbances) such as food intake, it is hypothesized that the blood insulin concentration level at any given time is a nonlinear function of prior food intakes and the historical traces of the insulin and blood glucose levels. To properly account for the effect of prior food ingestion to the blood insulin level, a historical window of six hours was adopted. To resolve the variability issue in the number of meals (and hence number of inputs) taken within the previous 6 hours, a soft-windowing strategy is adopted to partition the six hours historical windowing and weighting function into three conceptual segments, namely: *Recent Window* (i.e. previous 1 hour), *Intermediate Past Window* (i.e. previous 1 to 3 hour) and *Long Ago Window* (i.e. previous 3 to 6 hour), resulting in only three food history inputs. The names of the segments are chosen to intuitively represent the human conceptual understanding and perception of time based on these windows, three weighting functions are introduced to compute the carbohydrate content of meal(s) taken within the recent, intermediate past or long ago periods. Figure 13 depicts the weighting function for each of the segmented windows.

Three computing networks were constructed to model the dynamic blood insulin profile: a PSECMAC network of size 8 per dimension and two CMAC networks of size 8 and 12 per dimension respectively. The 100 days of collected metabolism data was then used in the training and testing of the PSECMAC and the two CMAC networks.

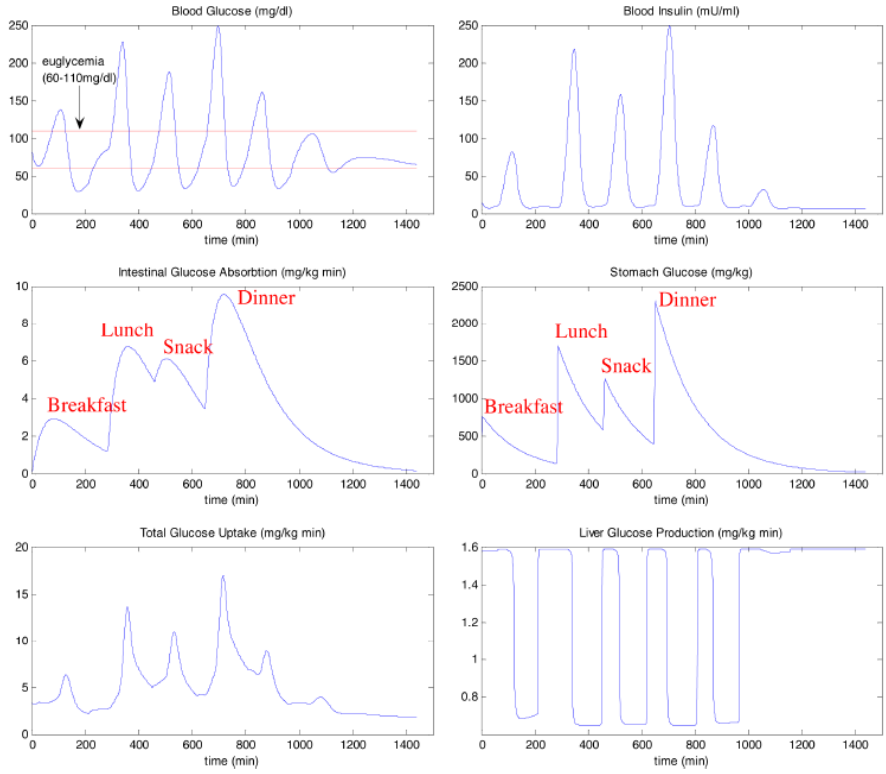


Fig. 12. Sample glucose metabolism data output from the GlucoSim simulator.

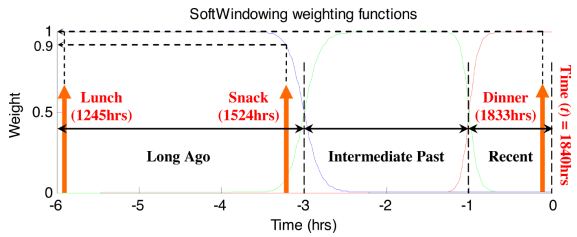


Fig. 13. Soft-windowing weighting functions to compute the carbohydrate content of meal(s) in the segmented windows of the 6-hours food history

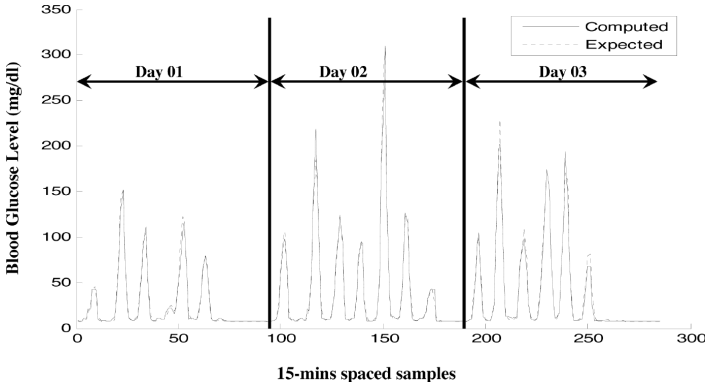
Table 2. Computations for the generation of GlucoSim input parameters. (Note: 100 sets of input parameters are generated. U(x,y): a uniformly distributed random number between x and y inclusively; and N(μ,σ): a normally distributed random number with mean μ and standard deviation σ.

No	Glucosim Input	Notation	Value	Remarks
	Meal Timings			Only four meals[1] per day and meal timings are typical of an office worker
1.	Breakfast Time	BkTime	U(0700hrs,0900hrs)	Meal timings are uniformly randomized within their specific ranges
2.	Lunch Time	LunTime	U(1130hrs,1200hrs)	
3.	Afternoon Snack Time	ASTime	U(1500hrs,1600hrs)	
4.	Dinner Time	DinTime	U(1830hrs,2030hrs)	
	Total Carbohydrate Intake Per Day			TotalCarb = 350g + N(μ=0g,σ=50g) (RDA for Subject A is approx. 350g)
5.	Breakfast Carbohydrate	BkCarb	U(12%,18%) x TotalCarb	Carbohydrate percentages are uniformly randomized within their specific ranges and normalized so that total sum is 100%
6.	Lunch Carbohydrate	LunCarb	U(25%,35%) x TotalCarb	
7.	Afternoon Snack Carbohydrate	ASCarb	U(13%,19%) x TotalCarb	
8.	Dinner Carbohydrate	DinCarb	U(35%,45%) x TotalCarb	
	Other Inputs			
9.	Body Weight	BW	67kg + N(μ=0kg,σ=0.5kg)	Weight is normally randomized
10.	Duration of Simulation	DSimu	24 hours	Constant

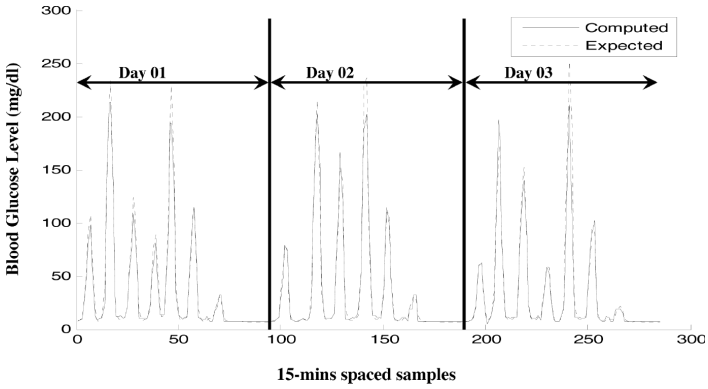
[1]It is assumed that Subject A does not take morning and evening snacks. Hence the morning and evening snack timings are kept constant at -----and -----hours during input to the simulator, and their respective carbohydrate contents are preset to - g.

Table 3. The Parameter Settings for the trained Networks

Parameter Name	Notation	Parameter Value
Neighborhood constant	N	0.1
Width of Gaussian weighting function	γ	0.5
Learning constant	α	0.1
Number of training epoch	Ep_{max}	1000



(a). Recall performance



(b). Generalization performance

Fig. 14. 3-days modeling performances of the PSECMAC network in modeling the insulin profile of a healthy person

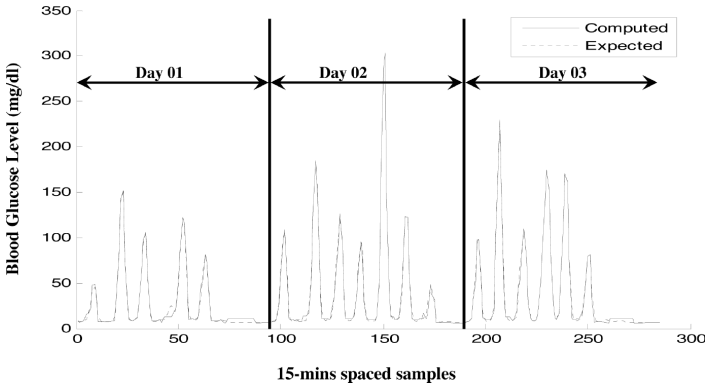
In order to obtain an objective comparison on the performances of the three models, all of the networks are trained and tested using the same parameter settings and the weighted Gaussian update and retrieval mechanisms (i.e. WGNO and WGNU respectively). The parameters of the networks are outlined in Table 3.

Figure 14 depicts a 3-days snapshot of the recall and generalization accuracy of the proposed PSECMAC network in comparison to its CMAC counterpart (Figure 15) on modeling the metabolic insulin profile. Each of the networks has 8 memory cells per dimension. To quantify the performance quality of the networks, two performance indicators are used: the *root mean-squared error* (RMSE) and the *Pearson correlation coefficient* between the desired and the computed metabolic insulin profile. The modeling accuracy of the PSECMAC network is evaluated against those of the basic CMAC and the results are tabulated in Table 4.

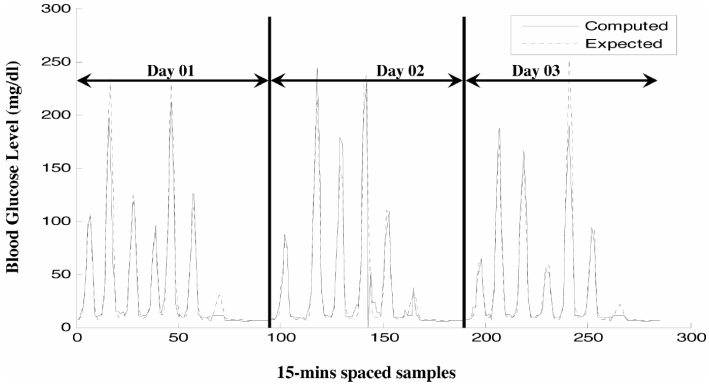
From the plots of Figure 14 and Figure 15, as well as the results tabulated in Table 4, it can be observed that there are slight performance degradations as the evaluation emphasis shifted from recall to generalization in the modeling performances of both the PSECMAC and CMAC networks. This is a common phenomenon since generally; computational models tend to have poorer modeling and prediction performance to data samples that have not been previously encountered in the training phase. However, it is clearly demonstrated that the generalization capability of the PSECMAC network surpasses that of the basic CMAC networks in both RMSE as well as the Pearson correlation coefficient. In fact, the PSECMAC network manages to obtain a rather good fit to the actual blood insulin concentration level required, as indicated by a high correlation of 97.69% and a relatively low RMSE of 10.3349 mU/ml of blood insulin concentration. Moreover, it is observed that there is degradation in the performance of the basic CMAC network as the network size grows from 8 to 12. This is due to the fact that in the basic CMAC network, memory partitioning is performed without taking into consideration the inherent structure and characteristics of the problem domain. These results have sufficiently demonstrated the ability of the PSECMAC network to efficiently capture the dynamics of the glucose metabolism process of a healthy person and are subsequently able to accurately decide on the appropriate level of insulin concentration based on the acquired knowledge. Specifically, in contrast to the basic CMAC, the proposed PSECMAC network provides a more meaningful and efficient method of managing the limited memory resource to model and capture the characteristics of a given problem domain.

Table 4. Simulation results of the modeling of the insulin response of the healthy glucose metabolic process

Architecture	Evaluation Mode	Memory Size (per dimension)	RMSE (mU/ml)	Pearson Correlation
PSECMAC	Recall	8	4.8039	0.9942
	Generalization	8	10.3349	0.9769
CMAC	Recall	8	3.7044	0.9965
	Generalization	8	16.4373	0.9405
	Recall	12	2.5443	0.9983
	Generalization	12	16.9316	0.9383



(a). Recall performance



(b). Generalization performance

Fig. 15. 3-days modeling performance of the PSECMAC network in modeling the insulin profile of a healthy person

6 Conclusions

This chapter proposes a novel brain-inspired, cerebellar-based computational model named PSECMAC to functionally model the autonomous decision making process in a complex, dynamic and uncertain environment. Dynamic decision making processes are characterized by multiple, interdependent and real-time decisions, which occur in an environment that changes independently as a function of a sequence of actions. Research has established that such a decision making process appears to be a cognitive skill that can be developed through training and repeated exposures to a series of decision episodes.

The human procedural memory system is a facet of the brain's information computing fabric, and exhibits the capacity for knowledge acquisition and information retention. An important component of the human procedural memory system is the cerebellum, which represents a learning memory system for habits, skills and procedures. It has characteristics of rapid and unconscious memory recalls, and is responsible for many human's subconscious behavioral responses. This provides the motivation to use PSECMAC, a cerebellar-based learning memory model, as a computational tool for autonomous decision making to dynamic, complex and ill-defined problems.

Inspired by the cerebellar learning mechanisms established through neurophysiological studies, the proposed PSECMAC learning memory model employs an experience-driven memory management scheme, which has been demonstrated to be more efficient in capturing the inherent characteristics of the problem domain for effective decision making. The PSECMAC network employs a density-based memory cell allocation procedure, which subsequently translates to finer and more precise representations of frequently encountered features of the problem being modeled. Such an allocation procedure in turn results in a more accurate representation of the important knowledge related to the problem domain. The performance of the proposed PSECMAC network is subsequently evaluated by employing it to model the dynamics of the metabolic insulin regulation mechanism of a healthy person when perturbed by food intakes. The regulation of the human glucose metabolic process via insulin control can be perceived as an autonomous decision making process, in which the body dynamically decides the appropriate amount of insulin to secrete in response to the food intakes. Simulation results have sufficiently demonstrated the effectiveness of the proposed PSECMAC model in capturing the complex interacting relationships between the blood glucose level, the food intake and the required blood insulin concentration for metabolic homeostasis. The modeling capability of the PSECMAC network is subsequently benchmarked against those of the basic CMAC and significant improvement is noted.

As part of the future work, the PSECMAC based insulin model will be used as a reference model to develop an intelligent control regime for an algorithmic-driven insulin pump for the treatment of Type I diabetes. These various research attempts are currently actively underway at the Centre of Computational Intelligence (C2i) [89] located at the School of Computer Engineering in Nanyang Technological University, Singapore. The C2i lab undertakes intense research in the study and development of advanced brain-inspired learning memory architectures [90–92] for the modeling of complex, dynamic and non-linear systems. These techniques have been successfully applied to numerous novel applications such as automated driving [93], signature forgery detection [94], gear control for the continuous variable transmission (CVT) system in an automobile [95], bank failure classification and early-warning system (EWS) [96], as well as in the biomedical engineering domain [97-98].

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