Prediction of Oral Food Challenges via Machine Learning

Justin Zhang\textsuperscript{a}, Deborah Lee\textsuperscript{b}, Kylie Jungles\textsuperscript{c}, Diane Shaltis\textsuperscript{d}, Kayvan Najarian\textsuperscript{d,e,f,g,h}, Rajan Ravikumar\textsuperscript{b}, Georgiana Sanders\textsuperscript{h,c,i} and Jonathan Gryak\textsuperscript{j,*}

\textsuperscript{a}Department of Electrical and Computer Engineering, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{b}Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{c}Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{d}Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{e}Michigan Institute for Data Science, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{f}Department of Emergency Medicine, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{g}Department of Computer Science and Engineering, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{h}Max Harry Weil Institute for Critical Care Research and Innovation, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{i}Mary H. Weiser Food Allergy Center, University of Michigan, Ann Arbor, MI, USA
\textsuperscript{j}Department of Computer Science, Queens College, City University of New York, New York, NY, USA

ARTICLE INFO

Keywords: 
Oral Food Challenges 
Machine Learning 
Learning Using Concave and Convex Kernels 
SHAP

ABSTRACT

Oral Food Challenges (OFCs) are essential to accurately diagnosing food allergy in patients. However, patients are hesitant to undergo OFCs, and for those that do, there is limited access to allergists in rural/community healthcare settings. The prediction of OFC outcomes through machine learning methods can facilitate the de-labeling of food allergens at home, improve patient and physician comfort during OFCs, and economize medical resources by minimizing the number of OFCs performed. Clinical data was gathered from 1,112 patients who collectively underwent a total of 1,284 OFCs, and consisted of clinical factors including serum specific IgE, total IgE, skin prick tests (SPTs), symptoms, sex, and age. Using these clinical features, machine learning models were constructed to predict outcomes for peanut, egg, and milk challenge. The best performing model for each allergen was created using the Learning Using Concave and Convex Kernels (LUCCK) method, which achieved an Area under the Curve (AUC) for peanut, egg, and milk OFC prediction of 0.76, 0.68, and 0.70, respectively. Model interpretation via SHapley Additive exPlanations (SHAP) indicate that specific IgE, along with wheal and flare values from SPTs, are highly predictive of OFC outcomes. The results of this analysis suggest that machine learning has the potential to predict OFC outcomes and reveal relevant clinical factors for further study.

1. Introduction

The prevalence of food allergies has increased in the United States over the past few decades. Food allergy affects 8% of US children and 4% of the general population [6]. Because incorrect food allergy diagnosis has been shown to increase anxiety and unnecessary food restrictions for patients and their families [2], appropriate diagnosis and management of reactions to foods is important to reducing risk and improving quality of life.

The diagnostic evaluation of food allergy involves careful review of reaction history, physical examination, and allergy testing - including skin prick tests (SPTs) and the quantitation of specific food IgE. These allergy tests have high sensitivity and positive predictive value, but poor specificity and negative predictive value. The combined presence of multiple clinical risk factors for food allergy can improve the accuracy of diagnosis of true allergy [17].

Given the limitations of these methods, oral food challenges (OFCs) remain the gold standard for determining the clinical response to food allergies in a monitored setting. However, the lack of widespread use of OFCs remains problematic. With approximately 4,000 board-certified allergists in the US, many patients with suspected food allergies have limited access to OFCs. While the majority of patients administered OFCs pass with minor or no symptoms, OFCs carry the risk of severe reactions including epinephrine-refractory anaphylaxis [4], which requires them to be administered in a clinical setting. A recent study suggested that fear and anxiety among patients and caregivers are

*Corresponding author 
\textsuperscript{*}jgryak@qc.cuny.edu (J. Gryak) 
\textsuperscript{ORCID(s):} 0000-0002-5125-7741 (J. Gryak)
a significant barrier to considering OFCs [11]. Furthermore, the risks associated with OFC may contribute to high no-show or cancellation rates, wasting limited clinical resources.

Predictive models based on logistic regression have shown that the presence of readily available EHR data including demographics, IgE levels, and SPTs can predict OFC failures with up to 80% accuracy [9]. Additionally, machine learning has found great success in predicting patient outcomes in many clinical settings [5]. In this study, we seek to utilize machine learning to predict OFC outcomes for three common allergens - peanut, milk, and egg. Clinical features such as demographics, comorbidities, IgE levels, and SPT results, were extracted from electronic health record (EHR) data. The machine learning method Learning Using Concave and Convex Kernels (LUCK) [16] was used to accurately predict OFC outcomes for individual patients, achieving an Area under the Curve (AUC) for peanut, egg, and milk OFC prediction of 0.76, 0.68, and 0.70, respectively. Model interpretation via SHapley Additive exPlanations (SHAP) indicate that specific IgE, along with wheal and flare values from SPTs, are highly predictive of OFC outcomes. The results of this analysis suggest that machine learning has the potential to predict OFC outcomes and reveal relevant clinical factors for further study.

2. Data

The secondary use of the data in this study was approved by the Michigan Medicine IRB under application HUM0019636. The patient cohort consists of patients between 0 to 80 years of age who underwent oral food challenges for evaluation of possible IgE-mediated allergies at the Michigan Medicine Allergy Clinic from January 2001 through March 2022. Patients diagnosed with Food Protein-Induced Enterocolitis Syndrome (FPIES) were excluded. Food challenges for testing food intolerance or proximity were excluded, as were blinded challenges or those administered under food allergy immunotherapy trials. Physician labelling identified patients with passed, failed, and ambiguous/inconclusive OFC results.

Due to changes in challenge protocol over time and idiosyncrasies between physicians, testing for IgE components is more prevalent and detailed for more recent OFCs. A portion of IgE and SPT data were read and entered into the system from stored paper records. Characteristics of these complexities in the older dataset include varying resolution (e.g., range and precision), and missing features (e.g., peanut components, wheal, and flare).

OFCs of relevance to this study include those from peanut, combined cooked and baked egg (any egg), combined baked and other milk (any milk). The final database contained 495 peanut OFCs, 558 any egg OFCs, and 231 any milk OFCs. In total, 1,112 patients and 1284 OFCs were included in this study. There was a 86% OFC pass rate and 62% of patients were male and 38% of patients were female. The median patient age was 5.6 years, and the lower and upper quartiles were 3.1 years and 5.6 years, respectively.

The available clinical variables in the dataset that were deemed salient to predicting OFCs were selected by board-certified allergists for inclusion in our analyses, and can be grouped into the following five categories:

- Demographics, including patient age, gender, race, and ethnicity
- Comorbidities
- Clinical Rationale for Food Challenge
- Total and specific serum IgE tests
- Wheal and flare components of Skin Prick Tests (SPTs)

In the following results and discussion, comorbidities are suffixed with "condition", while the clinical rationales for ordering a food challenge are prefaced with "Reason:". An OFC is interpreted to have "passed" and belong to the positive class when the patient did not experience a severe physiological reaction to the food allergen.
Table 1
Serum-specific IgE test and Skin Prick Test factors by allergen.

| Allergen | IgE test factors                               | SPT test factors                  |
|----------|------------------------------------------------|-----------------------------------|
| Peanut   | Total peanut                                   | Peanut                            |
| Egg      | Egg White, Egg Yolk, Ovalbumin, Ovomucoid      | Egg White (Needs Confirmation)    |
| Milk     | α-Lactalbumin, β-Lactoglobulin, Cow Milk, Casein, Whey | Cow Milk, Casein                 |

Table 2
Number of clinical factors in each category by dataset.

| Allergen | Demographics | Comorbidities | OFC Reason | IgE tests | SPT Components | Total |
|----------|--------------|---------------|------------|-----------|----------------|-------|
| Peanut   | 11           | 19            | 8          | 2         | 2              | 42    |
| Egg      | 11           | 19            | 8          | 5         | 2              | 45    |
| Milk     | 11           | 19            | 8          | 6         | 4              | 48    |

3. Methodology

3.1. Overview

The overall framework of the proposed method is depicted in Figure 1. First, feature selection is performed to evaluate features by their redundancy, dependency, and relevance. Second, an optimal selection of features and hyperparameters is determined for the machine learning classifier to use in predicting the outcome of Oral Food Challenges (OFCs). The optimized ensemble models are then evaluated on the test set. The dataset is then shuffled and the entire process (feature selection, training and validation, testing) repeated 10 times, with an aggregate performance produced to compare with those of benchmark methods. Final model behavior is analyzed using SHapley Additive exPlanations (SHAP) values, which can be used to estimate the contribution of each variable to the final decision [12].

![Figure 1: A schematic diagram of the proposed method.](image)

3.2. Data Preprocessing

OFCs that were missing feature values were removed from the dataset. SPT score, compiled from existing and recorded wheal, flare and pseudopod components, was deemed redundant and excluded from the data. All remaining challenges underwent data preprocessing, including the standardization of recorded serum specific and total IgE values, such as ‘<0.35’ being set to 0.175, and ‘>100’ set to ‘101’. ‘Yes/No’ and ‘Checked/Unchecked’ features were converted to binary. Personally identifiable information (PII) such as dates and names were removed. Features such as ‘patient age’ were extrapolated from the patient birthday and OFC date features. The most recent test data prior to challenge were selected to ensure information is not result-informed, i.e., to prevent data leakage. The final dataset is then partitioned for feature selection, training/validation, and testing as depicted in Figure 2a.

3.3. Feature Selection

Features were ranked in importance using the minimum Redundancy Maximum Relevance (mRMR) method, which determine features that have maximum mutual information with respect to the given classes and minimum mutual information with each other [14]. This feature selection occurs prior to training and validation. The optimal feature combination is then found by surveying the model performance on the validation set with number of most important features through the elbow method heuristic. The entire process is repeated with every data shuffle.
3.4. Machine Learning

3.4.1. Random Forest

Random forest, a commonly used machine learning model that works well with high-dimensional data [7], was used as the performance benchmark. Five hyperparameters were optimized via grid search in training random forest models: number of trees, split criterion, minimum leaf size, number of variables to sample, and the maximum number of splits.

| Parameter                          | Range                                |
|-----------------------------------|--------------------------------------|
| Number of Trees                   | 20, 40, 80, 100, 160                 |
| Split Criterion                   | Gini impurity, Information gain       |
| Minimum Number of Leaf Node       | 1, 2, 5                              |
| Node Observations                 |                                       |
| Number of Variables per Split     | 6, 12, 24                            |
| Maximal Number of Splits          | Size of Training Set ($N$), $\log_2 N$ |

3.4.2. Learning Using Concave and Convex Kernels

In addition to random forest, the Learning Using Concave and Convex Kernels (LUCCK) model was also evaluated. LUCCK has been shown to outperform other machine learning methods when using features that may be prone to large measurement errors [10] or weakly correlated with desired outcomes [3]. In the LUCCK algorithm, similarity functions generate models for each feature separately. These functions take parameters that adjust their concavity and convexity within the feature space, which are then proportionally weighed according to information extracted from each feature.

In the proposed framework, hyperparameters used for concavity and convexity of the classifier and the proportional weight of importance of each feature during classification are optimized via grid search. Parameters were selected from 30 logarithmically-space samples for theta between the ranges of $10^{-2}$ to $10^{3}$, 30 samples for lambda between $10^{-2}$ to $10^{4}$, and 18 samples for the weight of the negative class between 0.5 and 2.

The performance metrics for each model generated in the grid search are compared with each other, with the highest combined ranking of specificity and sensitivity values having their hyperparameter combination selected for testing. For smoothing, performance metrics are averaged with those of its closest neighbors (kernel distance 1) before selection occurs.

3.4.3. Model Training and Validation

The experimental design follows a 3-fold patient-wise cross-validation scheme. To correct the 86%/14% positive/negative class imbalance, the training data uses the SMOTE algorithm, which synthesizes new samples for the minority class from currently existing samples [8]. No resampling was performed on the feature selection or test sets.

Additionally, we compared this cross-validation method with a bagging ensemble method, where an ensemble predictor is taken from each fold and the mode of their test set predictions is the final predicted outcome. The model creation process is depicted in Figure 2b.

3.5. Model Interpretation

Our analysis is based on SHAP, a popular prediction explaining technique [12]. SHAP uses cooperative game theory to distribute predicted outcomes. Positives distributions can indicate greater contribution to a predicted outcome, and vice versa for negative distributions. SHAP values can provide insight into how individual features contribute to LUCCK decision making. This extends to the original kernelSHAP, which uses conditional values instead of interventional ones [1]. The latter method is used instead of the original kernelSHAP to create more realistic samples and fits models where features are not independent from one another. In this study, SHAP values were calculated using the extension to the original kernelSHAP available in MATLAB Statistics and Machine Learning Toolbox [13]. Each features’ total contribution to the LUCCK model predictions are summed and averaged to illustrate the most influential and impactful clinical features, as can be seen in Figures 6, 7, and 8.
4. Results

Performance metrics, including Area under the Curve (AUC) and Positive Predictive Value (PPV), of the LUCCK models for predicting OFC outcomes for all three food allergens are reported in Tables 4 and 5. Table 4 displays the performance of models trained and tested with the Ensemble method, while Table 5 displays the performance of models trained and tested with the cross-validation method. Table 6 provides a performance comparison of the LUCCK and random forest final models trained and tested with the cross-validation method. Feature importance trends, as determined by mRMR prior to model creation, for peanut, any egg, and any milk OFC data are provided in Figures 3, 4, and 5, respectively. In these figures, lower mRMR values indicate greater feature importance. Model interpretations via SHAP for peanut, any egg, and any milk OFC prediction are provided in Figures 6, 7, and 8, respectively. In these figures, a higher mean absolute Shapley value indicates that a feature made a greater contribution to the model’s OFC prediction.

The best performance achieved for any food allergen was the peanut Ensemble method model (0.76 AUC and 0.87 F1 score) followed by the peanut cross-validation method model (0.76 AUC and 0.85 F1 score). Across the ten shuffles of the dataset, the best performing models with respect to the elbow method utilized 5 to 15 features. The relatively low standard deviations on the test set indicate the utility of the elbow method heuristic in preventing over-fitting. In all cases, LUCCK equaled or outperformed the Random Forest classifier in AUC, F1, and accuracy metrics, as seen in Table 6. There is a larger difference in AUC of LUCCK and Random Forest for milk OFCs (0.70 to 0.60), which can be attributed to the milk OFC data’s higher complexity in terms of IgE and SPT variables, along with a smaller sample size, both of which are better handled by LUCCK’s algorithmic advantages.

| Allergen | AUC     | F1      | Sensitivity | Specificity | Accuracy | PPV     |
|----------|---------|---------|-------------|-------------|----------|---------|
| Peanut   | 0.76 (0.04) | 0.87 (0.02) | 0.80 (0.05) | 0.72 (0.10) | 0.79 (0.03) | 0.94 (0.03) |
| Egg      | 0.68 (0.05) | 0.81 (0.05) | 0.72 (0.08) | 0.63 (0.10) | 0.71 (0.06) | 0.92 (0.03) |
| Milk     | 0.66 (0.15) | 0.88 (0.04) | 0.83 (0.07) | 0.50 (0.30) | 0.80 (0.07) | 0.94 (0.04) |

5. Discussion

We analyzed the predictor importance value of the top 15 features ranked most important by the mRMR feature selection algorithm, where lower value indicates higher importance. Total IgE, wheal, flare, and age consistently rank...
Table 5
Mean (standard deviation) performance metrics of the cross-validation method in predicting OFC outcomes.

| Allergen | AUC     | F1      | Sensitivity | Specificity | Accuracy  | PPV     |
|----------|---------|---------|-------------|-------------|-----------|---------|
| Peanut   | 0.76 (0.04) | 0.86 (0.04) | 0.79 (0.07) | 0.72 (0.11) | 0.78 (0.05) | 0.94 (0.02) |
| Egg      | 0.68 (0.05) | 0.79 (0.06) | 0.69 (0.09) | 0.67 (0.12) | 0.68 (0.07) | 0.93 (0.03) |
| Milk     | 0.70 (0.11) | 0.84 (0.07) | 0.76 (0.11) | 0.64 (0.27) | 0.75 (0.09) | 0.95 (0.03) |

Table 6
A comparison of mean (standard deviation) performance metrics of the LUCCK and Random Forest cross-validation models in predicting OFC outcomes.

| Allergen | LUCCK AUC | LUCCK F1 | LUCCK Accuracy | Random Forest AUC | Random Forest F1 | Random Forest Accuracy |
|----------|-----------|---------|----------------|-------------------|------------------|-----------------------|
| Peanut   | 0.76 (0.04) | 0.86 (0.04) | 0.79 (0.07) | 0.68 (0.06) | 0.87 (0.02) | 0.79 (0.04) |
| Egg      | 0.68 (0.05) | 0.79 (0.06) | 0.69 (0.09) | 0.60 (0.06) | 0.77 (0.03) | 0.69 (0.05) |
| Milk     | 0.70 (0.11) | 0.84 (0.07) | 0.76 (0.11) | 0.60 (0.08) | 0.82 (0.04) | 0.74 (0.07) |

Figure 3: mRMR trends for Peanut OFCs

among the most important clinical factors across all food challenges. Categorical factors were consistently less relevant than more quantitative factors. For egg challenges, ovalbumin and egg white serum IgE tests were found to be more significant than Egg Yolk and Ovomucoid tests. For milk challenges, whey and cow milk IgEs were found more significant than other types of serum specific IgEs.

Post-hoc analysis of model performance via SHAP agrees with mRMR predictions in that categorical features contribute less to model predictions than numerical features. For peanut challenges, wheal and flare were found to be the most influential. For egg challenges, both mRMR feature selection and SHAP analysis agreed that ovalbumin IgE and Egg Wheal are important features. For milk, these two disagreed on the importance of whey, and agreed on the importance of the Food Sensitization Condition.

The skin prick test components – wheal and flare – were consistently found to be influential in model predictions for all three challenge foods, although significantly more for peanut OFCs. The significance of flare is novel, as flare
is typically given low importance by clinicians. In [15], a peanut wheal of $\geq 8$ mm resulted in a likelihood of a failed peanut challenge of 17.25. For our dataset, the highest likelihood for a failed peanut OFC with respect to peanut wheal was 12.06 (95% CI 11.23-12.89), which occurred when the wheal was $\geq 15$ mm, while the highest likelihood for a failed peanut OFC with respect to peanut flare was 4.452 (95% CI 4.070-4.835), which occurred when the flare was $\geq 31$ mm.

Analysis was also conducted where OFC data were stratified by age and test date values (for SPT, Total and specific serum IgE tests) to assess their influence in model performance. Trials were conducted where models were trained and tested that including OFC data from patients between the ages of 0 to 2 years, 2 to 18, and above 18 years, in an effort
Prediction of OFCs via Machine Learning

Figure 6: SHAP values for Peanut OFC

...to address distributional drift. Creating separate models for these age brackets did not improve model performance. Neither the inclusion of the time elapsed between the collection of IgE/SPT data the OFC, nor adding an indicator variable marking tests occurring more than 6 months prior to the OFC, had a significant impact on model performance.

A limitation in our trials is that the OFC data for training and testing were collected from a single-site study. Additionally, the data was collected over a twenty-one year period, during which changes occurred in the clinical practice of administering OFCs that has likely affected the accuracy and consistency of the collected data. Given that there were an insufficient number of challenges to create separate models for baked vs. raw egg (similarly for milk), the relative importance of specific features for those individual allergens may be different than those as determined using the combined models.

6. Conclusion

In this study, machine learning models were developed to predict OFC outcomes for three common allergens - peanut, milk, and egg. Clinical features such as demographics, comorbidities, IgE levels, and SPT results were obtained from 1,112 patients who collectively underwent a total of 1,284 OFCs. The machine learning methods Learning Using Concave and Convex Kernels (LUCCK) and random forest were evaluated for their predictive performance, with a LUCCK ensemble model achieving AUCs for peanut, egg, and milk OFC prediction of 0.76, 0.68, and 0.70, respectively. Model interpretation via SHapley Additive exPlanations (SHAP) indicate that specific IgE, along with wheal and flare values from SPTs, are highly predictive of OFC outcomes. The results of this analysis suggest that machine learning has the potential to predict OFC outcomes and reveal relevant clinical factors for further study. In future work, other influential features from data modalities such as genomic data and other immunologic measures will be extracted. Additionally, the models will be validated on external datasets from multiple healthcare systems.
Prediction of OFCs via Machine Learning

Figure 7: SHAP values for Egg OFC

Figure 8: SHAP values for Milk OFC
Acknowledgements

Author Contributions: Conceptualization: JG, DL, RR, GS; Methodology: JZ, JG; Software: JZ; Validation: JG, DL, RR, GS; Formal analysis: JZ; Data curation: JZ, DS, JG, DL, KJ, JG; Writing - Original Draft: JZ, JG; Supervision: GS, JG; Funding acquisition: JG, KN, RR, GS. All authors have discussed the results and contributed to the final manuscript.

Funding: This work was supported by the University of Michigan’s Mary H. Weiser Food Allergy Center through its M-FARA Pilot Grant Program.

References

[1] Aas, K., Jullum, M., Løland, A., 2021. Explaining individual predictions when features are dependent: More accurate approximations to shapley values. Artificial Intelligence 298, 103502.
[2] Akuete, K., Guffey, D., Israelsen, R.B., Broyles, J.M., Higgins, L.J., Green, T.D., Naimi, D.R., MacGinnitie, A.J., Vitalpur, G., Minard, C.G., et al., 2017. Multicenter prevalence of anaphylaxis in clinic-based oral food challenges. Annals of Allergy, Asthma & Immunology 119, 339–348.
[3] Alge, O., Soroushmehr, S.R., Gryak, J., Kratz, A., Najarian, K., 2020. Predicting poor sleep quality in fibromyalgia with wrist sensors, in: 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), IEEE. pp. 4290–4293.
[4] Alviani, C., Burrell, S., Maceo, A., Edees, S., Roberts, G., Turner, P.J., Erlewn-Lajeunesse, M., 2020. Anaphylaxis refractory to intramuscular adrenaline during in-hospital food challenges: A case series and proposed management. Clinical & Experimental Allergy 50, 1400–1405.
[5] Belle, A., Thiagarajan, R., Soroushmehr, S., Navidi, F., Beard, D., Najarian, K., 2015. Big data analytics in healthcare. biomed research international, 2015.
[6] Boyce, J.A., Assa’ad, A., Burks, A.W., Jones, S.M., Beck, L.A., Byrd-Bredbenner, C., Camargo Jr, C.A., Eichenfield, L., 2010. Guidelines for the diagnosis and management of food allergy in the united states: Summary of the niaid-sponsored expert panel report. J Allergy Clin Immunol 126.
[7] Breiman, L., 2001. Random forests. Machine learning 45, 5–32.
[8] Chawla, N.V., Bowyer, K.W., Hall, L.O., Kegelmeyer, W.P., 2002. Smote: synthetic minority over-sampling technique. Journal of artificial intelligence research 16, 321–357.
[9] DunnGalvin, A., Daly, D., Cullinane, C., Stenke, E., Keeton, D., Erlewn-Lajeunesse, M., Roberts, G.C., Lucas, J., Hourihane, J.O., 2011. Highly accurate prediction of food challenge outcome using routinely available clinical data. Journal of allergy and clinical immunology 127, 633–639.
[10] Hernandez, K., Tokcan, N., Derksen, H., Biesterveld, B.E., Croteau, A., Williams, A.M., Mathis, M., Najarian, K., Gryak, J., 2021. Multimodal tensor-based method for integrative and continuous patient monitoring during postoperative cardiac care. Artificial Intelligence in Medicine 113, 102032.
[11] Hsu, E., Soller, L., Abrams, E.M., Protudjer, J.L., Mill, C., Chan, E.S., 2020. Oral food challenge implementation: the first mixed-methods study exploring barriers and solutions. The Journal of Allergy and Clinical Immunology: In Practice 8, 149–156.
[12] Lundberg, S.M., Lee, S.I., 2017. A unified approach to interpreting model predictions. Advances in neural information processing systems 30.
[13] MATLAB, R2021a. Statistics and machine learning toolbox. The MathWorks Inc., Natick, MA, USA.
[14] Peng, H., Long, F., Ding, C., 2005. Feature selection based on mutual information criteria of max-dependency, max-relevance, and min-redundancy. IEEE Transactions on pattern analysis and machine intelligence 27, 1226–1238.
[15] Roberts, G., Lack, G., of Parents, A.L.S., Team, C.S., et al., 2005. Diagnosing peanut allergy with skin prick and specific IgE testing. Journal of Allergy and Clinical Immunology 115, 1291–1296.
[16] Sabeti, E., Gryak, J., Derksen, H., Biwer, C., Ansari, S., Isenstein, H., Kratz, A., Najarian, K., 2019. Learning using concave and convex kernels: applications in predicting quality of sleep and level of fatigue in fibromyalgia. Entropy 21, 442.
[17] Sporik, R., Hill, D., Hosking, C., 2000. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. Clinical & experimental allergy 30, 1541–1546.