

(続紙 1)

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論文題目	Interpretable machine learning approaches to high-dimensional data and their applications to biomedical engineering problems		
(論文内容の要旨)			
<p>Machine learning techniques have led to developments of algorithms that can learn from datasets alone to perform various pattern recognition, classification, and prediction tasks under rapid increase in computational power. In the field of biomedical engineering, they are expected to be promising solutions to deal with data growth associated with high-throughput experiments and high-resolution imaging techniques. However, there are still difficulties in applying machine learning techniques to the large amount of high-dimensional data.</p> <p>The first is about high-dimensionality, that is, the number of features may be much larger than that of samples while the most of features could be irrelevant to the phenotypes. In this situation, imposing sparsity-inducing regularization on machine learning models is able to remove irrelevant features automatically and effective in yielding insights into underlying biology to allow experimentalists to have a new working hypothesis. The next is about co-linearity, that is, a feature is linearly correlated with others, leading to unstable estimation of model parameters. One of the solutions is to apply dimension reduction that maps the original dataset onto a low dimensional space while keeping most of important information, under assuming that the entire dataset has been generated by a dominant system with a fewer dimensionality. The last is a nonlinearity inherent in biological phenomena. Since many biological phenomena could be nonlinear, it is worth introducing a nonlinear assumption into the models. Here, kernel-based methods are used for this purpose which deal with various types of nonlinear transformation within a unified framework.</p> <p>This thesis explored interpretable machine learning methods that can be applied to high-dimensional data with a particular interest in analyses of human brain activities, and presented a novel method for multimodal analyses that can be seen in the biomedical engineering field.</p> <p>Chapter 3 focused on diagnosis of depression based on human functional magnetic resonance imaging (fMRI). In order to achieve both accurate diagnosis and identifying relevant anatomical regions for depression, the current study introduced region-wise sub-kernels that corresponded one-to-one to anatomical brain regions, and an associated learning method as an extension of multiple kernel learning. This method achieved reasonably good accuracy in terms of leave-one-out cross-validation and also identified a restricted number of anatomical regions which will be profitable for depression diagnosis in the future study.</p> <p>Chapter 4 presented a method to predict a number of clinical scores from resting-state functional connectivity, with an interest in knowing the relation between the psychiatry scores and patient's brain activities. To ease the effects</p>			

from co-linearity in the functional connectivity, partial least squares regression (PLSR) and its kernel variants were applied. As a result, it was successfully demonstrated that they provided significantly better prediction of psychiatry scores than that by ordinary linear regression after applying a low-dimensional feature extraction.

Chapter 5 discussed the problems that often occur when nonlinear correlation analyses are applied to high-dimensional data. A novel method called two-stage kernel canonical correlation analysis was proposed, such to introduce an appropriate design of kernels within the framework of multiple kernel learning. Using synthetic datasets, it was confirmed that this method was able to remove irrelevant features. An application to gene expression analysis for the mice metabolic system was also demonstrated.

As a summary, this thesis explored machine learning algorithms that allowed the users to interpret the obtained results and to simultaneously deal with co-linearity and nonlinearity in high-dimensional datasets. Specifically, this thesis discussed the relationship between clinical diagnosis, scores, and fMRI data of depression patients with an attempt to reveal a physiological basis of traditional psychological evaluations in chapters 3 and 4. Moreover, to obtain deeper understanding of biological phenotypes in a data driven manner, a novel method based on multiple kernel learning was presented in chapter 5, which was able to obtain non-linear associations in the given biomedical data. Thus, the studies shown in this thesis could be new methodologies for dealing with high-dimensional and multimodal data in the field of biomedical engineering.

注) 論文内容の要旨と論文審査の結果の要旨は1頁を38字×36行で作成し、合わせて、3,000字を標準とすること。
論文内容の要旨を英語で記入する場合は、400～1,100 wordsで作成し
審査結果の要旨は日本語500～2,000字程度で作成すること。

(続紙 2)

(論文審査の結果の要旨)

医用工学分野では、サンプル数に比べて次元数が非常に高い高次元データの解析に加え、さらなる科学的発見につながる解釈可能なモデルの構築が求められている。本論文は、高次元データである脳活動データについてうつ病患者の診断及び心理指標に基づく重症度の評価を可能とする解釈可能なアルゴリズムを構築すると同時に、それらを遺伝子発現などその他の生理指標を含めたマルチモーダルな解析へと拡張する手法を提案するものである。その中で、以下のような成果を得ている。

1. 生理学的データに基づくうつ病の診断を目的として、脳画像データを入力として疾患の有無を判別する2値判別器を構築した。その際、脳の解剖学的領域に一对一対応させた領域カーネルを用いた多カーネル学習モデルを適用することにより、診断と同時に、それに関わる脳領域の特定を可能とする手法とした。これによれば、判別精度はサポートベクトルマシンと同程度だったものの、複数の重要な脳領域の特定に成功した点で、解釈可能であり、実際の医療応用への指針を提供できる手法となっている。

2. 部分最小二乗法を用いて、うつ病に関連する心理指標を機能的結合から高い精度で予測することに成功した。その過程で得られる低次元潜在空間表現を用いることで、診断精度が向上することを示した。また、回帰係数の大きさをもとに、心理指標の予測に関わる重要な脳の領野間機能的結合を特定することができ、結果が解釈可能となった。

3. カーネル正準相関分析では、適切なカーネル関数の設計が必要である。本論文では、高次元データに対してノイズに強くかつ解釈性のあるカーネル関数の設計手法を提案した。マウスの遺伝子発現の実データに適用した結果、従来のスパース加法モデルを仮定した手法に比べてロバスト、かつ重要な遺伝子を抽出可能なものとして動作することを確認した。

以上を要するに、本論文はサンプル数に比べて次元数が非常に高い高次元データ解析のための解釈可能な機械学習法であって、脳の機能画像から遺伝子発現などのマルチモーダルな実データ解析に個別適用することで、全体として一般性を有する手法の開発をおこなったという点で重要であり、博士(情報学)の学位に値するものと認める。平成30年1月18日に、論文内容とそれに関連した口頭試問を行った結果合格と認めた。

注) 論文審査の結果の要旨の結句には、学位論文の審査についての認定を明記すること。更に、試問の結果の要旨(例えば「平成 年 月 日論文内容とそれに関連した口頭試問を行った結果合格と認めた。」)を付け加えること。

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