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More Haphazard Thoughts

When I was in school, biology was not a favorite subject of mine. I am not sure about the exact reason for this–whether it was the topics that we were taught, the way those were taught, or my limitation and interest. However, in 2002 I made a short trip to National Chiao-Tung University, Taiwan to visit Prof. Chin-Teng Lin. While interacting with him and his group, I found them working on the protein folding problem among other topics. I found the topic very interesting and challenging. This made me interested in the use of machine learning to protein folding. In fact, I became interested in other problems in biology, and bioinformatics, in particular. The more I read, the more I realized that to understand biology one needs to exploit physics, chemistry, mathematics, statistics, and computer science. As of today, I know very little of the subject. In biology, in my view, the most amazing and at the same time the most complex thing is the human brain. That is why the brain is often referred to as the most complex object in the known universe. The brain is responsible for our ability of reasoning, understanding, sensing, cognition, learning, and emotion–the list goes on. The brain consists of about one hundred billion neurons and about one hundred trillion synapses (the number varies with age). Scientists all over the globe are trying to understand this most complex and mysterious object. There have been some interesting attempts to provide probabilistic models for perceptual computation. For example, Knill and Pouget [1] made a Bayesian coding hypothesis. The information received by sensory organs from the environment is represented in the brain by a conditional probability density function. Thus, the brain is a kind of probabilistic machine, which makes predictions and then based on the information that it gets via its sensory organs, it updates the predictions using the Bayesian principle. Although it is beyond my capability to assess how general such a theory is to explain all aspects of the brain, certainly there are activities related to perception and recognition where such an approach appears a very plausible one. Even for activities like crossing a road without a traffic signal, we look at the cars and other conditions, and then make a hypothesis/prediction whether it is the right time to cross. Then we update our prediction with sensory inputs and take action depending on the traffic situation. Moving further, Friston and his team [2], [3] attempted to unify ideas and concepts about how brain processes information to reason and decide. In this context, a "free energy principle" is proposed which can be viewed as a unified theory of perception and learning in the brain [2], [3]. According to the free energy principle, any self-organizing system must minimize its free energy to reach its equilibrium state, here the free energy is defined in terms of information theoretic quantities. This theory can bring several other theories under the same umbrella, which is very important. However, to establish this as the theory of the brain, a lot more needs to be done in terms of experimental verification. In fact, Friston himself wrote "If the arguments underlying the free-energy principle hold, then the real challenge is to

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understand how it manifests in the brain" [3]. In my view, there is a huge scope for us to exploit these theoretical advancements in biological science to design "intelligent" systems for engineering applications. In this context, it is worth noting that a Hopfield network minimizes such an energy to reach an equilibrium state.

There are many experimental investigations in brain science that can also help and/or pose challenges in designing of intelligent systems for various applications. Next I briefly touch on a few such experiments. Understanding of the brain has been both challenging and an exciting problem and has attracted many researchers to study experimentally different facets of the brain. There is growing evidence that different brain regions can take over functions that they are genetically not destined to perform. Many studies have demonstrated some reorganization of sensory and motor cortical maps following limb amputation [4]–[6]. It is well known that subjects with traumatic amputation of limbs develop phantom limbs when the amputation took place in adulthood [7]. There are also other studies on the reorganization of cortical maps for subjects with congenital missing limbs [6], [7]. For example, Montoya et al. [6] considered subjects with congenital missing of one of the upper limbs, traumatic amputees with phantom limb pain, and healthy controls. They concluded that congenital absence of a limb did not lead to cortical reorganization but traumatic amputees with phantom limb pain exhibited shifts of the cortical areas near the amputation zone. More specifically, traumatic amputees exhibited a significant shift of the cortical map representation of the lower lip, but this was not the case for subjects with congenital upper limb atrophy. They inferred that there is no significant difference in the organization of somatosensory cortex of subjects with congenital limb atrophy and that of healthy subjects. Flor et al. [7] also reported an extensive reorganization of cortical maps for traumatic amputees with phantom limb pain. But for traumatic amputees without phantom limb pain, they practically could not find any reorganization of the cortical maps. In fact, there are other studies such as [8] related to cortical reorganization of a language network that is associated with acquired language disabilities. A large percentage of stroke survivors develop aphasia-loss of language ability. In [8] subjects with stroke-induced aphasia and healthy subjects were given a picture naming task, and their blood-oxygen-level dependent (BOLD)- fMRI (functional Magnetic Resonance Imaging) was analyzed. Compared to the healthy controls, the activation in the left hemisphere of subjects with aphasia was significantly smaller. For aphasia subjects, the activation frequency and intensity in the regions that are related to language were much smaller compared to those of the controls. On the other hand, for the patients, the right superior temporal gyrus and the bilateral superior parietal lobule exhibited significantly higher activation than the controls. All these findings may not be too surprising. However, a recent study reported some strikingly different observations than what we used to believe [9]. These findings may influence the way we develop BCI (Brain Computer Interface) applications using machine learning. It considered 17 congenital one-handed subjects and 24 two-handed control subjects. One-handed people often use other body parts to compensate for the missing hand. These subjects were given five tasks like wrapping a gift and taking out money from a wallet and were asked to complete them as quickly as possible. Some important and striking findings of this study are: compared to the control, one-handers were found more likely to use their lower face, lower limbs, and the environment to compensate for their missing hand's function. Thus multiple body parts are involved in the compensatory behavior. More surprisingly, compared to the controls, movements of residual arms, lips, and feet when used for compensatory behavior, triggered a high activation in the missing hand-territory! Generally, it is believed that different parts of the brain (cortex) are organized based on different body parts–different areas of the cortex are responsible for motor functions or sensory functions for different parts of the body (cortical homunculus). In other words, different parts of the brain control different body parts. Thus, corresponding to a hand, say the left hand, there is a brain area, which is in charge of the left hand functions. But the above study revealed a completely different representation–the left hand area is not in charge of the left hand but is in charge of the activities that are normally carried out by the left hand! This is a very important finding. This is in sharp contrast to findings from several other studies as discussed earlier. Note that, this is not a topological reorganization but a functional reorganization. For example, other studies could not find any mapping of the lip movement into the missing hand territory [6], [7]. Flor et al. [7] reported not to find any cortical reorganization for congenital amputees. Here, the observations are limited to subjects with congenital missing hands. So the discovery reported in [9] has remarkable consequences. Can this be taken as a strong indication that the brain organization is not in terms of body parts but in terms of functions? What happens with other kinds of disability? For example, we have discussed the issue of cortical reorganization with stroke-induced language disability. What happens with congenital speaking disability? If it turns out that in general (or just for people with congenital disabilities) the brain is organized in terms of the functions then this may have a significant impact on the way we design BCI systems. Often we analyze motor imagery EEG data from normal subjects and design BCI systems. What would happen if we try to transfer such knowledge (via a trained machine learning system) to subjects with congenital missing limbs or to traumatic amputees? What about designing BCI games? It is possible that the games designed based on normal subjects (that is what is normally done) may not do well when the games are played by people with missing limbs or people with language disorder. Even factors like how the disorder is

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President's Message

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caused, whether it is congenital, or acquired in childhood or adulthood, is likely to play important roles and influence the performance of the system. Note that a BCI game is more important for a person with missing upper limbs. The situation becomes more challenging if we consider the fact that a particular area of the brain is no more in charge of a body part but in charge of activities that are done by that body part. Thus if we want to design a BCI based system, as an example, for people with missing upper limbs, it appears that we should use data from subjects with missing limbs. But this certainly poses a challenge to generate adequate data for designing such a system. This raises other important questions: To design a machine learning system for motor imagery, can we use imagination of lip movement or movement of the feet to do the same task? Using a BCI system how can we analyze what a person is actually doing (not functionally, but physically)? I have no answer to all these questions but they all appear to be challenging and are likely to impact designing of AI systems based on BCI.

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