Methods of diffusion-weighted and functional magnetic resonance imaging investigated in the human brain at ultra-high-field

Appendix A

Knowledge valorization

As I see it, there are three main motivations for us neuroscientists to study the brain: First, there is a philosophical aspect to it. For hundreds and thousands of years, great thinkers have been occupied with various existential questions. Historically, the authorities in answering those have been philosophers, shamans and priests. Modestly starting at the time of the renaissance and with ever increasing pace since then, the sciences have become another major authority. Nowadays, physicists for example develop theories about the origins of the universe and biologists about the genesis of life and mankind. Neuroscience in this regard is often concerned with questions related to the mind, such as how consciousness emerges and whether or not we have a "free will" (whatever this term means). Such questions are extremely hard to answer and my intention is not to say that science is particularly successful in doing so. However, humans crave to find the meaning of life and against this background, even incomplete, suboptimal or simply wrong answers can be more satisfying than not having an answer at all. Therefore, the pure attempt to solve the mysteries of our existence in a professional manner bears some societal value.

Second, and more importantly, there is the vast field of clinical applications of neuroscience. As mentioned in my introduction, MRI has been developed as a diagnostic tool, initially with the intention to detect tumors in regions which are otherwise hard to investigate. Even though nowadays MRI, particularly functional MRI, has many research applications without a clinical context as well, in its core it has kept this role. Improving the possibilities to diagnose pathological conditions in a fast, noninvasive way is without any doubt a significant achievement for our society. Aside of that, the health system is a huge economic sector. Therefore, neurodiagnostic methods certainly have a considerable economic value, too.

In this regard, for an imaging method to actually become a clinically applicable tool, several criteria have to be met: First of all, it has to be valid, providing robust and meaningful information about the examined tissue. Second, the method has to be sufficiently operable. This means there have to be a set of reasonably standardized parameters which allow users with only basic knowledge about its theoretical background to obtain good results. Finally, the interpretation of the results has to be clear, it has to be precisely known what information is contained in the acquired image volumes. These requirements cannot be guaranteed solely based on theories, but it has to be investigated in practice whether a method lives up to its expectations. Thus, making an imaging method good not only requires research and development, but also quality control, i.e. validation. This is precisely what I was concerned with in the first pillar of my doctorate, the validation of diffusion MRI. I showed first of all that a particular method of dMRI – DTI – works as it was theoretically assumed to do. I also helped towards optimizing model parameters and pointed out future directions to enhance the scope of this method. Therefore, I hope that this part of my work will play a role in the further development of dMRI and facilitate its establishment as a widely used clinical tool.

It also has to be mentioned that the clinical applications of neuroscience are not limited to only diagnostics anymore. For quite a few diseases of the brain or the mind, therapies based on neuroscience findings have been developed over the last decades. A prominent example of this is deep brain stimulation, which has proven helpful for example in cases of Parkinson's disease and major depression.

Third, there is the field of computational neuroscience. There have been many analogies for brain activity in the past. While the ancient Greeks thought of the brain as a blood cooler, in modern times the crucial link between its activity and our mind was recognized and people started to think of the brain as a steam engine, clockwork or whatever the cutting-edge machine of their time was. Today, the brain is most often seen in analogy to a computer. As such, it might not be the most powerful exemplar in terms of hardware specifications like processing speed or storage space (although this is hard to quantify). But qualitatively, the brain has some very powerful features, most notably being intelligent and able to learn. Particularly intelligence, which might be described as a set of very effective heuristics, allowing us to quickly find solutions to any kinds of new problems, is something which has not remotely been achievable with computers so far. Therefore, computational models of how the brain works can inspire software development, especially into the direction of artificial intelligence. In recent years, we have seen this in the example of so-called deep learning. Essentially a resurgence of old neuronal network paradigms, combined with state-of-the-art processing power, these networks show an unprecedented level of classification performance, being able to distinguish between various seen objects, faces, or heard words. These programs are still quite “dumb” in an AI sense, effectively doing little more than extracting patterns from huge data sets. However, doing this well enough to beat for example grandmaster Go players (something which some years ago was regarded as impossible), deep learning networks already show a vague resemblance of intelligence and are certainly a promising step towards a true AI.

What might sound like a rather playful field of application has in fact both a huge impact on our society and an equally huge economical potential. Many big companies have over the last decade started to acquire enormous sets of data about their (factual or potential) customers, such as which websites they visit, where they are at certain times of the day or what they like on social networks. States’ security services gather similar data and store who we are talking to and when with the aim to anticipate terrorist attacks. Their main problem though is that they often lack the methods to even rudimentarily analyze all the collected data and here, the potential of semi-intelligent, neuronally inspired pattern classifiers starts to be fully recognized. I want to point out that this is a very delicate matter since our society might at the moment stand at a crossroads. With ever growing capabilities to infer various facts from seemingly innocuous personal data, the question which data we allow to be collected and what to be done with them might determine which world we live in tomorrow. Will it be comparable to how we live today, or are we going to be automatically classified on a wide range of dimensions, such as professional aptitude, healthiness or psychological fitness, by our governments and, possibly worse, all kinds of companies? Are you and me going to be able to apply for the same jobs and buy the same products at the same prices, or will this depend on the output of algorithms determining how likely we are to succeed and how much we would be willing to pay? We are already seeing big steps into the second direction today and I am sometimes a little concerned about the future development. The more severe the responsibility of researchers is who develop and improve classifiers. They should not be blind to how their work is utilized and make their efforts depend on the continuous assessment whether their inventions will rather help us or put us in self-made chains.

Another practical application of the brain-computer analogy is to develop actual brain-computer-interfaces, which can work in two directions: One can transform digital data into nerve stimulation, as it is done with retina and cochlea implants. Or one can acquire brain activity data (such as fMRI data) and classify them in real time. This is very interesting in several clinical contexts. For example, BCIs of this kind could allow locked-in patients to communicate at least their basic needs with others, potentially increasing their quality of life by a large margin. Also, a new device to translate trained neuronal output into muscle stimulation has recently been successfully tested in a paraplegic patient, giving him back the ability to move his hand. So far, the practicability and efficiency of BCIs is still very limited. They require data acquisition techniques such as fMRI scans or permanent electrode implants which are very cumbersome from the perspective of daily life, and the amount of information which can be transmitted in a given time is very limited. For this reason, BCIs are contemporarily worthwile mostly as technical aids for people who have no other means of signal transmission. However, should this technology advance towards a level where operating machines cognitively becomes more comfortable than by using keyboards etc., BCIs could see a much wider range of application, completely revolutionizing the way people work and spend their leisure time.

My fMRI study, described in chapter 4, is a piece of fundamental research which aims to provide basic knowledge for both branches of computational neuroscience outlined above. With regard to the first part, I described and tested methods aimed to analyze the inner working of classifiers and eventually come to a better understanding of their performance. With regard to the second part, I used classifiers to decode visual stimuli from brain activity, and I enhanced the classification capabilities described in earlier studies by demonstrating decodability on small subsets of the visual cortex. While this study might be too methodologically focused to be directly translatable into concrete products, I hope to have convincingly argued that studies like this are the cornerstones of invaluable future developments.

Let me finally say that with the simplifying view brought about in this section, essentially reducing neuroscience to three subfields, I certainly forgot branches of neuroscience which might be just as valuable for society and economically profitable. I therefore want to stress that my intention is not to belittle any left-out branches but rather to show the most important reasons which I personally identified why we as a society should spend ressources into neuroscientific research.