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Neuroscience, Virtual Reality and Neurorehabilitation: Brain repair as a validation of brain theory

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Abstract—**This paper argues that basing cybertherapy approaches on a theoretical understanding of the brain has advantages. On one hand it provides for a rational approach towards therapy design while on the other allowing for a direct validation of brain theory in the clinic. As an example this paper discusses how the Distributed Adaptive Control architecture, a theory of mind, brain and action, has given rise to a new paradigm in neurorehabilitation called the Rehabilitation Gaming System (RGS) and to novel neuroprosthetic systems. The neuroprosthetic system considered is developed to replace the function of cerebellar micro-circuits, expresses core aspects of the learning systems of DAC and has been successfully tested in in-vivo experiments. The Virtual reality based rehabilitation paradigm of RGS has been validated in the treatment of acute and chronic stroke and has been shown to be more effective than existing methods. RGS provides a foundation for integrated at-home therapy systems that can operate largely autonomously when also augmented with appropriate physiological monitoring and diagnostic devices. These examples provide first steps towards a science based medicine.**

Introduction

The brain is considered to be the most complex physical device in the known universe. Indeed, we have only scratched the surface of understanding it as is witnessed by our limited capabilities to effectively repair and heal the brain. One developing trend in neuroscience is the use of computational and theoretical models to interpret specific aspects of neuronal anatomy, physiology and/or behavior. One fundamental challenge of theoretical studies is to find sufficient constraints to assess the uniqueness of a model or the problem of indeterminancy [1]. Computational neuroscience is no exception and in response a growing number of computational studies include real-time behavior as a constraint relying on robots [2]. One additional source for constraints of theoretical neuroscience is the clinic, where it can provide a theoretical base on which neurorehabilitation and brain repair can be based. Neuropathology provides very explicit possibilities to test our theories and hypothesis on brain function in health and disease. Although this claim looks rather uncontroversial, practically no theoretical models of the brain has made a successful transition into clinical practice. One exception to this rule is the, so called, Rehabilitation Gaming Station (RGS), a virtual reality based system that has been developed for the rehabilitation of instrumental activities of daily living after brain lesions. Thus far RGS has been successfully applied in both the acute and chronic stages of stroke and shown to speed up recovery as compared to other available methods. RGS is based on an extensive theoretical framework, of mind, brain and behavior called the Distributed Adaptive Control architecture that has been under development since the early 1990ies. In addition, key aspects of DAC have been translated into a novel neuroprosthetic system or the silicon cerebellum.

The Distributed Adaptive Control architecture provides an integrated real-time model for perception, cognition and action [3, 4] (Figure 1) that is consistent with our current understanding of brain architecture [5, 6]. DAC considers the brain as a wired control system that mediates between the needs of the internal environment (the body) and the external environment it has to exploit for survival through generating action. The brain is implemented as a collection of interconnected cells that exploit a combination of spatial organization of connectivity and temporal properties provided by its biophysics to achieve transformations from sensory states, derived from the internal and external world, into actions. The key variable the brain controls is the integrity of the body that hosts the brain, the organism, in the face of the needs of the organism, overall environmental challenges and the second law of thermodynamics. The brain is the result of a centralization of this mediation following the increasing complexity of the morphology, sensory repertoire, sensori-motor capabilities and the niche the organism exploit.

In order to explain these properties of brains DAC comprises three tightly coupled layers: reactive, adaptive and contextual which can roughly be mapped onto brainstem, midbrain and forebrain (Figure 1). At each level of organization increasingly more complex and memory dependent mappings from sensory states to actions are

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generated dependent on the internal affective state of the agent.

Compared to many other proposals the DAC architecture is fully grounded since it autonomously generates representations of its primary sensory inputs using a fully formalized neuronal model based on the objectives of prediction and correlation [7]. It has been demonstrated that the dynamics of these memory structures are equivalent to a Bayesian optimal analysis in foraging [4]. The DAC architecture has been deployed in a range of systems from robots, to a human accessible space to generate adaptive social behaviors [8], generalized to operate with multiple sensory modalities [9], and augmented with an integrated top-down bottom-up attention system [10]. Using DAC a novel non-neuronal feedback loop in the organization of perception and action has been identified, i.e. behavioral feedback, that explains how habits changes perception through biasing input sampling [4].

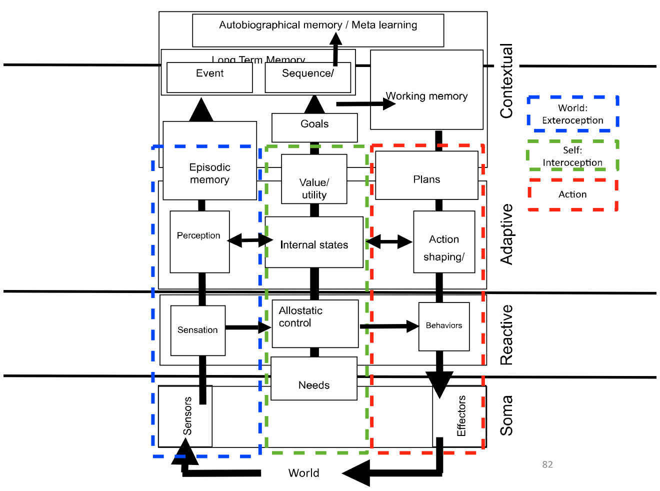

Figure 1. The DAC architecture. At the level of the *Soma* the direct interfaces to the world are defined combined with the needs of the organism. The *Reactive* layer endows a behaving system with a prewired repertoire of reflexes, low complexity stimuli and responses, that enable it to display simple behaviors. The activation of any reflex, however, also provides cues for learning that are used by the *Adaptive* layer via representations of internal states, i.e. valence and arousal. This second layer provides the mechanisms for the adaptive classification of sensory events and the reshaping of responses or in other words to construct a state space of sensing and acting. The sensory and motor representations formed at the level of adaptive control provide the inputs to the *contextual* layer that acquires, retains, and expresses sequential representations using systems for short- and long-term memory that store sequences of sense-act couplets. DAC distinguishes three columns of organization: The sensation and perception of the world, the perception of self and their integration in goal oriented action.

The DAC architecture has been generalized towards the neuronal substrate through a series of models on the cerebral cortex duff [11-14], hippocampus [15], thalamus [16] and cerebellum [17] and the combined roles of the amygdala and cerebellum in emotional learning [18]. Of particular interest here is that the cerebellar model, that has mapped key features of the adaptive layer of DAC to the neuronal substrate, has been implemented in aVLSI form [19]. Based on this realization a neuroprosthetic device for the cerebellum has been developed and successfully tested in in vivo studies [20]. The key objective of the cerebellar neuroprosthetic is to read data from the input structures to the cerebellum, the Pons and the Inferior Olive, to perform the basic operations implemented by the cerebellar microcircuits on the device (learning of a well timed response to a discrete stimulus) and to drive from the device the output pathways of the cerebellum (See Fig. 2.).

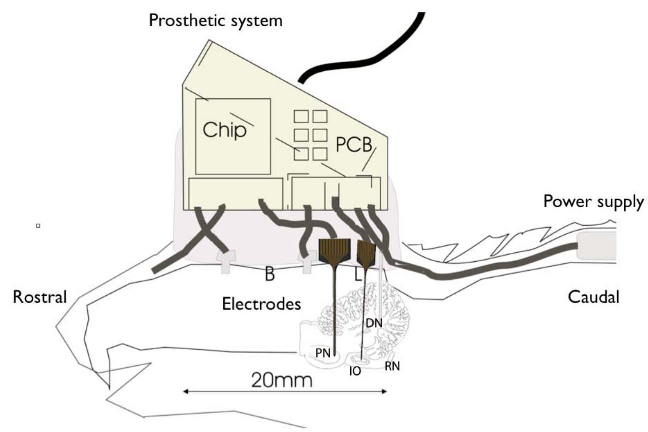

Figure 2: The design for a cerebellar neuroprosthetic. An integrated computational system emulates the circuit properties of the cerebellum based on a theoretical model. This emulated cerebellar micro-circuit is interfaced to the input and output structures, the Pons (PN) and Inferior Olive (IO) and Deep Nucleus (DN) respectively. Adapted from [20]

Given this broad range of validation studies it seemed appropriate to assess the ability of the DAC framework to inform the rehabilitation of stroke.

Stroke represents one of the main causes of adult disability and will be one of the main contributors to the burden of disease in 2030 [21]. Following stroke, patients initially show a variety of deficits, including motor deficits, sensory impairments aphasia spasticity chronic pain, mood disorders and depression and there are a considerable variety of treatment concepts and therapies addressing stroke without a clear consensus (see [22] for a review).

The initial impetus to the development of RGS was the observation that large-scale Virtual reality (VR) based immersive systems can be very effective in modulating human behavior, learning and experience [8]. Secondly the discovery of the human Mirror Neuron System (MNS) showed that a direct transduction channel existed between perception and action. The MNS is a system that is active during both goal-oriented action execution and action observation performed with a biological effector [23]. RGS was based on the assumption that this transduction channel can be exploited to drive effective reorganization after stroke. The further realization of RGS was informed by the theoretical work elaborated in the DAC architecture. One of these is that the hypothesis that the brain is organized around a limited number of learning systems. One example are the relatively uniform statistical learning mechanisms of the neocortex and the critical dependence of learning on the specific statistical structure of inputs [24, 25]. With respect to exploiting this feature of cortical learning this can be reformulated in terms of the specific and parametric control of the sensorimotor contingencies the brain is exposed to [26]. In addition, RGS exploits the phenomenon of behavioral feedback mentioned earlier. Lastly, RGS is built around the notion of task dependent and goal-oriented learning to exploit the role of neuromodulation in the regulation of plasticity [12]. Further learning is tightly regulated by systems that relate to motivation and arousal, the role of "self" in learning. This implies that learning must be individualized.

RGS integrates these different considerations outlined above in a VR based rehabilitation system integrating a paradigm of action execution with motor imagery and action observation [27-29] where the movements of the arms of the subject are mapped to a virtual character (Figure 3). The VR system in this way generates new sensori-motor contingencies that we assume will drive motor execution pathways affected by stroke through the MNS. The user is facing a computer screen on which they can view the virtual arms. The movements of these arms and hands are coupled to their own through a video based tracking system and data gloves (see [28] for a more detailed description). Using the virtual arms the users are asked to perform specific tasks such as intercepting spheres in the Spheroids scenario or playing puzzles. The tasks have been structured around the key concepts of elucidated in the DAC architecture outlined above. The clinical trials that have been performed thus far using stroke patents in both the acute and chronic stages show that RGS accelerates recovery of stroke patients as measured on the Chedoke Arm and Hand Activity Inventory while it is at least as effective in recovery of movement speed as intense - and therapist dependent - occupational therapy [29, 30].

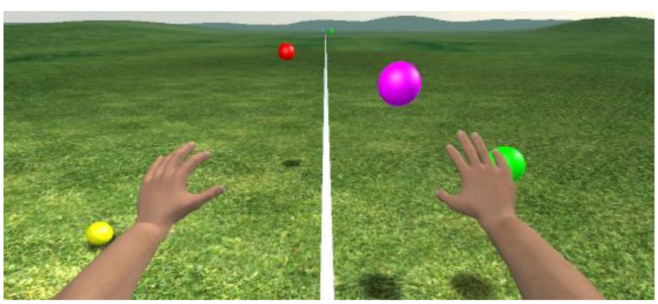

Figure 3. Users view during Spheroids. Spheres of variable sizes approach the virtual arms with variable velocities, at variable intervals and at different distances from the centerline. Users are exposed to an automated and graded training regime ranging from exercising of elbow and shoulder to precision grip.

Discussion

This paper presented an integrated approach towards a theory-based medicine of neurorehabilitation. It was demonstrated how the theoretical framework of Distributed Adaptive Control that aims at understanding mind, brain and action provided a foundation for the development of a novel neurorehabilitation approach called Rehabilitation Gaming Station. Currently we are transforming RGS into an autonomous solution for the at-home treatment of a range of neurological disorders. One key step in this direction is to equip it with more advanced physiological monitoring systems using wearable devices. The first experiments to achieve this are currently being performed. Once successful this will dramatically change the services we provide for care and quality of life management and facilitate a more open, cost effective and user driven approach towards how we deal with the brain in health and disease.

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