Mesoscopic Brainformatics

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Abstract. Brain science is a well-recognized frontier science with extensive and profound contents. For the past hundreds years, biological experimental studies are the main ways to understand the brain, but now, neuro-data and computing have grown up to be almost an equivalent important tool for uncovering the brain and brain disorders. It means that a fuse of "Brain" and "Informatics", Brainformatics, is becoming an area of science. In this paper, we take the brain research driven by information science as a new discipline – BraInFormatics – with "brain information acquisition", "Brain information decoding" and "brain information applications" as the main contents, and meso-scale problems are the main space waiting for this discipline. This paper explains the concept, scope and challenges with some examples, such as EEG zero-reference technique, brainwave music etc. developed in our lab.

Keywords: Brainformatics · Information acquisition · Information decoding · Information application · Meso-scale brain science

1 Introduction

Brain science covers problems of various spatial scales, from microscopic level (gene, biomolecule, neuron), mesoscopic level (neural mass) and macroscopic system level (Fig. 1). Each scale works specifically and acts differently, and requiring different research tools to look in. For the microscopic scale, gene sequencing, biochemistry, optical microscopy, electron microscopy and patch clamp etc. are the main research tools. For the macroscopic system level, electroencephalogram (EEG), magnetoencephalogram (MEG), magnetic resonance imaging (MRI), functional near - infrared spectroscopy (fNIRS), psychological and behavioral analysis are the main research technologies. Usually, microcosmic analysis typically processes off-body samples which are invasive and non in-situ analysis, but it can dip into the gene, protein molecule, synapse, ion channel, membrane potential etc. Macroscopic techniques may face the human brain directly as it is generally non-invasive and in-situ analysis, thus of more clinic values and cognitive science application.

For micro-scale brain science, constrained by biology, complete measurement of all activity and microstructure remains a wishful thinking. And even if such measurements were made possible, one could as easily get lost in the detail of a forest as in a large data set, just like one blind man feeling an elephant [1]. At the macro-scale, leading by

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psychology (Statistics), many fundamental progresses are also made without having to account for costly physiological or anatomical measurements (Fig. 1). However, the limited information available outside the brain also remains much secret under the observed. Another prominent question is whether there is a meso-scale area which do not just fills up the physical gap between the micro- and macro-scales, but also opens a new world to fly our dream? Unfortunately, there is no effective tool for the meso-scale brain information acquisition, mathematical model and computation simulation are therefore the main tools in current practice. Thus meso-scale brain science is mainly an information science driven brain science, that's the main body of BraInformatics (Fig. 1).

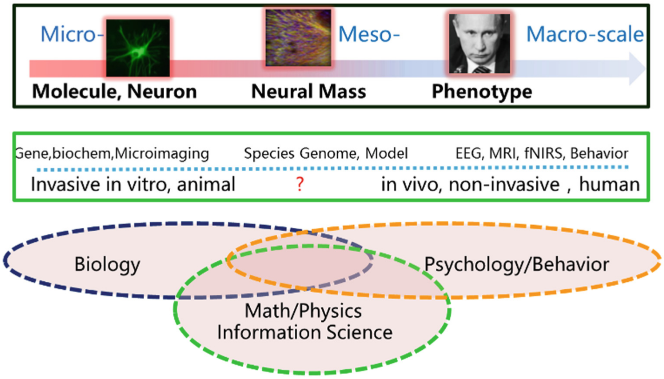

Fig. 1. Brain Science at different scales.

2 Meso-Scale Brainformatics

The meso-scale knowledge of brain is of specific significance not only because it is the critical bridge from the micro-scale details to the macro-scale phenomena, but also due to the fact that it may lead us to see the trees as well as the wood, based on its tight links with the micro- and Macro scales. As noted above, the three scale-dependent approaches are constrained respectively by genome/biology/biochemistry, mathematics/information Science, and Psychology/behavior (statistics) for the micro-scale, meso-scale and macro-scale efforts (Fig. 1), some scale-dependent sub-disciplines of brain science have been setup, such as cellular neurobiology, computational neuroscience and cognitive neuroscience in the past decades (Fig. 2). And some more specific sub-disciplines are emerging.

Actually, "when a workman wishes to get his work well done, he must have his tools sharpened". For brain science, the tool you are having would determine what kingdom you may be involved. In fact, if we look again at the brain science from the perspective of the main tools involved (Fig. 1), we will have a new view of the sub-disciplines: "Computational Neuroscience or Neurocomputing Science" driven by mathematics, "Electroencephalogram and Magnetoencephalogram" based on electromagnetism, "Neurobiology" on chemistry and biology, and "Cognitive Neuroscience" on psychology and neuroimaging. In this way, the brain science study induced by information science would be titled as "Brainformatics", a new discipline founded on the fusion of information and brain science, thus we may take Brainformatics as an information driven brain science discipline [2], the main body being the knowledge of the meso-scale brain.

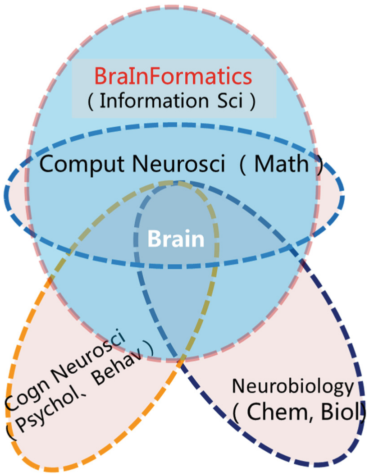

Fig. 2. Various sub-disciplines of Brain Science. Sub-disciplines and the main tools adopted in parentheses. Brainformatics is the one driven by information science as the main tools.

3 The Scope of BraInformatics

Information science, which is based on information theory, system theory and cybernetics, covers the theory, method and system for information acquisition, transmission and processing, and various applications. Information science covers information theory founded by Shannon but not limited to it. Therefore, brainformatics is not limited to entropy theory, but to include brain information acquisition, decoding (the information mechanism of brain function and brain disorder) [3] and application (brain-like technology, brain-inspired technology, brain-computer interface technology and translational medicine) (Fig. 3). What should the brainformatics include in general? It can be listed according to the information detecting technologies we have. The existing technologies cover the behavioristics, mechanics (ultrasound), thermotics (infrared), electricity, magnetism, optics, biochemistry, metabolism and gene, such a scope is far beyond the well-known "neuron" or "neural network", thus the brainformatics is not the neuroinformatics. After obtaining the brain information, the coming challenge is the explanation or decoding of the data. It involves all aspects of the brain function and brain disease, and the knowledge will contribute to our understanding and protection of our brain. In the past decades, new experimental techniques are generating a wealth of information about the brain at different scales – from the levels of genome, single cells to brain circuits to behavior – but neuroscience still lacks effective tools for managing these massive data sets. We need to find new ways to organize, analyze, and extract meaning from neurodata, thus open a new big data-driven neuroscience and in so doing accelerate the pace of discovery [4]. Thirdly, how could we verify the decoding and understanding of the brain information? It depends on the generalization of the obtained model and assumption in facing various new aspects of brain function and new intervention of brain disorder.

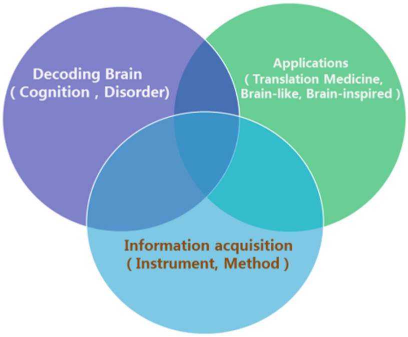

Fig. 3. The scope of Brainformatics. The main domains are the three: decoding brain to understanding cognition and disorder; information acquisition and the instrument, method behind; applications in both intelligent technique and clinical practice.

4 Brain Information Acquisition and EEG Zero-Reference Technique

Brain information acquisition involves two aspects: instrument and method. In recent years, driven by USA BRAIN Project [5] etc., a few breakthrough technologies emerged for accessing brain information, they are CLARITY technology, optogenetics technology, high field MRI brain imaging technology, flexible electrode technology, gene editing technology (such as CRISPR-9, Clustered Regularly Interspaced Short Palindromic Repeats). In this aspect, the Chinese advances include high resolution optical sectioning imaging technology [6], EEG-MRI information fusion technology [7], EEG zero reference technology [8] and so forth.

As an example, let's get into a little more details of EEG zero reference techniques [8]. EEG is a scalp potential recordings, as potential can only be measured as the potential difference between two points, we need to have one point as base, the reference electrode, and the other as the active electrode, and only when the reference is zero or constant, we can get the true activities at the active electrode (Fig. 4). However, there is no point on the body surface including the brain scalp where the potential is constant, thus no point on the body surface can be used as the gold reference. Figure 4 shows that for the same neural activities inside, the waveforms may be quite different when different references are adopted.

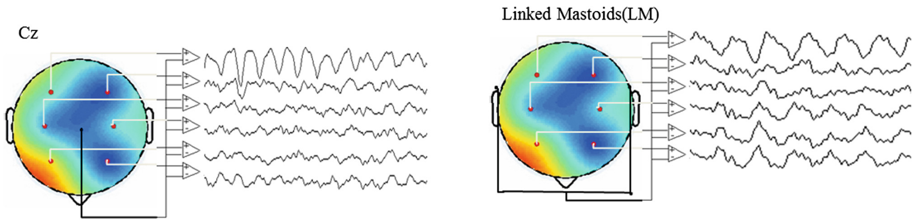

Fig. 4. EEG recordings with different reference. Left: Cz as reference, Right: Linked mastoids as reference. With the same sources underneath, EEG recordings may be quite different when different references are adopted.

EEG non-zero reference problem is a historical and fundamental problem since the human EEG discovered in 1924 by Hans Berger. In 2001, we took the lead to adopt the information science knowledge, the brain electric theory, that the scalp potential recordings, no matter what reference adopted, are generated by sources inside the brain, thus the different recordings with different references can be bridged together by the sources inside, then we developed a software method (reference electrode standardization technique–REST: www.neuro.uestc.edu.cn/rest) [8, 9] which was later repeatedly confirmed to be able to transfer an actual non-zero reference recordings to approximate zero reference based recordings [10], and now it was directly adopted more and more to get the true activities on the scalp surface to improve the later brain function or disorder discovery in many labs around the world.

5 Brain Information Decoding and Brainwave Music

Brain information decoding is in fact the understanding of brain information in a sense of brain cognition and brain disorder. The existing neural coding and decoding theory is a typical example. The current coding theory, including frequency coding, time coding, mode coding, collaborative coding, still cannot work in consent with the large amount of data accumulated in neuro-electro-physiological domain. In other words, the development of decoding theory is still at a relatively delayed situation than the data accumulation. Another issue is the brain network theory. It has now been recognized that the brain function is networked [11], which follows "small world" and "rich club" rules, and the networks are hierarchical, but the whole story of brain network is still blurred. The third problem is the brain's "Schrodinger equation" or "Einstein's equation" problem. Are there a few simple equations or principles which control the human brain's function? In past few decades, Dr. Karl Friston proposed "Bayesian brain" and "the principle of minimum free energy" [12]. Could they be the simple equation? All these problems are core problems in brainformatics in the future. In recent years, there are a lot of works conducted in understanding the information mechanism of brain function and brain diseases in China, such as Brainwave music [13], bi-directional regulation mechanism of absence epilepsy [14], effects of game training on insula plasticity [15] as well as the EEG brain network theory [16].

As an example, let's show you the relation between brain signal and music. Since the dawn of human civilization, music evolved along with the human evolution, human signals such as EEG would have intrinsic hints of the music, and thus music might be a tricky way to decode the human brain (Fig. 5).

Fortunately, it is easy to find that both EEG and music signal follow power-law thus we may establish a bridge between EEG and music directly [13], and the resulted music also follows power law, and can be used to discriminate (decode) different brain state [17].

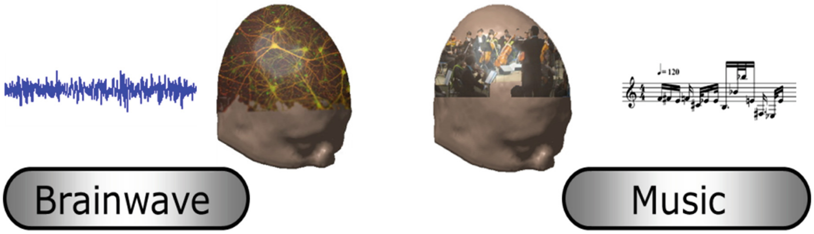

Fig. 5. Brainwave music. Left: brainwave, right: music. With the intrinsic relation(both EEG and music following power-law), the brainwave (left) is translated to music (right).

6 Exploratory Application of Brainformatics and Apparatus-Brain Conversation

For the exploratory application of brainformatics, the EU human brain project (HBP) is a good example [18]. One task of HBP is to explore the internal cognitive mechanism of the brain through simulating normal brain function, for example, to understand the causality mechanism of cognitive behavior by comparison of various aspects between 'dummy human or SimAnimals' and 'real man or real animal'. The second goal is to simulate the brain mechanism of brain disease. It tries to find biomarker of brain disease, determine new targets, and explore the curative effect of new drugs or side effects by combining pharmacokinetics and systematic simulation study from healthy brain to morbid brain. The third point focuses on neural morphology, which aims to develop human-like control technology, such as automatic driving technology.

In general, any application of brainformatics is about the interaction between brain science and the environment, the most well-known concept is the so-called brain-computer interface (BCI). However, interface cannot characterize the whole story, we propose to use apparatus-brain conversation (ABC) (Fig. 6), where apparatus is not just computer or machine, it also represents the biological organs of a living system, and conversation represents both one-way and bi-directional communication in nature. In this way, ABC may have three categories, such as ABC-1 for "activating brain", here we assume the brain at good state, the problem is to have normal channel to let it activate, thus to get the neural signal pass through the channel to interact/control something outside, such as the brain-signal P300, SSVEP etc. based armchair control, and various artificial limb, visual or auditory prosthesis; ABC-2 for "modulating brain", such as animal robot, various neurofeedback; ABC-3 for "brain enhancement", such as the previous brainwave music, and action game where a brain decision becomes action through the biological organ, the hand, and the results feed-back to the brain through ears and eyes, the repeating practice would enhance the related brain function and even change our brain [15].

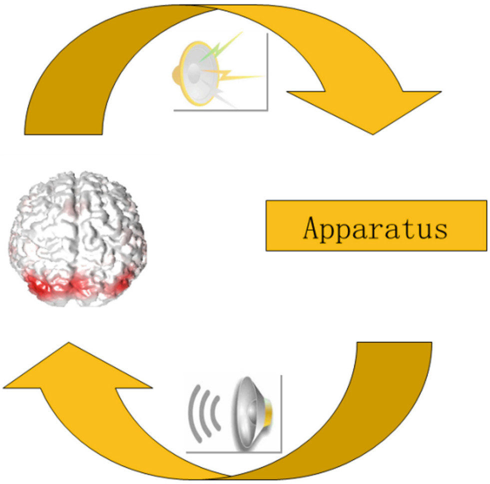

Fig. 6. Apparatus-brain conversation (ABC). Left: brain functionalized with perception/execution, making decision, memory and consciousness etc. Right: apparatus including both biological organs within normal health person and machine like computer outside the body. Conversation covers both one-way and bi-direction communication.

7 The Opportunities

Why should Brainformatics be assigned as an independent sub-discipline? Actually, "substance, energy, information" have now been recognized as the three basic elements of the world though the initiation of information science is later than that of physics, mathematics, chemistry and biology. It means that information science is now as important as the other main basic disciplines. In fact, our life and cell, including our brain and neuron, is actually a unity of "substance, energy and information". In this sense, publicizing Brainformatics is more than necessary, it would be an important routine to drive both the brain science and information science, making them help each other and fastening each other. Essentially, the journal "Brain Informatics" setup a few years ago already partly play the role to drive computational technologies related to human brain and cognitive [19].

In the wave of artificial intelligence, the brain information mechanism is the thinking spring of the artificial intelligence technology, Brainformatics will play an important role in such an age. The European Human Brain Project (HBP) initiated in 2013 took the brain simulation as the core, it actually reflects the European scientists' judgment of the future science and its economic and social values. Currently, with the development of society and economy, health, especially brain health, becomes the sign of the level of social development. It is estimated that brain disease may cost about 25% of the total medical burden in years 2020. Therefore, research on brain disease mechanism is already a timely crucial topic. In the past decades, various international enterprises have put in a lot of resources to identify the molecular target, so as to design a medicine for the therapy of brain diseases. Unfortunately, almost all of these efforts failed in the past decades. These challenges are actually the main background of the USA BRAIN project (Brain Research through Advancing Innovative Neurotechnologies) initiated in 2013, too. The "brain information acquisition" was put at the core of the BRAIN project and the aim is to search for new breakthrough for both brain disease and brain function from new information to be obtained.

In general, the importance of information science for brain study is already the consensus of the international community. Systematically pushing the new sub-discipline, Brainformatics, can not only satisfy the scientists' curiosity, but also meet the giant need of brain health, and such researches would receive much attention and support, and make a significant breakthrough in the near future.

8 Potential Challenges

What are the challenges of brainformatics - the brain research and application driven by information science? For such a question, each one may have specific opinion, however, the following issues are likely to be widely accepted.

(1) Brain aging: due to the desynchronized aging between physiology and brain function, brain aging disease is becoming a big challenge problem for the whole world. What are the determining factors of the brain aging, and are there any intervention techniques which can be adopted to stop or delay the brain aging process? The drug intervention is more emphasized in current medical system, but more and more people realized that it may not be the most effective method. How about to have some information-based technologies and methods to intervene brain aging?

(2) Major neuropsychiatric disorders enlarged by current rapid social informationization: We have to face more and more patient population with neuropsychiatric disorders and their medical burden getting heavier when we enjoy convenience brought by informationization. For these diseases caused by informationization, should we focus on using information approach to remit them?

(3) How to further improve imaging to dynamic, noninvasive, natural and multimodal integration. For example, the spatial resolution of the current functional magnetic resonance image is about 3 mm, how can we reach the desired 0.1 mm for functional column of brain in the coming ten years?

(4) The big data in brain science: Brain information covers multi-level, large-scale heterogeneous datasets ranging from gene to behavior, thus brainformatics is a typical issue of big data [20]. What can artificial intelligence technology do in this respect? What new development does artificial intelligence technology need to explore?

(5) Reverse and emulation brain: ‘Reverse brain engineering’ is one of the big challenges in the 21st century [21]. For brainformatics researchers, no matter ‘brain-like’, ‘brain emulation’ or ‘brain-inspired’ technologies are worth to develop, each of them has its own special target, and they all try to feedback the society to promote social progress and make human life better.

9 Conclusions

In conclusion, brainformatics, founded by the brain research driven by information science, on one side owes its growth to progress of information science in information-acquisition technology and computational capacity. On the other side, it also forces innovation of information science theory and method. Thus, it will facilitate the understanding of the brain information mechanism and develop engineering applications and clinical translation. Obviously, the development of the brainformatics discipline needs researchers with multiple discipline backgrounds and spirits of innovation to devote themselves to this work. In the brewing Chinese brain project, brainformatics will play an important role as the information mechanism of the brain is one of the main contents. This fact also means that Chinese scientists also attach great agreement on the importance of this crucial sub-discipline for the future.

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