Machine learning for biomedical problems, including radiomics and (radio)genomics

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What is Machine Learning?

- ML is the science (art?) of discovering actionable models/patterns/knowledge directly from data.

- ML methods try to:
  - Make as few assumptions and be as computationally efficient as possible (vis-à-vis traditional statistical methods)
  - Be as unbiased w.r.t. current knowledge as possible (vis-à-vis traditional bioinformatics and computational biology methods)

- Several types of (machine) learning:
  - Supervised: Classification, regression.
  - Unsupervised: Clustering, anomaly detection.

Supervised learning

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Learning algorithm

Induction

Learn Model

Deduction

Apply Model

Model
Evaluation of supervised ML models

- Evaluation setups:
  - Training-test sets
  - Cross-validation

- Evaluation metrics:
  - Accuracy
  - ROC Curve
    - Shows relationship between True Positive Rate (Sensitivity) and False Positive Rate (1-Specificity) across a variety of thresholds applied to classifier output scores.
    - Area Under the Curve (AUC)
      - Ideal: AUC = 1
      - Random: AUC = 0.5
    - Model with higher AUC generally considered better

- More specialized metrics needed for unbalanced data sets
  - Typical biomedical problems (e.g., healthy-vs-diseased) are unbalanced
  - Right metrics to use: Precision-Recall-Fmeasure


Unsupervised learning: Clustering

- Finding groups of objects such that the objects in a group will be similar (or related) to one another and different from (or unrelated to) the objects in other groups

- Intra-cluster distances are minimized
- Inter-cluster distances are maximized

Why should we care? Because we are awash in biomedical data

- Several images taken from the web
Abundant data and ML provide opportunities to address problems related to personalized/precision medicine

- **Supervised learning**
  - Discovery of factors affecting/related to health/disease (biomarkers)
    - Genetic/genomic factors
    - Environmental factors (exposome)
    - Gene X Environment interactions
  - Prediction of disease phenotypes, progression, survival rates etc:
    - Imaging data (radiomics, deep learning etc)
    - Genetic, EMR and other data types
  - Prediction of drug sensitivity/efficacy and adverse/side effects

- **Unsupervised learning**
  - Disease subtype discovery
  - Deconvolution of cell types in a mixture
  - Drug repositioning and discovery of effective drug combinations
  - Clustering of (disease-related) gene/proteins into functions/pathways etc.

Some applications of ML in biomedical problems

Discovering gene expression biomarkers of diseases

![Diagram of gene expression biomarker discovery process]

- RNA-Seq → Healthy/diseased patients' gene expression data
- Feature (Gene) Selector → Classifier
- Wrapped classification (predictive) model learning
- Patient classification
- Diagnostic panel (e.g., MammaPrint & Oncotype DX)

Several images taken from the web
Accurate diagnostic panel for (mild/moderate) asthma

Specificity of diagnostic panel to (mild/moderate) asthma vis-à-vis respiratory diseases with similar symptoms

Discovering air pollutant combinations affecting children’s health

“You Can’t Change Your Genes, but You Can Change the Environment: How the Environment Affects Your Health”: Dr. Linda S. Birnbaum, Director, National Institute of Environmental Health Sciences and National Toxicology Program
Pollutant combinations can help define at-risk population profiles

Stigone et al, Environmental Pollution, 2017

Radiomics and ML for tumor classification

- Data set: 68 prostate tumor captured using mpMRI (ADC and T2)
  - 54 low and intermediate
  - 14 highly aggressive tumors

- 116 radiomics features derived from images:
  - Mostly feature-based (Histogram analysis, GLCM, GLDM and Fourier analysis)

- Goal: Can supervised ML methods be applied to this data set to improve tumor classification by identifying a combination of radiomics features?

ML methodology and current results

Bino Varghese and Vinay Duddalwar (USC)
Challenges with biomedical ML

- Type and amount of data being analyzed should be relevant and representative for the target problem.
- Interpretability of ML models: "Black Box" characterization
  - Much of this comes from incomplete understanding of how ML methods work
- Data issues:
  - Noise
  - Missing data
  - Incompatibility of data from different sources
    - Same data type: Different scales/distributions (batch effects, normalization etc.)
    - Different data types: Different representations, not always clear how to integrate
  - Integral to any data analysis, not just ML
    - Best practices should be followed, unless better solutions available

Summary

- ML methods of several types hold great potential in the data-rich era of biomedical sciences to address challenging problems and derive actionable knowledge directly from data.
- Several useful applications:
  - Development of diagnostic gene expression panels for diseases (e.g. asthma)
  - Identification of air pollutant combinations that affect children’s health
  - Tumor classification based on radiomics data derived from mpMRI images
- Substantial challenges remain and efforts are being made!

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